



More bronchopulmonary dysplasia with improved survival in extremely preterm infants

Ga Won Jeon^a, MD, PhD, Yun Sil Chang^b, MD, PhD

^aDepartment of Pediatrics, Inha University Hospital, Inha University College of Medicine, Incheon, Korea; ^bDepartment of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Abstract

Objective: Although advances in neonatal intensive care have significantly reduced mortality in preterm infants, the incidence of bronchopulmonary dysplasia (BPD) is increasing. This study evaluated mortality, BPD, and the combined incidence of BPD or mortality among extremely preterm infants in Korea.

Methods: We analyzed extremely preterm infants with gestational ages of 23–27 weeks using data from the Korean Neonatal Network. BPD was diagnosed at 36 weeks' postmenstrual age. Trends in mortality, BPD incidence, and associated risk factors were assessed from 2014 to 2021.

Results: The mean gestational age was 25.7 ± 1.2 weeks, and the mean birth weight was 870.7 ± 194.2 grams. The incidence of BPD among survivors increased from 51.2% in 2014 to 62.7% in 2021 ($P < 0.001$), while mortality decreased from 28.3% to 19.5% ($P < 0.001$). The combined incidence of BPD or mortality also increased, from 63.6% in 2014 to 66.9% in 2021 ($P = 0.006$). Although the duration of invasive ventilation, the incidence of endotracheal intubation at birth, and intubation for surfactant administration decreased, the duration of non-invasive ventilation and ventilatory support increased.

Conclusion: Although the mortality decreased, the incidence of BPD and the combined incidence of BPD or mortality increased, likely due to the longer duration of ventilatory support.

Introduction

We hypothesized that over the past decade, as the mortality rates for extremely preterm infants (EPIs, gestational age < 28 weeks) have decreased, the incidence of BPD has increased, resulting in a consistent ratio of mortality or BPD incidence among these infants.

To test this hypothesis, we examined trends in the incidence of BPD, mortality, and BPD or mortality in EPIs using data from the Korean Neonatal Network (KNN) from 2014 to 2021.

We also analyzed these trends in the context of policy changes aimed at reducing BPD and investigated the factors contributing to any observed changes.

Methods

We utilized the KNN, a nationwide large cohort of preterm infants in Korea, database for EPIs with gestational ages ranging from 23 to 27 weeks, born between January 1, 2014, and December 31, 2021.

BPD was diagnosed at 36 weeks' postmenstrual age according to the Neonatal Research Network's 2019 definition by Jensen et al., which classified it into three grades: grade 1 (requiring oxygen via nasal cannula at < 2 L/min), grade 2 (requiring non-invasive ventilation, including nasal cannula oxygen at ≥ 2 L/min), and grade 3 (requiring invasive ventilation).

Results

Trends in BPD, mortality, and BPD or mortality

The overall incidence of BPD among surviving EPIs increased over time, from 51.2% in 2014 to 62.7% in 2021 (P for trend < 0.001). Conversely, the mortality rate of EPIs decreased from 28.3% in 2014 to 19.5% in 2021 (P for trend < 0.001). The combined incidence of BPD or mortality also increased.

Trends in BPD, mortality, and BPD or mortality stratified by gestational age.

The incidence of BPD among surviving EPIs born at 24–27 weeks significantly increased over time, while in those born at 23 weeks, it rose without statistical significance. Mortality rates significantly decreased for infants born at 24–26 weeks. Although mortality for those born at 25 weeks showed an initial rise until 2016, it then steadily declined. Mortality trends for infants born at 23 and 27 weeks also decreased but were not statistically significant. BPD or mortality increased in infants born at 25 and 27 weeks but remained stable over time for those born at 23, 24, and 26 weeks.

Risk factors for BPD, mortality, and BPD or mortality

Multivariable logistic regression identified the duration of ventilatory support and supplemental oxygen as risk factors for BPD. Risk factors for mortality included invasive ventilation duration, sepsis, high-grade IVH (\geq grade 3), and NEC (\geq stage 2). The duration of invasive ventilation, ventilatory support, and supplemental oxygen were all risk factors for BPD or mortality.

Trends in factors associated with BPD

Among survivors, invasive ventilation and supplemental oxygen durations decreased over time, while non-invasive ventilation and total ventilatory support durations increased. Invasive surfactant administration and endotracheal intubation at birth decreased, whereas postnatal corticosteroid therapy increased.

Trends in other morbidities

The rates of sepsis and IVH (grade ≥ 3) decreased. The rates of NEC (stage ≥ 2), ROP (stage ≥ 3), and ROP requiring operation remained stable.

Discussion

In conclusion, while the mortality rate among EPIs in Korea has decreased over time, there has been a concurrent increase in the incidence of BPD among survivors and in the combined outcome of BPD or mortality.

The decrease in mortality was particularly significant for infants born at 24 and 26 weeks of gestation, with no corresponding increase in BPD or mortality observed in these infants.

This suggests a trade-off, where improved survival rates among EPIs lead to a higher incidence of BPD among survivors. This trend is likely due to decreasing trends in mortality risk factors over time, such as the duration of invasive ventilation, sepsis, and IVH. Despite efforts to reduce BPD, these have not yet had a strong impact on its incidence.

The significant risk factor of ventilator duration in EPIs remains a major challenge.

References

- Jensen EA, Dysart K, Gantz MG, et al. The Diagnosis of Bronchopulmonary Dysplasia in Very Preterm Infants. An Evidence-based Approach. *Am J Respir Crit Care Med*. Sep 15 2019;200(6):751-759.
- Isayama T, Iwami H, McDonald S, Beyene J. Association of Noninvasive Ventilation Strategies With Mortality and Bronchopulmonary Dysplasia Among Preterm Infants: A Systematic Review and Meta-analysis. *JAMA*. Aug 9 2016;316(6):611-24.
- Nakashima T, Inoue H, Sakemi Y, Ochiai M, Yamashita H, Ohga S. Trends in Bronchopulmonary Dysplasia Among Extremely Preterm Infants in Japan, 2003-2016. *J Pediatr*. Mar 2021;230:119-125.e7.
- Jeon GW, Oh M, Lee J, Jun YH, Chang YS. Comparison of definitions of bronchopulmonary dysplasia to reflect the long-term outcomes of extremely preterm infants. *Sci Rep*. Oct 27 2022;12(1):18095.