An Algorithm for Predicting Neonatal Mortality in Threatened Very Preterm Birth

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Abstract

Objective: To develop a prediction model for neonatal mortality using information readily available in the antenatal period.

Methods: A multiple logistic regression model of a complete population-based geographically defined cohort of very preterm infants of 23+0 to 30+6 weeks' gestation was used to identify antenatal factors which were predictive of mortality in this population. Infants < 23 weeks and those with major anomalies were excluded.

Results: Between 1996 and 2012, 1240 live born infants < 31 weeks' gestation were born to women residing in Nova Scotia. Decreasing gestational age strongly predicted an increased mortality rate. Other factors significantly contributing to increased mortality included classification as small for gestational age, oligohydramnios, maternal psychiatric disorders, antenatal antibiotic therapy, and monochorionic twins. Reduced neonatal mortality was associated with antenatal use of antihypertensive agents and use of corticosteroids of any duration of therapy given at least 24 hours before delivery. An algorithm was developed to estimate the risk of mortality without the need for a calculator.

Conclusion: Prediction of the probability of neonatal mortality is influenced by maternal and fetal factors. An algorithm to estimate the risk of mortality facilitates counselling and informs shared decision making regarding obstetric management.

Résumé

Objectif : Élaborer un modèle prédictif en ce qui concerne la mortalité néonatale au moyen de renseignements faciles à obtenir au cours de la période prénatale.

Méthodes : Nous avons eu recours au modèle de régression logistique multiple d'une cohorte exhaustive, populationnelle et définie géographiquement de nouveau-nés très prématurés (âge gestationnel : de 23+0 à 30+6 semaines) pour identifier les facteurs prénataux permettant de prédire la mortalité au sein de cette population. Les nouveau-nés dont l'âge gestationnel était inférieur à 23 semaines et ceux qui présentaient des anomalies majeures ont été exclus.

Résultats : Entre 1996 et 2012, 1 240 enfants nés vivants à moins de 31 semaines de gestation ont été issus de femmes résidant en Nouvelle-Écosse. La baisse de l'âge gestationnel constituait un facteur solide permettant de prédire une hausse du taux de mortalité. Parmi les autres facteurs contribuant de façon significative à la hausse du taux de mortalité, on trouvait l'hypotrophie fœtale, l'oligohydramnios, les troubles psychiatriques maternels, l'antibiothérapie prénatale et les jumeaux monozygotes. La baisse du taux de mortalité néonatale était associée à l'utilisation prénatale d'antihypertenseurs et à l'utilisation de corticostéroïdes (peu importe la durée du traitement) administrés au moins 24 heures avant l'accouchement. Nous avons élaboré un algorithme pour estimer le risque de mortalité sans avoir recours à une calculatrice.

Conclusion : La prévision de la probabilité de la mortalité néonatale est influencée par des facteurs maternels et fœtaux. Le fait de disposer d'un algorithme pour estimer le risque de mortalité facilite le counseling et éclaire le processus décisionnel partagé en ce qui concerne la prise en charge obstétricale.

Key Words: Neonatal mortality, infant, premature, population-based, logistic regression

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INTRODUCTION

Decisions in pregnancies complicated by threatened preterm labour in very preterm infants are often based on gestational age because mortality increases with decreasing gestational age.[1–5] However, it has long been recognized that mortality rates in preterm infants may be modified by other maternal and fetal factors.[6] Logistic regression techniques have shown that the presence of modifiers such as polyhydramnios, congenital malformations, grand multiparity, low birth weight,[7] small for gestational age, and male sex[8] are risk factors for increased mortality, while antenatal corticosteroid therapy[9] and hypertension in pregnancy[8,10] are associated with decreased mortality. Thus, a more useful guide for advanced treatment decisions would be a predictive model for mortality derived from gestational age and modified by factors that increase or decrease mortality.

Attempts at using logistic regression to evaluate factors increasing or decreasing the risk of mortality have been reported. The interpretation of the relationship between risk factors and outcome is limited because the cohorts used in these studies were either not population-based[7,9] or used information unavailable in the antenatal period.[7–9] A recent study from Israel was population-based[11]; however, it was restricted to the most immature infants (23 to 26 completed weeks) and only considered a limited number of risk factors.

The purpose of the current study was to estimate neonatal mortality based exclusively on available antenatal fetal and maternal information for decision making (such as performing a Caesarean section or carrying out neonatal resuscitation). A practical and simple-to-use risk score was generated and tested for clinical use.

METHODS

Nova Scotia has a population of approximately 1 million people.[12] Infants born alive between January 1, 1996, and December 31, 2012, to mothers who resided in Nova Scotia at the time of birth and who were very preterm (23+0 to 30+6 weeks' gestational age, which will be referred to as 23 to 30 weeks) were included in the study. These gestational age limits were used because survival below 23 weeks' gestation was virtually zero, and infants above 30 weeks' gestation were not enrolled in the Perinatal Follow-Up Program from which the data for this study were generated. This study included infants who died in the delivery room, whether or not resuscitation was attempted. Infants with major anomalies, defined as congenital anomalies that require significant medical or surgical interventions, were excluded. The majority of these anomalies included pulmonary hypoplasia, cardiovascular anomalies, chromosomal abnormalities, neurologic anomalies, and club feet.

All live born infants from 23 to 30 weeks' gestation born to residents of Nova Scotia during the 17-year era were included in the Perinatal Follow-Up Program database using a proprietary product, Scientific Information Retrieval software (SIR version XS.01.12, Australia). The database was modelled on the Nova Scotia Atlee Perinatal Database, which has been previously validated.[13,14] The Perinatal Follow-Up Program database included illnesses and treatments for mothers during the pregnancy and for newborns during the postnatal period (noted in Table 1). Neonatal mortality was defined as death before 28 days' postnatal age.

Other terms in Table 1 requiring definitions were:

1. families in need: those requiring social services;
2. maternal anemia: hemoglobin concentration < 100 g/L at any time during pregnancy;
3. maternal drug abuse: abuse of either illegal substances or non-prescribed pharmaceuticals;
4. oligohydramnios: an ultrasound finding of single deepest pocket of amniotic fluid < 2 cm or an amniotic index < 5;
5. polyhydramnios: an ultrasound finding of single deepest pocket of amniotic fluid ≥ 8 cm or an amniotic index > 20; and
6. maternal psychiatric disorders: as documented on the Nova Scotia prenatal form or in the history of the mother's inpatient chart for the current pregnancy.

More than 80% of psychiatric disorders in the current study were depression or anxiety; the remainder included schizophrenia, bipolar disorders, eating disorders, and other psychiatric disorders.

The relevant data were extracted from SIR using SPSS version 15.0 (IBM Corp., Armonk NY) for analysis. Variable correlations by univariate analysis with mortality of $P < 0.20$ (Table 1) were entered in a multiple backward stepwise logistic regression model using a generalized estimating equation.

A scoring system to predict the risk of mortality was developed based on the established method of Sullivan et al.[15] The score was developed from the beta coefficients (Table 2) of the logistic regression model to generate points for each risk factor (Table 3). For gestational age, 30 weeks was used as the reference. For each individual infant, a risk score was calculated based on the value for each factor and the sum of their individual points assigned and the mortality (Table 4).