School Entry Age Outcomes for Infants with Birth Weight ≤800 Grams

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Objective To evaluate the mortality and long-term morbidity rates of extremely low birth weight (ELBW) infants admitted to neonatal intensive care units (NICUs).

Study design This was a longitudinal cohort study of all admissions born between 1983 and 2003 with birth weight ≤ 800 g at a single tertiary NICU. Trends in survival and neurodevelopmental outcome rates at school entry in four 5-year epochs were analyzed.

Results Of 917 admissions, 552 survived to NICU discharge, with significantly increasing survival rates from 46% in epoch 1 to 71% in epoch 4 ($P < .0001$). Although the overall impairment rate of 30% did not change, the pattern of impairments did. Cognitive ($P = .017$) and hearing ($P = .014$) impairment rates increased. Visual impairment rates decreased ($P = .042$), with a trend toward decreasing cerebral palsy from 20% to 12% ($P = .061$).

Conclusions Improved survival of low birth weight preterm infants has been associated with different types of neurodevelopmental impairments, including increased cognitive impairment rates. *(J Pediatr 2010;157:989-94)*.

Survival of extremely premature and low birth weight infants has improved with advances in perinatal and neonatal treatment and technology. For example, before the introduction of surfactant in the 1980s, Hack et al[1] reported survival rates of 18%-20% in newborns with birth weight <750 g. The National Institute of Child Health and Human Development Neonatal Research Network demonstrated a survival rate of 41% in the early 1990s, 54% in the mid-1990s, and 55% in 1997-2002.[2] Adverse neurodevelopmental outcomes are common, however. Trends in long-term morbidity rates, including cerebral palsy, and early childhood and school age outcomes, have shown mixed results, with reports of increases, no change, and decreases over time.[3] Most of these studies evaluated changes in impairment rates in children age 2 years and younger. Because the diagnosis of cerebral palsy may change over time,[4] follow-up beyond 2 years is desirable. In addition, the predictive validity of developmental tests, such as the Bayley Scales of Infant Development (BSID) for cognitive function, at school age is poor.[5] Thus, there is a need for more information on trends in long-term impairment rates in extremely low birth weight (ELBW) infants.

Since 1983, the regional Neonatal Follow-up Program at Children's and Women's Health Centre of British Columbia (C&W) has performed standardized sequential multidisciplinary assessments in preterm ELBW survivors (birth weight ≤800 g). We examined trends in survival and neurodevelopmental status at school entry of ELBW infants born at C&W between January 1983 and May 2003. Our hypothesis is that there has been an increase in survival but no change in the incidence of motor, cognitive, visual, and hearing outcomes in this ELBW population born during this 20-year period.

Methods

British Columbia, Canada, has a publicly financed health care system with universal health care access. There are approximately 40 000 births per year in British Columbia. Neonatal intensive care is regionalized, and C&W is the largest maternal and neonatal tertiary referral unit. Before 1993, C&W was the only neonatal intensive care unit (NICU) in British Columbia that cared for ELBW babies. Since 1993, two additional NICUs in British Columbia have provided this level of NICU care.

The study population comprised all infants with a birth weight of ≤800 g admitted to the C&W NICU between January 1983 and May 2003. All infants who were discharged alive were invited to attend the Neonatal Follow-up Programme between 1983 and 2008 at standardized ages: 4 months, 8 months, 18 months, 3 years corrected age (CA), and 4.5 years chronological age.

BSID	Bayley Scales of Infant Development	NICU	Neonatal intensive care unit
C&W	Children's and Women's Health Centre of British Columbia	OR	Odds ratio
CA	Corrected age	PDI	Psychomotor Development Index
CI	Confidence interval	ROP	Retinopathy of prematurity
ELBW	Extremely low birth weight	SD	Standard deviation
MDI	Mental Development Index	SGA	Small for gestational age
		WPPSI	Wechsler Preschool and Primary Scales of Intelligence

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University and hospital Ethics Review Board approval was obtained. Neonatal data were collected prospectively and entered into a computerized NICU database. Each family was given a questionnaire soliciting information about ethnic background and parental education. Assessment outcomes were entered into the neonatal follow-up database. Information was retrieved and validated from hospital charts when necessary. Assessments performed at other institutions were included when information from C&W was not available.

Standardized assessments of motor, cognitive, and sensory function were performed by an experienced multidisciplinary team of pediatricians, nurses, physical and occupational therapists, psychologists, psychometricians, audiologists, and speech and language pathologists. Vision assessments were carried out by pediatric ophthalmologists, usually at the 8-month and 4.5-year visits. At all visits, a detailed history was obtained, and general and neurologic exams were performed. Visual and hearing status were reviewed by history at each visit. Hearing was evaluated with behavioral audiometry at the 8-month visit and with ear-specific behavioral audiometry at 3 years. At 18 months CA, the Psychomotor Development Index (PDI) and the Mental Development Index (MDI) of the BSID were used to assess motor and cognitive abilities, respectively. The BSID-I[6] was used for 1983-1993, and the BSID-II[7] was used thereafter. At 4.5 years chronological age, the Wechsler Preschool and Primary Scales of Intelligence (WPPSI)[8] was used to measure intelligence. The first edition of the WPPSI was used until March 1990, the WPPSI-R[9] was used from April 1990 to December 2002, and the WPPSI-III[10] was used thereafter. The Performance, Verbal, and Full-Scale IQ scores were calculated. All of these assessment scales have a mean of 100 and a standard deviation (SD) of 15, except for the BSID-I, which has a SD of 16. The WPPSI was not administered in children with severe visual, hearing, and/or motor impairments and/or clinically severe global developmental delay.

Definitions

Small for gestational age (SGA) was defined as a birth weight below the third percentile for gestation based on the British Columbia Provincial intrauterine growth charts.[11] Impairment rates were calculated using the most recent visit. Cerebral palsy included all definite abnormalities of tone and reflexes compatible with a clinical diagnosis of cerebral palsy on neurologic examination.[12] Cognitive impairment was defined as a cognitive test score below -2 SD (score <70) or based on neurologic exam when a child's impairment(s) precluded standardized assessment. Blindness was defined as acuity worse than 20/200 in the better eye with optimal refractive correction. Deafness was defined as sensorineural hearing loss requiring amplification or a cochlear implant.

Statistical Analysis

Descriptive survival and impairment rates were calculated for the entire time period and for four 5-year epochs based on date of birth: 1983-1987, 1988-1992, 1993-1997, and 1998 to May 2003. Cerebral palsy, motor, cognitive, visual, and hearing impairment rates were calculated individually and collectively as the number of impairments (cognitive, visual, hearing, and either cerebral palsy or motor impairment) based on results of the most recent assessment for children seen at 18 months CA or older. The proportion of children with standard scores <70 was calculated for subjects with BSID and WPPSI test results. Survival-free impairment rates were calculated by multiplying the impairment-free rate and the rate of survival to 4.5 years.

The statistical analyses of changes in survival and impairment rates over time using the 4 epochs were performed with the Cochran-Armitage test for trend using SAS version 9.2 (SAS Institute, Cary, North Carolina).[13] The effects of gestational age, SGA, sex, and epoch on cognitive and motor impairment were evaluated using stepwise logistic regression analysis. Results are expressed as adjusted odds ratios (ORs) and 95% confidence intervals (CIs). A difference of $P < .05$ was considered statistically significant.

Results

Of the 917 ELBW infants born in British Columbia between 1983 and 2003 and admitted to the NICU at C&W, 552 (60%) survived to NICU discharge (**Table I**). The birth weight of the smallest survivor, born in 1997, was 400 g, and the most premature survivor, born in 1998, was born at 22 weeks, 4 days gestation. The median birth weight of 668 g was lower in the most recent epoch compared with a median birth weight of 690-700 g in the earlier 3 epochs. The survival rate was 54% in males and 66% in females. The overall survival rate increased significantly across the 4 time periods from 46% to 71% ($P < .0001$, Cochran-Armitage test). Sixteen percent of the cohort was SGA. Information about families' self-identified ethnic background was available for 305 survivors (55%): 71% Caucasian, 16% Indian, 6% Asian, 3% aboriginal, 1% black, and 3% other. The average years of maternal education was 13 years for the 300 subjects who provided this information.

Of the 552 NICU survivors, 11 died after NICU discharge, and 483 (89%) were assessed at age 18 months CA or older (**Figure**). Characteristics of the subjects lost to follow-up are given in **Table II** (available at www.jpeds.com). Of the 58 subjects not included in the analyses, 18 were assessed at <18 months CA. Five of these 18 children (28%) were clinically thought at that time to have at least one impairment. Not all subjects were able to complete standardized assessments either because of a major motor, visual, or hearing impairment; behavior; or a different assessment at another institution. Of the 16 subjects seen at 18 months who did not have a BSID assessment, 69% were classified as impaired, and 77% of the 44 subjects who had the 4.5-year assessment but did not have a WPPSI assessment were categorized as impaired.

Table III gives the impairment rates for the 4 epochs. The overall impairment rate of 30% did not vary significantly across time periods. The type of impairment changed over