Perinatal Risk and Severity of Illness in Newborns at 6 Neonatal Intensive Care Units

ABSTRACT

Objectives. This multisite study sought to identify (1) any differences in admission risk (defined by gestational age and illness severity) among neonatal intensive care units (NICUs) and (2) obstetric antecedents of newborn illness severity.

Methods. Data on 1476 babies born at a gestational age of less than 32 weeks in 6 perinatal centers were abstracted prospectively. Newborn illness severity was measured with the Score for Neonatal Acute Physiology. Regression models were constructed to predict scores as a function of perinatal risk factors.

Results. The sites differed by several obstetric case-mix characteristics. Of these, only gestational age, small for gestational age, White race, and severe congenital anomalies were associated with higher scores. Antenatal corticosteroids, low Apgar scores, and neonatal hypothermia also affected illness severity. At 2 sites, higher mean severity could not be explained by case mix.

Conclusions. Obstetric events and perinatal practices affect newborn illness severity. These risk factors differ among perinatal centers and are associated with elevated illness severity at some sites. Outcomes of NICU care may be affected by antecedent events and perinatal practices. (*Am J Public Health.* 1999;89:511–516)

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Wide differences in morbidity and mortality among neonatal intensive care units (NICUs) have been observed.[1,2] Newborn population risk, or case mix, is primarily a function of gestational age and illness severity—that is, how small and how sick the newborn is—at the time of NICU admission.[3]

The case mix admitted to an NICU, in turn, depends on the obstetric case mix presenting to that hospital, the obstetric care practices at that hospital, and the quality of delivery room stabilization. The obstetric population can be characterized in terms of adequacy of prenatal care, maternal illnesses, gestational age at onset of premature rupture of membranes or preterm labor, and frequency of multiple gestations. These factors tend to determine the rate and gestational ages of preterm deliveries. In addition, regional referral centers attract high-risk maternal transports and women with identified fetal anomalies. Even when delivery becomes inevitable, perinatal care practices may directly affect the neonatal condition. For example, obstetric practices may differ in terms of administration of antepartum corticosteroids, timing of delivery, intrapartum management, selection for operative delivery, and skill at delivery room stabilization.[4] These delivery-related events will be reflected in the illness severity of the infants who are admitted to the neonatal intensive care unit.

Both Richardson et al.[5] and Kaaresen et al.[6] have recently shown striking changes in the condition of very preterm newborns over time in regional perinatal centers. This implies an improvement in the obstetric population, better perinatal management, or both. This multicenter prospective study addresses the following 3 questions: (1) Are there differences in admission illness severity among NICUs (i.e., are some NICUs challenged with a more difficult task)? (2) What are the obstetric antecedents of those sicker infants? (3) After adjusting for these antecedent risk factors, can we fully explain differences in admission severity among NICUs?

Methods

Population

The study population consisted of all babies born at a gestational age of less than 32 weeks who were delivered in 6 regional perinatal centers in Massachusetts and Rhode Island during a 21-month period (October 1994–June 1996). Infant medical records were abstracted prospectively by use of a strictly defined protocol and were subjected to rigorous data quality checks. We eliminated 37 infants because records were missing or incomplete, leaving a final study group of 1476 infants. We ascertained separately all delivery room deaths, including infants who were considered moribund on

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admission (died within hours without mechanical ventilation). These were further classified as less than 500 grams or less than 24 weeks (previable) or more than 500 grams or more than 24 weeks (potentially viable). Institutional review board approval, which included assurances of confidentiality for the identity of the study sites, was obtained at all participating institutions. For this reason, easily identifiable institutional characteristics (e.g., cohort size, racial profile) were analyzed but are not presented individually in the results.

Score for Neonatal Acute Physiology

The Score for Neonatal Acute Physiology (SNAP) is a physiology-based illness severity index specific for neonatal intensive care.[7] It scores the degree of derangement in 34 routinely collected vital signs and laboratory tests. SNAP is the sum of score points in the first 12 hours of admission and reflects the overall degree of illness severity in several organ systems. It is significantly associated with mortality and morbidity risks.[3,5,7] Thus, SNAP represents both the condition of the newborn within the first 12 hours following admission and his or her risk of adverse outcome. For models that included admission hypothermia as a predictor of SNAP, we excluded the SNAP points directly attributable to admission temperature.

Other Variables

We abstracted a number of markers of maternal health and perinatal practice. These fall into 2 general categories: prenatal demographics and pregnancy risks that existed before hospitalization (race, prenatal care, multifetal pregnancy, maternal hypertension, fetal growth restriction, fetal presentation, gestation at delivery, and congenital anomalies) and hospital-related care practices (antenatal corticosteroid administration, mode of delivery, delivery room resuscitation as reflected in the Apgar scores, and temperature on admission to the NICU, reflecting hypothermia following delivery). These markers were selected because they are frequent, clearly identifiable, and related to traditional risk factors for adverse pregnancy outcome.

Gestational age was defined as the "best estimate" in completed weeks recorded by the obstetrician at the time of delivery. Maternal hypertension was considered present if either chronic or gestational hypertension in pregnancy was noted. Newborn anomalies were classified as acutely life threatening or not.[8,9] Antenatal corticosteroid treatment was classified as (1) none, (2) partial (treatment received, but less than 24 hours or more than 7 days before delivery), or (3) full (treatment received more than 24 hours but less than 7 days before delivery). Small for gestational age was defined as a weight of less than the fifth percentile by the Brenner standard.[10] Hypothermia consisted of an infant axillary or rectal temperature on admission to the NICU of less than 96°F (35.5°C). Low Apgar score was treated as a categorical variable (i.e., less than or greater than 5 for the 1-minute score and less than or greater than 7 for the 5-minute score). Prenatal care was assessed conservatively as the presence of at least 1 previous prenatal visit. Other outcome variables followed conventional uses. (For information on the data forms and abstracting protocol, contact the corresponding author.)

Statistical Techniques

All data management was carried out with SAS (SAS Corporation, Cary, NC). Our principal model was a multivariate linear regression predicting admission illness severity as a function of (1) gestation achieved (gestational age, birthweight), (2) pregnancy characteristics (maternal hypertension, multiple gestation, small for gestational age, fetal anomalies), (3) antepartum management (maternal corticosteroids), (4) delivery characteristics (fetal presentation, cesarean delivery), (5) delivery room management (Apgar scores at 1 and 5 minutes, and hypothermia on NICU admission), and (6) site. Because birthweight and gestational age are highly correlated, we retained gestational age, consistent with the greater importance of fetal maturity than weight as indicated in population-based research.[11] Residual effects of birthweight are conveyed by inclusion of the term *small for gestational age*, defined above. We also modeled low Apgar scores and hypothermia as a function of these factors. We characterized the differences in physiologic stability between infants receiving and not receiving antenatal corticosteroids by analysis of variance, using the generalized linear models procedure. For regressions that controlled for site, we repeated our analyses with SUDAAN (Research Triangle Institute, Research Triangle, NC), which adjusts estimates of standard errors for clustering at the sites.

Results

Population and Care Practices

The sites were ranked and labeled as sites U to Z according to overall mean admission illness severity (Table 1). Lower gestational age was associated with greater illness severity. Moreover, significant differences in severity remained when the same gestational age stratum was compared between sites. Specifically, sites U and V had significantly higher illness severity for all gestational ages by post-hoc multiple range tests. (To preserve the confidentiality of sites, sample size is not displayed.)

Table 2 presents the characteristics of the patients at the 6 sites. The mean gestations differed significantly among sites (range = 27.4–28.3 weeks, $P < .001$), so that even within this narrowly defined very premature population, the average infant admitted at site Z was 0.9 weeks older than the average infant admitted at site W. Few of the other pregnancy characteristics differed among the 6 sites. No significant differences were observed in rates of absent prenatal

TABLE 1—Mean Illness Severity (SNAP) by Site and Gestational Age Group: Massachusetts and Rhode Island, 1994–1996

		Site						
	n	U	V	W	X	Y	Z	P^a
All	1476	12.9	12.6	12.0	10.2	9.4	8.3	<.001
Gestational age, wks								
<26	287	19.4	18.9	18.7	15.1	14.1	16.7	<.001
26–27	262	14.1	14.5	10.3	12.0	10.9	9.8	<.005
28–29	432	12.7	10.2	10.7	8.4	8.8	8.3	<.001
30–31	491	9.0	9.3	7.4	7.9	6.9	4.1	<.001

[a]Significance of differences among sites by analysis of variance. Post-hoc Duncan multiple range tests ranked sites U and V in the highest grouping in each gestational age stratum.

TABLE 2— Incidence of Pregnancy-Related and Practice-Related Risk Factors, by Site: Massachusetts and Rhode Island, 1994–1996

	Site						
	U	V	W	X	Y	Z	*P*
Obstetric case mix							
Gestational age, mean (SD), wks	28.0 (2.4)	27.7 (2.4)	27.4 (2.4)	27.9 (2.2)	28.2 (2.3)	28.3 (2.3)	<.001
Maternal hypertension, %	15	22	13	19	24	20	<.05
Small for gestational age, %	3	6	4	6	5	2	NS
Multiple birth, %	27	22	24	32	36	39	<.001
Life-threatening congenital anomaly, %	4	2	1	3	1	1	<.001
Breech presentation, %	26	26	27	25	20	24	NS
No prenatal care, %	2	3	4	2	2	2	NS
Perinatal care practices							
Antenatal corticosteroids,[a] %	88	63	56	87	82	78	<.001
Cesarean delivery, %	46	56	53	58	58	62	<.05
Apgar at 1 min <5, %	42	42	33	30	26	23	<.001
Apgar at 5 min <7, %	22	45	29	18	21	18	<.001
Newborn hypothermia (<96°F), %	16	28	33	30	12	17	<.001

Note. NS = not significant.
[a]Full or partial treatment.

care, small for gestational age, male gender (range = 52%–61%; not shown), and breech presentation. Multiple births and maternal hypertension differed, reflecting the effects of associated fertility programs and referral areas for several hospitals. Life-threatening congenital anomalies ranged from 1% to 4%, indicating differing regional referral patterns ($P < .05$). The proportion of White newborns ranged from 59% to 79% ($P < .001$), and medical assistance/self-pay insurance status ranged from 17% to 52% ($P < .001$) (both not shown for confidentiality of study site). Highly significant differences occurred among sites in every measure of perinatal care practices and delivery room stabilization. There were significant differences in rates of treatment with any antenatal corticosteroids, cesarean delivery, and low 1- and 5-minute Apgar scores. Hypothermia on NICU admission was also exceedingly common, and it differed among sites (Table 2).

Model of Illness Severity

We modeled the association between perinatal events and the illness severity scores of the newborns assessed at 12 hours of age, using all infants at all sites (Table 3). The calculated partial slope coefficient represents the number of SNAP points (i.e., the magnitude of physiologic derangement) attributable to that factor, independent of the effects of the other factors. Advancing gestation had a powerful impact on neonatal stability, with a drop of more than 1 SNAP point for each additional week of gestation ($P < .001$). No effects on neonatal illness severity at 12 hours of age were detected for maternal hypertension, multiple gestation, male gender, breech presentation, absence of prenatal care, payor status, or method of delivery. On the other hand, White race was associated with a 1.2-point increase (worsening) in SNAP ($P < .001$), and small for gestational age resulted in a 2.4-point increase in SNAP ($P < .001$). Presence of a life-threatening congenital anomaly had the largest impact, adding 4.0 points. As expected, antenatal corticosteroids had a significant beneficial effect on neonatal stability, lowering SNAP on average 2.1 points for any corticosteroid treatment ($P < .001$). The 3 delivery room stabilization variables (i.e., low 1- and 5-minute Apgar scores and hypothermia) had significant associations with neonatal illness severity. Despite their colinearity, low 1- and 5-minute Apgar scores both showed strong independent and additive effects and were associated with higher SNAP (by 2.4 and 2.2 points, respectively; $P < .001$) at 12 hours of age. Hypothermia on arrival to the NICU worsened SNAP by 2.3 points ($P < .001$). The model explained 38% of the variance in admission SNAP.

Model of Hospital Performance

We then examined whether the differences in obstetric case mix observed in Table 2 might explain the differences in admission severity among NICUs as noted in Table 1. To separate differences in intrinsic maternal and fetal factors (gestational age, maternal hypertension, fetal growth restriction, gender, multiple birth, anomalies) from the effects of perinatal care–related events (antenatal steroids, cesarean delivery, Apgar scores, hypothermia), we constructed a 3-stage model. As previously shown, neonatal physiologic stability (SNAP) served as the dependent variable. Stage 1 included all obstetric case mix variables (upper half of Table 3). In stage 2 we entered 5 dummy variables for site (with site X designated as the reference site).

By excluding the care-related predictors (the bottom part of Table 3), we reallocated their statistical effects to the sites with disproportionate numbers of such adverse events. Only the significant case mix predictors are presented in Table 4. Small for gestational age remained significant (+3.6 SNAP points), as did gestational age (decreasing 1.5 SNAP points per week older; $P < .001$) and congenital anomalies (+4.0 SNAP points; $P < .001$). When adjusted for obstetric case mix, sites U and V had significantly higher illness severities of +2.7 and +1.9 points, respectively. Sites W and Y did not differ from reference site X (selected as reference on the basis of large sample size). Site Z had a slightly lower illness severity, by 1.3 points ($P < .05$). We then extended the multivariate model to stage 3 (not shown) to include care-related events, specifically corticosteroids, Apgar scores, and occurrence of hypothermia. This step eliminated intersite differences in admission severity at site V but not at site U and improved the total R^2 to 0.40. Replicating the analyses with and without early deaths (less than 12 hours of age, affecting incomplete SNAP scores) did not alter these results.

Models of 5-Minute Apgar Score

We also constructed a logistic model predicting the occurrence of low 5-minute Apgar scores by using the same obstetric case-mix variables plus antenatal corticosteroids and cesarean delivery. Only gesta-

TABLE 3—Perinatal Predictors of Newborn Illness Severity (SNAP) by Multiple Linear Regression[a]

	Partial Slope[b] (SNAP Points)	95% CI	Partial R^2	P
Obstetric case mix				
Gestational age (per week)	−1.1	−1.2, −0.9	0.25	<.001
Maternal hypertension	−0.4	−1.3, +0.5	0.00	NS
Small for gestational age	+2.4	+0.8, +3.9	0.01	<.01
Multiple birth	−0.3	−1.0, +0.5	0.00	NS
Life-threatening congenital anomaly	+4.0	+2.1, +6.6	0.01	<.001
White race	+1.2	+0.5, +2.0	0.01	<.001
Male sex	−0.1	−0.8, +0.5	0.00	NS
Breech presentation	−0.2	−1.0, +0.6	0.00	NS
No prenatal care	+1.5	−0.7, +3.7	0.00	NS
Medicaid/self-pay	−0.5	−1.2, +0.3	0.00	NS
Perinatal care practices				
Antenatal corticosteroid treatment	−2.1	−2.9, −1.3	0.02	<.001
Cesarean delivery	+0.6	−0.1, +1.4	0.00	NS
Apgar at 1 min <5	+2.4	+1.4, +3.3	0.06	<.001
Apgar at 5 min <7	+2.2	+1.2, +3.2	0.01	<.001
Newborn hypothermia (<96°F)	+2.3	+1.4, +3.2	0.01	<.001

Note. NS = not significant.
[a]Model R^2 = 0.38, intercept = 39.2.
[b]Negative slope implies reduced severity, while positive slope implies increased severity.

TABLE 4—Newborn Admission Illness Severity Attributable to Obstetric Case Mix and Site, by Multiple Linear Regression[a]

	Partial Slope[b] (SNAP Points)	95% CI	Partial R^2	P
Impact of obstetric case mix[c]				
Gestational age (per week)	−1.5	−1.7, −1.4	0.25	<.001
Small for gestational age	+3.6	+1.9, +5.2	0.01	<.001
Congenital anomaly	+4.0	+1.5, +6.2	0.01	<.001
Impact of care practices allocated to				
Site U	+2.7	+1.5, +3.8	0.01	<.001
Site V	+1.9	+0.8, +2.9	0.01	<.001
Site W	+1.0	−0.2, +2.2	0.00	NS
Site X	0.3	−1.4, +0.8	0.00	NS
Site Y	(Reference)	...	...	...
Site Z	−1.3	−2.6, −0.02	0.001	<.05

Note. NS = not significant.
[a]Model R^2 = 0.30, intercept = 52.0.
[b]Negative slope implies reduced severity, while positive slope implies increased severity.
[c]Controlled for all risk factors. Significant variables are displayed; nonsignificant variables included maternal hypertension, multiple birth, White race, male sex, breech presentation, no prenatal care, and Medicaid/self-pay.

tional age and small for gestational age were found to be significant predictors of low 5-minute Apgar score. Anomalies had no effect. The odds ratios were 7.1 for gestations of less than 26 weeks (95% confidence interval [CI] = 5.1, 9.9) and 2.2 for gestations of 26 and 27 weeks (95% CI = 1.5, 3.1), relative to infants older than 27 weeks. Small-for-gestational-age infants were 4.1 times more likely to have poor 5-minute Apgar scores (95% CI = 2.3, 7.3) than infants of normal gestational age. Antenatal corticosteroids were protective; that is, administration was associated with a greater likelihood of better Apgar scores (odds ratio = 0.50; 95% CI = 0.37, 0.68). After accounting for obstetric case mix, cesarean delivery, and corticosteroid treatment, we found that the odds ratio for poor Apgar scores at site V were 2.8 (95% CI = 1.8, 4.1), meaning that babies of similar gestational age at site V were nearly 3 times more likely to have a low score than babies at other sites.

Model of Hypothermia

The obstetric case-mix variables significantly associated with delivery room hypothermia were as follows: gestational age, with odds ratios of 10.6 for less than 26 weeks of age (95% CI = 7.3, 15.3) and 2.1 for 27 to 28 weeks of age (95% CI = 1.4, 3.2); small for gestational age (odds ratio = 3.2; 95% CI = 1.8, 5.9); and maternal hypertension (odds ratio = 2.6; 95% CI = 1.8, 3.8). Antenatal steroid use was again slightly protective against hypothermia (odds ratio = 0.6; 95% CI = 0.5, 0.9). Adjusting for these factors could not account for intersite variation. Three of the 6 sites had significantly elevated risk-adjusted rates of delivery room hypothermia relative to the best-performing site Y. Site V had an odds ratio of 2.5 (95% CI = 1.5, 4.1), site W had an odds ratio of 3.6 (95% CI = 2.1, 6.2), and site X had an odds ratio of 3.5 (95% CI = 2.1, 5.7).

Effects of Corticosteroids

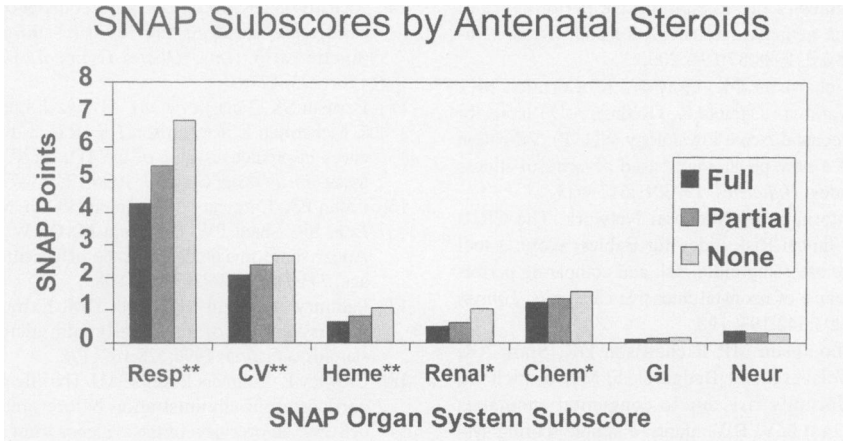
We examined the effects of antenatal corticosteroid treatment on the stability of multiple organ systems (Figure 1) by comparing the gestational age–adjusted severity for each organ system among fully treated, partially treated, and untreated pregnancies. The adjusted overall mean SNAPs for these 3 treatment groups were 9.2, 11.1, and 13.6, respectively. Each treatment level significantly differed from the other two ($P < .01$). The reduction in severity of respiratory illness was an expected finding, but the significant reductions in cardiovascular, renal, metabolic, and hematological instability (all $P < .05$) point to beneficial pansystemic effects of antenatal corticosteroids for very-low-birthweight newborns.

Delivery Room Deaths

Of the 173 pre-NICU deaths in the 6 hospitals, 145 were classified as previable (less than 500 grams or less than 24 weeks). Of the remaining 28 potentially viable births (more than 24 weeks or more than 500 grams), the rates of delivery room deaths were 1.8%, 4.5%, 0.5%, 1.2%, 0.9%, and 0.5%, respectively, for sites U, V, W, X, Y, and Z, with the incidence at site V being 2 to 9 times higher than at the other 5 sites ($P < .001$).

Discussion

We have shown significant differences in admission illness severity in very-low-birthweight infants among 6 regional tertiary perinatal centers. Only some of the sites' differences in illness severity on NICU admission can be explained by recognized obstetric population risk factors such as birthweight and gestational age distributions, racial composition, rates of multifetal pregnancies, incidence of maternal hypertension,



Note. Full treatment is defined as initiation of treatment more than 24 hours or less than 7 days before delivery. Partial treatment is defined as initiation of treatment less than 24 hours or more than 7 days before delivery. Organ system subscores: Resp = respiratory, CV = cardiovascular, Heme = hematologic, Renal = renal, Chem = metabolic/serum chemistries, GI = gastrointestinal, Neur = neurologic. The gestational age–adjusted differences in organ subscores are significant for each comparison (none vs partial and partial vs complete) for Resp, CV, and Heme ($P < .05$ for each, indicated by **). Differences between full treatment and no treatment are also found for Renal, and Chem ($P < .01$, indicated by *).

FIGURE 1—Score for Neonatal Acute Physiology (SNAP) organ-system subscores according to maternal treatment with antenatal corticosteroids.

fetal anomalies, and growth restriction. The residual interhospital variation is unexplained and, consequently, must be attributed to unmeasured factors such as differences in other population risks (e.g., socioeconomic status, maternal medical conditions, time of presentation in preterm labor, drug abuse), to differences in perinatal management (e.g., rates of fetal acidosis in labor, variations in anesthesia practices, tocolytic practices), or to both. This unexplained risk-adjusted variation in newborn illness severity suggests that some acute perinatal care practices can optimize or exacerbate the condition of the very premature infant in the first day of life. Our finding of an increase in risk-adjusted severity of 2.7 SNAP points in site U implies that every very premature infant admitted to site U was, on average, 2.7 points sicker than similar infants admitted to the reference NICU. This effect may be clinically meaningful because previous work has shown that 10 SNAP points convey an estimated 20- to 60-fold excess neonatal mortality.[3]

Similar findings have been reported by Kaaresen et al.[6] In a 16-year retrospective analysis of a region in Norway, they demonstrated that distinct changes in delivery room deaths, need for resuscitation, and Clinical Risk Index for Babies score at admission were associated with apparent changes in obstetric practices.[12] Measuring physiological derangements associated with lower gestational age, fetal growth restriction, and serious congenital anomalies helps to quantify the burden of illness passed on to the NICU, especially in situations where maternal transfers are regionalized.

The finding that White race is a risk factor for greater illness is consistent with several studies indicating lower susceptibility of African Americans to respiratory distress syndrome, compared to that of Whites within gestational age strata.[13–15] Interestingly, cesarean delivery did not, on average, affect illness severity. This could be the result of offsetting advantages and disadvantages conferred by mode of delivery that cannot be determined from our study design.

Apgar scores are recognized to be dependent on gestational age.[16] Differences in gestational age, however, do not explain the highly significant differences in Apgar scores among these NICUs. Intrapartum obstetric or anesthesia practices may influence the 1-minute Apgar scores. The higher rate of poor 5-minute Apgar scores at site U might also suggest a pattern of suboptimal resuscitation or of greater antecedent fetal sedation or compromise. The higher subsequent SNAPs associated with low Apgar scores (nearly 5 additional points could be added if both Apgar scores were low) indicate that physiologic disturbance persists over the ensuing 12 hours. Although we cannot exclude the potential bias of stricter Apgar scoring at site U, the higher rate of delivery room deaths, the more frequent occurrence of hypothermia in these very premature newborns, and the plausible association of site U's worse Apgar scores with higher SNAPs all support an explanation of suboptimal delivery room stabilization.

Our finding that maternal corticosteroids exert multiple organ system benefits in physiologic stability confirms previous studies.[17] These observations also offer further insight into the potential mechanisms for the observed protection against intraventricular hemorrhage conferred by antenatal corticosteroid treatment,[18,19] an effect that is independent of reductions in the rate and severity of respiratory distress syndrome.[20]

Our findings that similar regional tertiary perinatal centers exhibit significant differences in antenatal corticosteroid use, Apgar scores, and newborn hypothermia point out clear opportunities for quality improvement initiatives.[21] They also demonstrate the value of neonatal networks for benchmarking and for the development of practice guidelines.[22]

There are important limitations to this study. Obstetric case-mix factors such as best estimate of gestational age, maternal hypertension, and prenatal care were defined simply and do not permit fuller analysis. Important risk factors such as diabetes, chorioamnionitis, and cervical examination on admission to labor and delivery were not obtained because the data were derived from a study of NICU outcomes rather than obstetric outcomes. Measured risk factors such as antenatal corticosteroid use are influenced by the interval between maternal presentation and delivery and by access to care. A more detailed evaluation of the effects of these and other factors is under way at one of the study sites. However, it is unlikely that the prevalence of these unmeasured factors differs sufficiently among sites to explain the striking elevation in illness severity at sites U and V.

In summary, measures of newborn illness severity can serve as an indicator of obstetric outcome. Our findings make clear that a burden of excess neonatal mortality risk, in the form of elevated illness severity, is conveyed from obstetric events into the newborn period. Also, our findings suggest that perinatal and delivery room management can systematically mitigate or exacerbate the immediate condition of premature newborns and thereby influence neonatal outcome. □

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