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ORIGINAL ARTICLE

# Morbidity and mortality of very low birth weight infants in Taiwan—Changes in 15 years: A population based study



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## KEYWORDS

morbidity;  
mortality;  
very low birth weight  
infant

**Background/Purpose:** Very low birth weight (VLBW) infants account for over 50% of perinatal deaths in Taiwan. This study aimed to identify changes in parental characteristics, perinatal conditions, mortality, and major neonatal morbidities for VLBW infants in Taiwan, and to highlight the challenges faced by patients, families, and caregivers.

**Methods:** We conducted a retrospective cohort study to investigate the mortality and morbidity of VLBW infants registered in the Taiwan Premature Infant Follow-up Network from 1997 through 2011. The exclusion criteria included congenital anomalies and chromosome anomalies. Continuous data was represented as mean  $\pm$  SD, and changes over time in the variables were tested using one-way analysis of variance, with  $p < 0.05$  considered statistically significant.

**Results:** A total of 13,159 VLBW infants were enrolled. We found significant increases over time in the parental age and educational level, *in vitro* fertilization, first livebirth, multiple births, maternal transfer, cesarean section, and complete antenatal steroid use. Apgar scores at 1 minute and 5 minutes after birth increased, and the intubation rate decreased gradually. Decreasing mortality over time for each successive period was demonstrated. Incidence of some morbidities increased, such as respiratory distress syndrome and patent ductus arteriosus; in contrast, incidence of others decreased, such as sepsis, necrotizing enterocolitis,

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intraventricular hemorrhage, and chronic lung disease. However, retinopathy of prematurity (ROP) incidence remained constant.

*Conclusion:* Although the mortality and most of the morbidity of VLBW infants improved over time, the incidence of ROP remained constant. This requires us to further evaluate our strategy for preventing ROP in the future.

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## Introduction

In recent decades, advances in obstetrical and neonatal care have decreased the mortality rate of premature infants in many populations. In Taiwan, about 200,000 infants are born annually and the preterm birth rate is estimated to be 8–10%. Of these preterm births, very low birth weight (VLBW) infants, defined as those with a body weight of  $\leq 1500$  g at birth, represent 0.8% of live births yet account for over 50% of perinatal deaths in Taiwan.<sup>1</sup> Furthermore, many VLBW infants suffer from morbidities during their hospitalization, such as respiratory distress syndrome (RDS), patent ductus arteriosus (PDA), sepsis, necrotizing enterocolitis (NEC), intraventricular hemorrhage (IVH), retinopathy of prematurity (ROP), and chronic lung disease (CLD). These conditions not only expose the premature infants to a higher risk of mortality and lengthen their hospitalization period but also cause great psychological burden to their families and higher social costs. The Taiwan Premature Infant Follow-up Network (TPFN), called the Taiwan Premature Infant Developmental Collaborative Study Group before 2016, was founded in 1995 with the aim of improving the healthcare quality of premature infants by providing local statistical data about the mortality, morbidities, and long-term neurological outcome of VLBW infants. The healthcare system, healthcare training, and health insurance policies have changed significantly over the past 20 years;<sup>2,3</sup> thus, it is crucial to provide data that can be used to find ways to improve future outcomes of VLBW infants. We identified changes in parental trends, perinatal conditions, mortality, and major neonatal morbidities for VLBW infants born between January 1, 1997 and December 31, 2011 to provide better understanding of VLBW-infant mortality and morbidity in Taiwan and highlight the challenges faced by these patients, their families, and their caregivers.

## Methods

Participants in TPFN submitted data about infants born at their facilities or admitted before the age of 7 days. Maternal pregnancy/delivery data recorded by the hospital staff soon after birth and infant data from birth to death or discharge reported by case managers using uniform definitions and tables was also collected. This study was restricted to VLBW infants born between January 1, 1997 and December 31, 2011. Term and post-term infants [gestational age (GA)  $\geq 37$  weeks] and VLBW infants with known chromosomal abnormalities, congenital heart

disease requiring risk-adjusted congenital heart surgery-1 categories 2–6,<sup>4</sup> and other severe congenital anomalies were excluded from the study.

GA was determined as the best obstetric estimate using ultrasonography and the date of the last menstrual period. Infants with a birth weight below the 10<sup>th</sup> percentile for their age and sex, according to previously published growth charts,<sup>5</sup> were defined as small for gestational age. Mortality was defined as death before discharge. The following morbidities were included and diagnosed as follows: (1) RDS was diagnosed by clinical symptoms and chest X-ray findings; (2) PDA was diagnosed by cardiac sonography and treated at the discretion of the attending neonatologist; (3) sepsis was diagnosed by a positive blood culture result; (4) NEC was diagnosed by abdominal X-ray and clinical findings; and (5) IVH and periventricular leukomalacia were detected by brain sonography and graded according to the previously published scheme of Papile et al.<sup>6</sup> ROP was staged according to international classifications.<sup>7</sup> CLD was defined as oxygen dependence at 36 weeks of postmenstrual age.<sup>8</sup>

Continuous data was represented as mean  $\pm$  SD, and the changes in the variables over time were tested by one-way analysis of variance with a  $p$  value  $< 0.05$  considered statistically significant.

## Ethical statement

The study was approved by the Institutional Review Board of each participating hospital, which included the National Taiwan University Hospital, Taipei, Taiwan; Chang Gung Memorial Hospital, Taoyuan, Taiwan; China Medical University Hospital, Taichung, Taiwan; National Cheng Kung University Hospital, Tainan, Taiwan; Tri-Service General Hospital, Taipei, Taiwan; Chung Shan Medical University Hospital, Taichung, Taiwan; Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan; and Kaohsiung Medical University Chung-Ho Memorial Hospital, Kaohsiung, Taiwan; and by a Joint Institutional Review Board representing the remaining hospitals that provided data.

## Results

### Study group

A total of 13,159 VLBW infants, who were registered in TPFN between January 1, 1997 and December 31, 2011 met the inclusion criteria and were enrolled in this study. To compare the variables over time, study period was divided

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