Variations in mortality rates among Canadian neonatal intensive care units

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Abstract

Background: Most previous reports of variations in mortality rates for infants admitted to neonatal intensive care units (NICUs) have involved small groups of subpopulations, such as infants with very low birth weight. Our aim was to examine the incidence and causes of death and the risk-adjusted variation in mortality rates for a large group of infants of all birth weights admitted to Canadian NICUs.

Methods: We examined the deaths that occurred among all 19 265 infants admitted to 17 tertiary-level Canadian NICUs from January 1996 to October 1997. We used multivariate analysis to examine the risk factors associated with death and the variations in mortality rates, adjusting for risks in the baseline population, severity of illness on admission and whether the infant was outborn (born at a different hospital from the one where the NICU was located).

Results: The overall mortality rate was 4% (795 infants died). Forty percent of the deaths ($n = 318$) occurred within 2 days of NICU admission, 50% ($n = 397$) within 3 days and 75% ($n = 596$) within 12 days. The major conditions associated with death were gestational age less than 24 weeks (59 deaths [7%]), gestational age 24–28 weeks (325 deaths [41%]), outborn status (340 deaths [42%]), congenital anomalies (270 deaths [34%]), surgery (141 deaths [18%]), infection (108 deaths [14%]), hypoxic–ischemic encephalopathy (128 deaths [16%]) and small for gestational age (i.e., less than the third percentile) (77 deaths [10%]). There was significant variation in the risk-adjusted mortality rates (range 1.6% to 5.5%) among the 17 NICUs.

Interpretation: Most NICU deaths occurred within the first few days after admission. Preterm birth, outborn status and congenital anomalies were the conditions most frequently associated with death in the NICU. The significant variation in risk-adjusted mortality rates emphasizes the importance of risk adjustment for valid comparison of NICU outcomes.

Advances in perinatal and neonatal care have significantly reduced neonatal mortality rates and have especially benefited preterm infants admitted to neonatal intensive care units (NICUs).[1–5] Recent publications have highlighted these trends[6–8] but have also reported significant variations in mortality rates among NICUs.[8–10] Variations in mortality rates are important because they permit inferences about quality of care. Examination of care practices associated with variations in mortality rates can provide insights into how care practices might be changed to improve outcomes. However, comparisons between hospitals are valid only if there is adequate adjustment for differences in population characteristics and severity of illness. Previous reports of variation in NICU mortality rates involved only specific subpopulations of interest, such as infants with very low birth weight (up to and including 1500 g),[9,10] and did not fully adjust for differences in the characteristics of the baseline population and the severity of illness on admission.[8–10] Our purpose was to determine and report the incidence and causes of death and the

risk-adjusted variation in mortality rates for a large group of infants admitted to 17 NICUs in the Canadian Neonatal Network. The member units of the Canadian Neonatal Network account for 75% of all tertiary-level NICU beds in Canada and serve a total population of about 22 million people.[8] In 1996, at the time of our study, Canada had a total population of nearly 30 million people,[11] and the country had about 357 000 births in the fiscal year 1996/97.[12]

Methods

Canada has a highly regionalized system of perinatal and neonatal care. Tertiary-level NICUs serve distinct geographic regions and coordinate care with a network of primary- and secondary-level facilities. The 17 hospitals participating in this study represented all 5 geographic regions of the country, including British Columbia (3 hospitals), the Prairie provinces (4 hospitals), Ontario (7 hospitals), Quebec (1 hospital) and the Atlantic provinces (2 hospitals). Of the 662 NICU beds in these 17 hospitals, there were a total of 349 intensive care neonatal beds (range 2 to 45 per hospital) and 313 intermediate-level and continuing care neonatal beds (range 0 to 45 per hospital). Medical staff at the hospitals included 96 full-time equivalent neonatologists, 76 full-time equivalent housestaff (including clinical assistants, neonatal fellows and pediatric residents) and 31 full-time equivalent neonatal nurse practitioners or clinical nurse specialists. Three NICUs did not employ housestaff, and only 6 NICUs used neonatal nurse practitioners or clinical nurse specialists. Three NICUs admitted only outborn infants (those born at hospitals other than the hospital in which the NICU was located). General surgery was available in 13 hospitals, cardiac surgery in 9 hospitals, extracorporeal membrane oxygenation in 3 hospitals, and cryotherapy or laser therapy in 11 hospitals. In some hospitals, infants needing general or cardiac surgery were admitted to surgical or pediatric intensive care units instead of NICUs. Details about the participating hospitals and the study population have been presented in more detail elsewhere.[8]

The study population included all 19 265 infants admitted to the 17 participating NICUs during a 22-month period (from Jan. 8, 1996, to Oct. 31, 1997). A total of 172 infants (0.9%) were excluded because of incomplete data; this group included 11 infants (0.1%) who had not been discharged from hospital at the time the database was closed, on June 30, 1998. Seventy infants (0.4%) who were moribund on admission (i.e., a physician, in consultation with the parents, had made an explicit decision not to provide life support at the time of NICU admission) were also excluded from the analysis. The prevalence of infants moribund on admission to participating NICUs ranged from 0% to 2.7%. In comparison with the infants included in the study (for whom data are presented in Table 1), moribund infants had lower mean birth weight (924 g, standard deviation 867 g) and were less frequently born by cesarean sections (27%), but these infants more often were a member of multiple births (40%), had Apgar scores less than 7 at 5 minutes (87%), were female (54%) and were small for gestational age (15%). An admission was defined as a stay in the NICU for at least 24 hours or death or transfer to another NICU within 24 hours. Readmissions and transfers were tracked as data from the same infant.

Trained research assistants regularly abstracted patient information from the mothers' and infants' charts at each participating hospital. Data were directly entered into laptop computers at the bedside by means of a customized data entry program with built-in error checking and a standard manual of operations and definitions. Data were electronically transmitted to the Canadian Neonatal Network Coordinating Centre, at the British Columbia

Table 1: Characteristics of infants admitted to Canadian NICUs between January 1996 and October 1997

| Characteristic | Birth weight; overall mean %* (and range) for 17 NICUs† | | | | | |
	< 1000 g	1000–1499 g	1500–1999 g	2000–2499 g	≥ 2500 g	Total
No. of infants	1566	2158	2863	3485	9193	19 265
Outborn status	24 (2–100)	19 (0–100)	15 (1–100)	20 (2–100)	34 (1–100)	26 (3–100)
Perinatal risks						
No prenatal care	2 (0–7)	2 (0–7)	2 (1–13)	2 (0–9)	2 (0–9)	2 (1–8)
Maternal hypertension	18 (6–36)	19 (11–33)	18 (5–31)	14 (3–24)	8 (4–14)	13 (5–18)
Cesarean section	50 (22–73)	54 (41–77)	46 (38–51)	37 (26–45)	32 (26–47)	39 (30–46)
Multiple births	24 (5–46)	31 (12–40)	29 (8–38)	20 (9–27)	3 (1–6)	15 (7–25)
Apgar < 7 at 5 min	35 (21–73)	16 (8–33)	10 (4–26)	9 (5–22)	14 (8–23)	14 (9–23)
Infant characteristics						
Male sex	53 (36–77)	54 (44–65)	53 (45–67)	56 (51–64)	61 (57–67)	58 (55–63)
Small for gestational age	14 (6–27)	9 (0–14)	7 (3–12)	5 (2–13)	1 (0–1)	4 (3–6)
Congenital anomalies	11 (0–31)	11 (4–25)	10 (2–24)	12 (2–43)	19 (5–47)	15 (4–39)
Mean admission SNAP-II score†	21 (8–31)	11 (7–16)	6 (3–9)	4 (1–9)	5 (2–9)	7 (2–10)

Note: NICU = neonatal intensive care unit.
*Except where indicated otherwise.
†SNAP-II = Score for Neonatal Acute Physiology, version II.[13] For this variable, each range is the range of mean scores for the NICUs for that birth weight category. The overall range of scores for individual infants was 0 to 115.

Research Institute for Children's and Women's Health, for verification. Potential data errors were rechecked by research assistants on site. Data management was conducted by the Canadian Neonatal Network Coordinating Centre in concert with a steering committee of experienced researchers and with site investigators representing each of the 17 participating hospitals. Patient information was collected until death or discharge from the NICU. Patients transferred to another hospital were tracked until death or discharge home, and outcome information was collected. Data analysis was performed for each infant rather than for each admission. Approval was obtained from the ethics review board of each participating hospital before the study began.

Patient information included demographic information, antenatal history, mode of delivery and problems at delivery, status of infant and problems at birth, severity of illness on admission (according to the Score for Neonatal Acute Physiology, version II [SNAP-II][13]) and selected patient conditions. The study variables were defined according to the manual of operations and definitions for the project and are described briefly here. The value for gestational age was the best obstetric estimate based on early prenatal ultrasonography, obstetric examination and obstetric history, unless the postnatal pediatric estimate of gestation differed from the obstetric estimate by more than 2 weeks. In that case, the pediatric estimate of gestational age, based on the Ballard Score,[14] was used instead. An infant was defined as small for gestational age if the birth weight was less than the third percentile for gestational age, according to the British Columbia provincial growth charts established by Whitfield[15] in 1992. Prenatal care was defined as receipt of pregnancy-related care from a physician on at least one occasion during the pregnancy but not related to a visit for diagnosis of the pregnancy. SNAP-II[13] is a score for neonatal illness severity calculated from 6 empirically weighted physiologic measurements made during the first 12 hours after admission to the NICU. Higher scores indicate more severe illness. Congenital anomalies were classified according to the World Health Organization International Classification of Diseases, 9th revision (ICD-9),[16] and were categorized as lethal, high risk for death, low risk for death or no risk for death by a panel of 3 neonatologists. Outborn infants were those born at a hospital different from the hospital in which the NICU was located.

Univariate and bivariate analyses were performed to describe the characteristics of the study population and to explore the association between population characteristics and death. We compared risk-adjusted mortality rates among NICUs.[17] We used multiple logistic regression to develop a risk adjustment model for NICU death. The outcome was survival or death, and the independent variables were baseline population risks (sex, gestational age, size for gestational age, 5-minute Apgar score, outborn status, presence of congenital anomalies and antenatal treatment with steroids) and SNAP-II score on admission. The model was used to calculate the predicted probability of death for each infant admitted to a NICU. An expected mortality rate was then calculated from the average of the predicted probabilities of death for each hospital. The hospital-specific ratios of observed to expected mortality rates were then multiplied by the overall mortality rate for the study period to obtain the risk-adjusted mortality rate, which was plotted with 95% confidence intervals. Confidence intervals around the adjusted mortality rates were derived by means of propagation of errors (based on first-order Taylor series expansions) to provide an approximation to the variance of the adjusted mortality rate.

Results

Of the total study population, 26% were outborn, but only 2% had not received any prenatal care (Table 1). The incidence of maternal hypertension, cesarean section, multiple births and Apgar score less than 7 at 5 minutes was generally higher for infants with lower birth weights. More males than females were admitted to a NICU (58% v. 42%), and 4% of all infants were small for gestational age. Fifteen percent of the infants had congenital anomalies, but the prevalence of such anomalies was higher among infants with higher birth weights. The overall mortality rate was 4% (795 deaths). The mortality rate was 2% for infants with birth weight up to and including 1500 g but 51% for infants with birth weight less than 500 g. Forty percent of the deaths ($n = 318$) occurred within 2 days of NICU admission, 50% ($n = 397$) within 3 days and 75% ($n = 596$) within 12 days. Only 10% of deaths ($n = 79$) occurred after the first month of NICU admission.

Overall, the most prevalent conditions associated with death in the NICU were gestational age less than 24 weeks (310 deaths [39%]), gestational age 24–28 weeks (103 deaths [13%]), outborn status (334 deaths [42%]) and chromosomal or congenital anomalies (270 deaths [34%]). Other associated diagnoses were infection (111 deaths [14%]), hypoxic–ischemic encephalopathy (127 deaths [16%]) and small for gestational age (79 deaths [10%]). Twelve percent of the infants who died ($n = 95$) were treated surgically, 7% ($n = 60$) were treated with nitric oxide and 1% ($n = 4$) received extracorporeal membrane oxygenation. The prevalence of diagnoses associated with death varied with birth weight (stratified as up to and including 1500 g and greater than 1500 g) (Fig. 1). Outborn status, congenital anomalies and hypoxic–ischemic
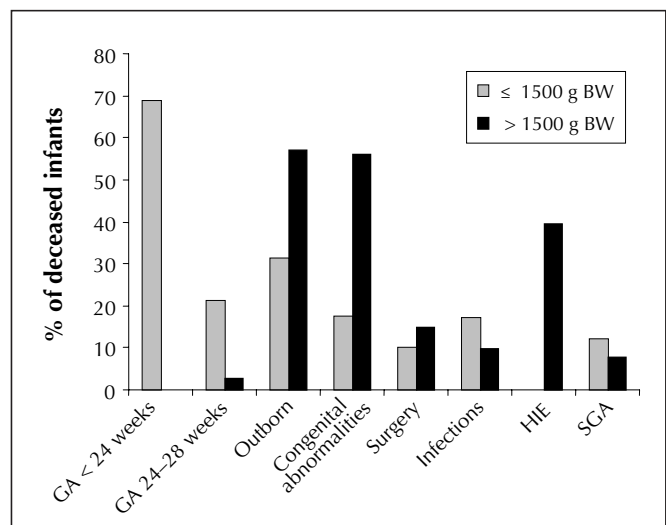

Fig. 1: Prevalence of major conditions associated with infant deaths in Canadian neonatal intensive care units (NICUs). BW = birth weight, GA = gestational age, HIE = hypoxic–ischemic encephalopathy, SGA = small for gestational age (less than the third percentile), outborn = born at a hospital other than the tertiary-level institution where the NICU was located.

encephalopathy were more common among infants with birth weight greater than 1500 g, whereas low gestational age and infections were associated to a greater extent with infants whose birth weight was up to and including 1500 g.

Risk factors significantly ($p < 0.01$) predictive of mortality are shown in Table 2. Sex was not a significant factor. Lack of antenatal corticosteroid treatment was correlated with outborn status. There was significant variation in crude mortality rates among the 17 NICUs (Fig. 2). Five NICUs (sites E, I, H, A and N) had crude mortality rates significantly greater than the mean for the 17 hospitals ($p < 0.05$), whereas 7 NICUs (sites M, J, D, P, C, Q and F) had crude mortality rates significantly lower than the mean ($p < 0.05$). One NICU (site H) had a risk-adjusted mortality rate significantly higher than the mean, but 4 NICUs (sites M, J, D and C) had risk-adjusted mortality rates significantly lower than the mean ($p < 0.05$) (Fig. 3).

Table 2: Risk factors predictive of NICU mortality on logistic regression analysis*

Variable	Crude OR (and 95% CI)		Adjusted OR (and 95% CI)	
Gestational age				
< 27 wk	16.3	(13.8–19.3)	6.4	(5.2–8.0)
27–29 wk	3.1	(2.4–3.8)	2.0	(1.5–2.5)
≥ 30 wk (reference)	1.0	NA	1.0	NA
Apgar				
< 7 at 5 min	9.2	(7.9–10.7)	3.1	(2.6–3.7)
≥ 7 at 5 min (reference)	1.0	NA	1.0	NA
Size in relation to gestational age				
Small for gestational age (< third percentile)	2.6	(2.1–3.4)	2.9	(2.1–4.0)
Not small for gestational age (reference)	1.0	NA	1.0	NA
Hospital of birth				
Outborn	2.1	(1.9–2.5)	2.2	(1.8–2.6)
Born at tertiary centre (reference)	1.0	NA	1.0	NA
Admission SNAP-II				
0–9 (reference)	1.0	NA	1.0	NA
10–19	5.6	(4.4–7.1)	3.2	(2.5–4.1)
20–29	13.4	(19.5–17.2)	5.7	(4.3–7.5)
≥ 30	45.1	(37.1–55.0)	18.7	(14.6–24.0)
Congenital anomalies				
Present, low risk of death	1.6	(1.3–2.1)	2.1	(1.6–2.8)
Present, high risk of death	4.7	(3.9–5.6)	4.4	(3.5–5.6)
Present, lethal	31.4	(17.2–56.7)	36.9	(17.6–77.2)
None present, no risk of death (reference)	1.0	NA	1.0	NA

Note: OR = odds ratio, CI = confidence interval, NA = not applicable.
*Variables included in the model were gestational age, Apgar score at 5 minutes, size in relation to gestational age, outborn status, severity of illness on admission and congenital anomalies.

Interpretation

Our study is unique because it included infants of all birth weights and because it compared NICU mortality rates that had been adjusted for both baseline population characteristics and severity of illness on admission. To our knowledge, this is the largest cohort study of deaths in Canadian NICUs serving a large proportion of the population and representing all regions of the country. Our results confirm that mortality rates for infants of all birth weights admitted to Canadian NICUs vary from one institution to another, even after adjustment for severity of illness on admission. Variations in outcomes are important because they are natural experiments representing the practice patterns of small groups of physicians. Wennberg and associates[18] showed that variations over small geographic areas can be used to study the relative effectiveness of differing medical practices and technologies and to provide insights into how to improve care. In a future study, we will examine practice differences among participating NICUs in more detail, to gain insights into ways of reducing NICU deaths.

The variations in mortality rates among Canadian NICUs appear as wide as those reported in the United States[9,10] and elsewhere,[19] even though Canada has more generous welfare entitlements, less income disparity, universal health coverage, and more highly regionalized and uniform standards of perinatal care than the United States.[8] It is unclear how differences in health care and social systems interact to affect NICU outcomes. Further study into variations in NICU practices and outcomes is needed to understand the sources of variation and to enable design of strategies to deal with them.

Our results also demonstrate the importance of adequate risk adjustment for both baseline population risks and severity of illness on admission in comparisons of NICU mortality rates. Omission of risk adjustment variables can unfairly penalize NICUs in audits to examine quality of care. Admission SNAP-II was significantly and highly predictive of NICU mortality rates, independent of other baseline population characteristics. However, one limitation of this score is that it is measured over a period of 12 hours after admission and may therefore reflect not only severity of illness on admission but also interventions during the measurement period, which may result in bias. However, illness severity cannot yet be measured at a single point in time, and SNAP-II is currently the best available method for assessing severity of illness on admission. Risk-adjusted trends in mortality rates also act as sentinels that can alert caregivers to potential problems and help guide the management of infants, particularly those at high risk of death. Longitudinal monitoring of NICU mortality rates can provide valuable information for audit and can yield important insights into how to improve efficacy and efficiency of care.

The strong association between NICU mortality rates on the one hand and preterm delivery and outborn status on the other indicates the importance of antenatal care, preven-

tion of preterm deliveries and transfer of mothers with high-risk pregnancies to tertiary-level perinatal centres before delivery.[8,20–23] Development of strategies aimed at addressing these issues is key to further reduction of NICU deaths. Congenital anomalies were present in 34% of NICU deaths, although only 15% of infants admitted to a NICU had such anomalies. These results are consistent with other reports[8–10] showing that congenital anomalies are important causes of NICU admissions and deaths, and they underscore the importance of developing strategies to reduce the occurrence of congenital anomalies and improve prenatal diagnosis. Infection and birth asphyxia (the major cause of hypoxic–ischemic encephalopathy) were also significantly associated with NICU deaths. These associations highlight the fact that many causes of neonatal death may be preventable. Sex was not a significant predictor of death on multivariate analysis. Jones and collaborators[24] recently reported no sex difference in death rates for infants greater than 24 weeks gestational age and suggested that treatment

with antenatal corticosteroids and artificial surfactant may be responsible for reducing the male biological disadvantage due to lung immaturity that existed previously. Finally, 50% of NICU deaths occurred within 3 days of admission and 75% occurred within 12 days. Actuarial survival curves published by Jones and collaborators[24] explicitly illustrate the change in day-by-day survival for different gestational-age groups and can be of assistance in counselling the parents and in decision-making for infants admitted to the NICU.

Study limitations

Our data were confined to infants admitted to the NICU and hence did not cover deaths of infants who were never admitted to a NICU. Combining data on NICU deaths with data on perinatal deaths occurring without NICU admission should yield information on expected survival at different gestational ages during pregnancy, which may be helpful to those who counsel pregnant women.
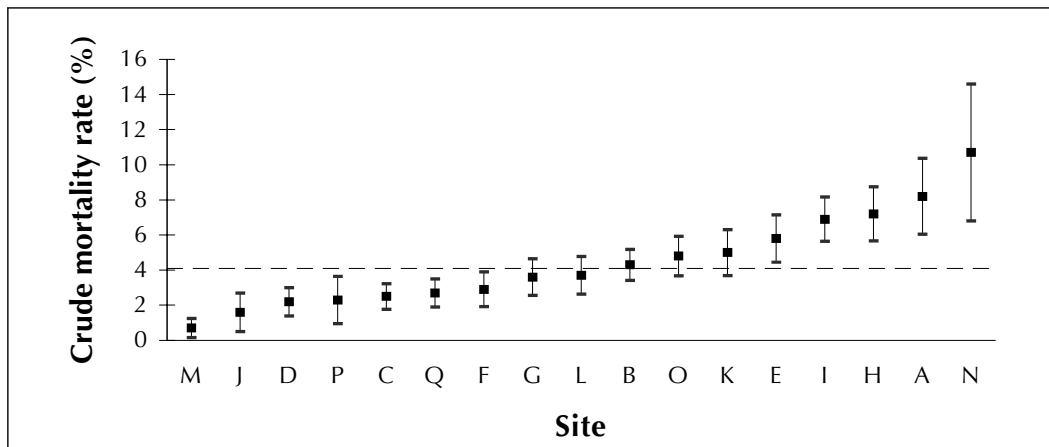
Fig. 2: Crude mortality rate (with 95% confidence intervals) for neonates admitted to 17 Canadian NICUs (identified by capital letters). The dashed line represents the mean for the 17 hospitals.

Fig. 3: Adjusted mortality rate (with 95% confidence intervals) for neonates admitted to 17 Canadian NICUs (identified by capital letters). The dashed line represents the mean for the 17 hospitals.

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