Outcomes of Very Low Birth Weight Infants with Severe Congenital Heart Disease

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Abstract

Using Korean Neonatal Network data (2013–2021), we analyzed 15,145 very low birth weight infants (VLBWIs), including 147 (1.0%) with severe congenital heart disease (CHD) confirmed by echocardiography and categorized by Vermont Oxford Network criteria. Cyanotic and shunt lesions were most common (36.7%). Mortality was significantly higher in CHD-VLBWIs compared to non-CHD infants (35.4% vs. 10.8%, p<0.001). CHD-VLBWIs also experienced higher rates of pulmonary hypertension, bronchopulmonary dysplasia, and necrotizing enterocolitis. Among survivors, growth and neurodevelopmental outcomes were significantly poorer, with increased rates of cognitive and motor delays and greater need for hearing aids. Unclassified and left-sided lesions showed the highest mortality, while surgically correctable defects such as total anomalous pulmonary venous return and atrioventricular septal defect had particularly high mortality rates. Overall, 57.8% of CHD-VLBWIs died or developed neurodevelopmental impairment by 24 months, highlighting the critical need for specialized neonatal management and long-term multidisciplinary follow-up in this high-risk population.

Introduction

- Very low birth weight (VLBW) infants and congenital heart disease (CHD) are each recognized as independent risk factors that increase mortality and morbidity.
- Although numerous studies have reported that preterm infants with congenital heart disease have higher mortality and are at increased risk of complications, most investigations have been limited by small sample sizes, and relatively few have been published in the past decade.
- In South Korea, national epidemiological data are scarce beyond single-center study, and research on neurodevelopmental outcomes has not yet been established.
- We aimed to describe the both short term outcomes and neurodevelopmental outcomes of CHD-VLBWI.

Methods

- **Study population**

  We included preterm infants with a birth weight of less than 1,500 g who were born in NICUs participating in the KNN between January 2013 and December 2021. In addition, follow-up data at 18–24 months of corrected age (CA), collected between 2015 and 2023, were also included.

- **Definition of severe CHD**

  We define severe CHDs as those structural cardiac defects that impose substantial hemodynamic burden, require surgical or catheter-based intervention within the first year of life.

- **Categorization of CHD (Vermont Oxford Network)**

  A) Left-sided lesions with impaired systemic output
  B) Cyanotic CHD
  C) Shunt lesions with pulmonary over-circulation
  D) Unclassified

- **In-hospital outcomes**

  Bronchopulmonary dysplasia (BPD), Pulmonary hypertension (PHT), Respiratory distress syndrome (RDS), Intraventricular hemorrhage (IVH), Necrotizing enterocolitis (NEC), Retinopathy of prematurity (ROP), Mortality until discharge

- **Neurodevelopmental outcomes**

  Blindness, Hearing loss, Cerebral palsy, Ability to sit and walk independently, BSID-II<70 or BSID-III<85. Neurodevelopmental impairment (NDI) was defined as the presence of any one of the above abnormalities.

Results

Results – Distribution of CHD and associated mortality

	Number	Mortality
Category A (Left sided lesion with impaired output)	17 (11.6%)	8 (47.1%)
Category B (Cyanotic lesion)	54 (36.7%)	22 (40.7%)
Category C (Pulmonary over-circulation)	54 (36.7%)	14 (25.9%)
Category D (Unclassified)	22 (15.0%)	12 (54.5%)

Results – In-hospital outcomes

	With CHD (N=147)	Without CHD (N=14998)	OR (95% CI)	P-value
PHT	35 (23.8%)	1260 (8.4%)	3.41 (2.32-5.00)	<0.001
RDS	119 (81.0%)	12368 (82.5%)	0.90 (0.60-1.37)	0.663
BPD	76/100 (76.0%)	4465/13436 (33.2%)	6.36 (4.02-10.08)	<0.001
NEC stage ≥ 2	17 (11.6%)	981 (6.5%)	1.87 (1.12-3.11)	0.027
IVH grade ≥ 3	15/136 (11.0%)	1205/14619 (8.2%)	1.38 (0.80-2.37)	0.27
Treated ROP	7/105 (6.7%)	1564/13459 (11.6%)	0.54 (0.25-1.17)	0.126
LOS	28 (19.0%)	2926 (19.5%)	0.97 (0.64-1.47)	1.00
Congenital anomaly	29 (19.7%)	435 (2.9%)	8.23 (5.42-12.49)	<0.001
Mortality until discharge	52 (35.4%)	1588 (10.6%)	4.62 (3.28-6.51)	<0.001

Results – Neurodevelopmental outcomes

	With CHD (N=147)	Without CHD (N=14998)	OR (95% CI)	P-value
Follow up rate	73/147 (49.7%)	9645/14998 (64.4%)	0.55 (0.40-0.76)	<0.001
Blindness	0/73 (0.0%)	21/9614 (0.2%)	-	-
Hearing loss	4/69 (5.8%)	77/9645 (0.8%)	7.61 (2.71-21.42)	0.003
Sit alone	63/72 (87.5%)	9264/9645 (96.0%)	0.29 (0.14-0.58)	<0.001
Walk alone	53/71 (74.6%)	8795/9612 (91.5%)	0.27 (0.16-0.47)	<0.001
Cerebral palsy	7/71 (9.9%)	450/9595 (4.7%)	2.22 (1.01-4.87)	0.047
BSID Cognitive delay	21/40 (52.5%)	1486/5182 (28.7%)	2.75 (1.47-5.13)	0.002
BSID Motor delay	15/40 (37.5%)	1016/5182 (19.6%)	2.46 (1.29-4.68)	0.008
NDI	29/73 (39.7%)	2456/9645 (25.5%)	1.93 (1.20-3.09)	0.006

Discussion

Severe CHD prevalence among VLBW infants was 1.0% (147/15,145). Categories B and C were the most common (54/147, 36.7%). Mortality in CHD-VLBWI was markedly higher than in those without CHD (38.1% vs. 11.4%). Pulmonary hypertension, moderate-to-severe bronchopulmonary dysplasia, and necrotizing enterocolitis were significantly more common. At 18–24 months, anthropometric indices were lower, independent sitting or walking was less frequent, and Bayley scores indicated worse outcomes, with higher rates of cognitive (52.5% vs 28.9%) and motor delay (37.5% vs 19.7%). Among subgroups, unclassified lesions had the highest mortality, while early surgically correctable defects (e.g., total anomalous pulmonary venous return, coarctation, atrioventricular septal defect) were particularly lethal.

References

[1] Polito A, Piga S, Cogo PE, Corchia C, Carnielli V, Da Frè M, et al. Increased morbidity and mortality in very preterm/VLBW infants with congenital heart disease. Intensive care medicine 2013;39(6):1104-12.
[2] Best KE, Tennant PW, Rankin J. Survival, by birth weight and gestational age, in individuals with congenital heart disease: a population-based study. Journal of the American Heart Association 2017;6(7):e005213.
[3] Pappas A, Shankaran S, Hansen NI, Bell EF, Stoll BJ, Laptook AR, et al. Outcome of extremely low birth weight infants with congenital heart defects in the Eunice Kennedy Shriver NICHD neonatal research network. Pediatric cardiology 2012;33(8):1415.
[4] Nakashima Y, Mori Y, Sugiura H, Hirose E, Toyoshima K, Masutani S, et al. Very low birth weight infants with congenital heart disease: A multicenter cohort study in Japan. Journal of Cardiology 2022;80(4):344-50.
[5] Norman M, Håkansson S, Kusuda S, Vento M, Lehtonen L, Reichman B, et al. Neonatal outcomes in very preterm infants with severe congenital heart defects: an international cohort study. Journal of the American Heart Association 2020;9(5):e015369.