An Epidemiological Study of Factors Associated with Preterm Infant In-Hospital Mortality

Abstract

Nationally representative in-hospital mortality rates among preterm infants are essentially unknown in Ireland. We examined preterm infants born in hospital and admitted to intensive care unit (ICU) between 2005 and 2008. Unadjusted in-hospital mortality rates were 9.5% (95% CI 4.9-16.8). Overall, 6,595 preterm infants were admitted to 13 ICUs of whom 256 (3.9%) died prior to hospital discharge. Infants with a birthweight less than 1,000g were 18.1 (95% CI 12.1-27.1) times more likely to die in hospital. Mortality was high among preterm infants diagnosed with Grade 3/4 intraventricular haemorrhage (43.6 deaths per 100 cases; 95% CI 31.0-56.7). Congenital anomaly diagnosis was associated with a five-fold increased risk (RR 5.1; 95% CI 4.0-6.6) of in-hospital mortality. Our population-based study provides reliable estimates of in-hospital mortality among preterm infants admitted to ICUs in Ireland over a four-year period. Specific focus was given to infant and health service characteristics, procedures, congenital anomalies, and pregnancy outcomes.

Introduction

The rate of preterm births is increasing worldwide. Advances in comprehensive neonatal intensive care have resulted in a substantial reduction in perinatal mortality. However, obsetric and neonatal mortality estimates for preterm infants can be challenging to ascertain, since more favourable outcomes, frequently reported from tertiary care centres, are not always reflective of general care units (ICUs) that offer mid- to high-level care in moderate to high obstetric volume hospitals. To date, the largest Irish study observed differences in survival across Irish centres among very low birth weight (VLBW) infants admitted to ICUs; however, secondary data sources such as hospital discharge records were used to assess in-hospital mortality in preterm infants. Thus, we conducted an epidemiologic study of factors associated with in-hospital mortality in preterm infants admitted to ICUs in Ireland over a four-year period. Specific focus was given to infant and health service characteristics, procedures, congenital anomalies, and pregnancy outcomes.

Methods

We reviewed hospital discharge records from the Economic and Social Research Institute Hospital In-Patient Enquiry (HIPE) dataset. HIPE contains nationally representative information on all infants admitted to ICU between January 1, 2005 and December 31, 2008. For the purposes of our analysis, we only examined preterm infants admitted to ICU between 0 and 28 days of age. Further, we restricted our analysis to infants weighing greater than 500g due to small numbers (<50 cases) and our cohort variable for gestational age at birth. Therefore, preterm infants were identified using diagnostic codes from the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM). Infants without a diagnosis code for gestational age at birth were excluded from the study. Since infant viability prior to 24 completed gestational weeks is unlikely, we excluded infants who were either diagnosed with <24 weeks gestation (ICD-10-AM code: P07.20) or were considered preterm if they were born between >24 and <37 weeks gestation, and were identified using ICD-10-AM codes P07.22 (24 but <28 weeks gestation), P07.31 (28 but <32 completed weeks gestation) and P07.32 (32 but <37 completed weeks gestation). Based on these criteria, data were available on 8,043 infants.

To prevent the potential analysis of duplicate cases, we excluded 1,444 infants who were discharged as a transfer to another hospital. Infants whose source of admission was recorded as a transfer from another hospital and who were admitted to ICU remained in the sample to capture all cases of in-hospital mortality. Thus, our final sample size included 6,595 preterm infants. Infant in-hospital mortality was our primary outcome and was derived from hospital discharge codes. Potential predictors included gender, age, admission weight, source of hospital admission (e.g., newborn, hospital ward, other settings), and length of stay in ICU. We also examined the influence of maternal high-risk conditions, infant conditions (clinician defined at hospital level) and procedures and major complications were identified. Major congenital anomalies were classified into 16 groups in accordance with the European Surveillance of Congenital Anomalies guidelines.

We calculated unadjusted incidence and exact 95% confidence intervals (CIs) for indications of delivery, co-morbidities, procedures, congenital anomalies and in-hospital mortality. The in-hospital mortality rate per 100 cases and corresponding binomial 95% CIs were derived. To evaluate the association between in-hospital mortality and complications of interest, we derived unadjusted relative risks and 95% CIs. Since extremely immature infants (<28 completed weeks gestation) face distinct clinical complications compared to more mature infants, we repeated the analysis for infants born >28 but <37 completed weeks gestation to compare differences in risk factor associations. Although overall mortality decreased, patterns in associated risk factors remained the same, and therefore results are shown for the entire cohort. Analyses were conducted using SAS software, Version 9.2.

Results

We identified 6,595 preterm infants admitted to ICU between 2005 and 2008. The majority (74.7%) were aged between 32 and 36 completed gestational weeks, one in five (19.3%) were aged 28 to 31 weeks and one in sixteen (6.0%) were aged 24 to 27 weeks. Congenital anomalies died prior to hospital discharge, translating to a mortality rate of 3.9% (95% CI 3.4-4.4). Marked variation in in-hospital mortality was observed by level of immaturity; 32.5% (95% CI 27.9-37.3) of infants aged 24 to 27 gestational weeks died prior to hospital discharge compared to 4.9% (95% CI 3.4-4.4). Mortality was highest among preterm infants diagnosed with Grade 3/4 intraventricular haemorrhage (43.6 deaths per 100 cases; 95% CI 31.0-56.7). Congenital anomaly diagnosis was associated with a five-fold increased risk (RR 5.1; 95% CI 4.0-6.6) of in-hospital mortality. Our population-based study provides reliable estimates of in-hospital mortality among preterm infants admitted to ICUs in Ireland over a four-year period. Specific focus was given to infant and health service characteristics, procedures, congenital anomalies, and pregnancy outcomes.

Note: Mortality rates given per 100 cases.

Abbreviation: CI, confidence interval
a Excludes babies < 500g or > 5,000g due to small numbers
b Includes admission source not elsewhere listed

There was a wide variation in the in-hospital mortality rates by maternal high-risk conditions, neonatal conditions and procedures (Table 2). The highest in-hospital mortality rate was among infants whose mothers were diagnosed with a placental disorder (7.4%) or where there was a multiple pregnancy (4.9%). Mortality was highest among infants diagnosed with intraventricular haemorrhage (IVH), necrotizing enterocolitis (NEC), or other brain haemorrhage (included subdural, cerebral and subarachnoid). One-third (33.3%) of infants who had a chest drain inserted died in hospital, compared to 7% of infants admitted to the ICU who were diagnosed with a major congenital anomaly, which the most frequently anomalous conditions reported were heart disease, chromosomal and genital (Table 3). Diagnosis of congenital anomalies varied according to gestational age; 6.9% of infants aged between 32 and 36 completed gestational weeks were diagnosed with a congenital anomaly compared to 11.3% of infants aged 28 to 31 weeks and 13.8% aged 24 to 27 weeks (data not shown). Among infants diagnosed with a major congenital anomaly, the overall in-hospital mortality rate was 14.9%. Mortality in infants with congenital anomaly diagnosis was identified, with mortality rates ranging from 4.1% among infants with genital anomalies to 53.3% among infants with respiratory anomalies.

Note: Mortality rates given per 100 cases.

Abbreviation: CI, confidence interval
a Gestational age > 24 but < 37 completed weeks
b Excludes placental translation disorders
c Includes respiratory distress syndrome, asphyxia, transient tachypnoea, pulmonary haemorrhage, other pulmonary heart disease, pneumonia, respiratory failure, hypoxia, pneumothorax, and other chronic respiratory conditions

d Includes infectious and parasitic diseases, meningitis, and unspecified acute respiratory infections

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e Includes subdural, cerebral and subarachnoid haemorrhage due to birth trauma

The risk of in-hospital mortality was significantly higher among infants aged one day and weighing <1,500g on admission (Table 4). In contrast, infants aged at least 8 days or weighing between 2,000 and 2,500g on admission were at the lowest risk. Infants transferred for ongoing care had a three-fold risk of in-hospital mortality relative to those transferred for ongoing care, while the association between maternal high-risk conditions and in-hospital mortality was insignificant. Risk of in-hospital mortality was nearly four-fold for infants diagnosed with select medical conditions and five-fold for infants diagnosed with major congenital abnormalities. Infant risk of death was severe enough to warrant ventilatory support or chest drain insertion were 31 times more likely to die in-hospital.

a) Premature delivery is identified as any infant with a gestational age > 24 but = 37 completed weeks.
b) Classification based on the European Surveillance of Congenital Anomalies.
c) Includes major congenital abnormalities not elsewhere classified.
d) Major congenital abnormalities of the ear, face, and neck are not shown due to small numbers (<5).

Abbreviation: RR, risk ratio; CI, confidence interval

- Adults aged at least 8 days or weighing between 2,000 and 2,500g on admission.
- Infants transferred for ongoing care.
- Maternal high-risk conditions.

Discussion

Our study is the first analysis of early and late preterm infants admitted to ICU over a four-year period in Ireland. We found that 3.9% of preterm infants did not survive to hospital discharge, and mortality varied significantly by level of immaturity. The mortality rates among infants aged 24 to 27 weeks, similar to rates reported for the European region of the northern Europe, was high at 32.5%. Similar high mortality rates may be attributed in part to the high risk of congenital abnormalities present in this particular gestational age group. Although our study’s goal was not to conduct an analysis at the clinical level, further investigation of NICU clinical practice and benchmarks that impact on infants undergoing ventilator support with major congenital anomalies is necessary. This high mortality rate may be consistent with prior research and demonstrate the importance of identifying and capturing important infant-related procedures and diagnoses during ICU stay. Similar to reports from the European Surveillance of Congenital Anomalies (EUROCAT) network, in our study cohort, heart, chromosomal and genital anomalies were the most commonly diagnosed. We found that one in twelve infants was diagnosed with a major congenital anomaly, which is nearly four-times higher than the international average reported by EUROCAT. Disparity is unsurprising, given the differences in the data collection strategy and sampling frame between our study and EUROCAT. Differences are further impacted by our focus on a high-risk study population and restrictive legislation on termination of pregnancy. Future research exploring the range of outcomes among preterm infants diagnosed with congenital abnormalities would be clinically important and useful for counselling purposes.

Maternal high risk conditions were not associated with infant mortality, which was unexpected given the known risks of maternal factors. The complications associated with preterm delivery. Since we were reliant on maternal data, we cannot comment on the impact of maternal factors.

Our study has several limitations. First, identification of preterm infants depends on ICD-10-AM codes and lack specific estimated gestational weeks at birth, which is problematic given the variation in mortality risk by gestational age. Second, there is potential selection bias, as preterm infants without an ICD-10-AM code indicating prematurity may have been unintentionally excluded from our study cohort. The absence of grading information for NEC coupled with missing IVD grading for a proportion of cases limited clinical interpretation. The lack of established maternal predictors in the dataset prevented the investigation of factors such as parity, age and hypertension. Moreover, although hospital discharge data have reportedly high accuracy, the de-identified nature of the hospital discharge data inhibited the ability to ascertain the impact of clinical practice and ICU characteristics on mortality. Further, large variability in case definitions between clinicians may be present. Larger hospitals may have better obstetric and care, with the ability to provide rapid emergency caesarean sections with associated increase in the risk of in-hospital mortality. Further, large variability in case definitions between clinicians may be present. Larger hospitals may have better obstetric and care, with the ability to provide rapid emergency caesarean sections with associated increase in the risk of in-hospital mortality. Further, large variability in case definitions between clinicians may be present. Larger hospitals may have better obstetric and care, with the ability to provide rapid emergency caesarean sections with associated increase.

The impact of maternal conditions on infant mortality may have been underestimated. This population-based ascertainment of deaths ensures provision of reliable estimates of in-hospital mortality among preterm infants admitted to ICU. Such risk estimates are useful for informing clinicians regarding the range of infant morbidities, risk of death, specialised care, prolonged infant hospital stays, and accompanying health service organisational planning and practice patterns.

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