Retinopathy of Prematurity Requiring Treatment Is Closely Related to Head Growth during Neonatal Intensive Care Unit Hospitalization in Very Low Birth Weight Infants

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Keywords

Retinopathy of prematurity · Infant · Very low birth weight · Risk factors · Anthropometry

Abstract

Background: Retinopathy of prematurity (ROP) is caused by prenatal sensitization and postnatal insults to the immature retina. This process can be associated with the postnatal growth of preterm infants. We investigated whether ROP requiring treatment was associated with the postnatal growth failure of very low birth weight (VLBW) infants. **Method:** From a cohort of VLBW infants (birth weight <1,500 g) registered in the Korean Neonatal Network from January 2013 to December 2017, 3,133 infants with gestational age (GA) between 24 and 28 weeks were included in the study. Postnatal growth failure was defined when the change in each anthropometric z-score between birth and discharge was <10th percentile of the total population. Propensity score matching (PSM) at 1:1 was performed to match the distribution of GA and postnatal morbidities between infants with and without ROP requiring treatment. Prenatal factors and ROP

were analyzed by conditional logistic regression. **Results:** Of 3,133 enrolled infants, 624 (19.9%) were diagnosed with ROP requiring treatment. After PSM, ROP requiring treatment was associated with postnatal growth failure assessed by head circumference (adjusted odds ratio [aOR] 1.91, 95% confidence interval [CI] 1.18–3.09), but not weight (aOR 1.45, 95% CI 0.97–2.17) and length (aOR 1.21, 95% CI 0.81–1.82). **Conclusion:** ROP requiring treatment was associated with poor head circumference growth, not with weight and length. Our findings suggest that ROP requiring treatment and poor head growth during NICU hospitalization are fundamentally related.

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Introduction

Retinopathy of prematurity (ROP) is a complication of prematurity caused by prenatal sensitization and postnatal insults to the immature retina that not only leads to visual disabilities but also is reportedly associated with poor neurodevelopmental outcomes [1, 2]. Small for ges-

Fig. 1. Flowchart of the study population. BPD, bronchopulmonary dysplasia; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; PMA, postmenstrual age; ROP, retinopathy of prematurity; VLBW, very low birth weight.

tational age, along with low gestational age (GA), is the most commonly reported significant risk factor for ROP [3]. In addition, low serum levels of insulin-like growth factor 1 (IGF-1) are known to be related to the development of ROP, and many studies are developing efficient ROP screening criteria by modeling to predict the occurrence of severe ROP using GA and postnatal weight gain instead of measuring IGF-1 levels [4–6]. However, few studies have investigated the relationship between ROP requiring treatment and postnatal growth in various anthropometric modes during NICU hospitalization, controlling for major comorbidities affecting growth.

Preterm infants with ROP requiring treatment are often preceded or accompanied by comorbidities such as intraventricular hemorrhage (IVH), sepsis, necrotizing enterocolitis (NEC), and bronchopulmonary dysplasia (BPD). These illnesses frequently hamper optimal nutritional support and are known to affect growth by lowering IGF-1 levels [7]. These morbidities are also related to postnatal inflammation and have been shown to be associated with severe ROP [8–10]. Studying the relationship between ROP requiring treatment and various postnatal anthropometric changes after controlling for the major prematurity-associated morbidities is important because it can help to determine which aspect of growth is associated with ROP.

Since 2013, the Korean Neonatal Network (KNN) has collected data from 70 hospitals to investigate the factors

related to mortality and morbidity in Korean VLBW infants [11]. We investigated the association between ROP requiring treatment and changes in postnatal anthropometric values in KNN data with 1:1 propensity score matching (PSM) to match the distribution of GA and postnatal morbidities in infants born between 24 and 28 weeks of GA.

Materials and Methods

Study Population

VLBW infants (birth weight <1,500 g) born in or transferred to the participating NICU of the KNN within 28 days after birth between January 2013 and December 2017 were prospectively registered in the KNN database by the staff at each hospital using a standardized electronic case report form. Infants whose parents did not want to register in the KNN were excluded. The inclusion criteria of this study were infants with GAs between 24 and 28 weeks. Infants with major congenital anomalies or who died before the postmenstrual age (PMA) of 36 weeks were excluded.

Of the total group of 9,374 VLBW infants, 4,547 who did not meet the GA criteria, 945 who died before 36 weeks PMA, 82 who had major congenital anomalies, 497 with incomplete data missing anthropometric values or ROP therapy, and 170 whose ROP status was not obtainable due to transfer to other hospitals after 28 days of birth were excluded. Finally, 3,133 VLBW infants were analyzed (shown in Fig. 1). The KNN registry was approved by the Institutional Review Board (IRB), and informed consent was obtained from parents upon enrollment at each participating hospital.

Table 1. Demographics of the study population

Characteristics	All infants (N = 3,133)		PSM (n = 944)		p value**	SMD
	ROP treated (n = 624)	ROP not treated (n = 2,509)	ROP treated (n = 472)	ROP not treated (n = 472)		
GA, mean (SD), weeks	26.00 (1.25)	27.37 (1.17)	26.34 (1.20)	26.32 (1.16)	0.661*	0.011
Birth weight, mean (SD), g	833.12 (193.55)	1,019.4 (207.16)	867.97 (195.16)	887.32 (188.64)	0.064*	
Birth weight z-score, mean (SD)	0.02 (1.03)	0.18 (0.88)	0.01 (1.06)	0.14 (0.94)	0.047*	
Male, n (%)	333 (53.4)	1,333 (53.1)	250 (53.0)	262 (55.5)	0.010	
Multiple pregnancies, n (%)	224 (35.9)	748 (29.8)	165 (35.0)	131 (27.8)	0.014	
IVF, n (%)	167 (26.8)	546 (21.8)	122 (25.9)	104 (22.0)	<0.001	
Maternal hypertension, n (%)	73 (11.7)	311 (12.4)	59 (12.5)	52 (11.0)	<0.001	
Maternal DM, n (%)	47 (7.5)	234 (9.3)	40 (8.5)	38 (8.1)	0.814	
Chorioamnionitis ^a , n (%)	277 (50.9)	999 (46.3)	199 (49.1)	211 (51.7)	0.872	
PROM ^b , n (%)	270 (43.6)	1,048 (42.0)	194 (41.4)	203 (43.2)	0.599	
No antenatal corticosteroid ^c , n (%)	98 (15.8)	384 (15.4)	72 (15.4)	62 (13.2)	0.327	
Oligohydramnios ^d , n (%)	85 (15.2)	311 (13.8)	63 (14.9)	59 (14.0)	>0.999	
Cesarean section, n (%)	467 (74.8)	1,859 (74.1)	352 (74.6)	349 (73.9)	0.824	
Duration of invasive ventilation, mean (SD)	36.07 (27.0)	14.76 (19.95)	32.12 (25.95)	26.85 (26.72)	<0.001*	
Days to achieve 100 mL/kg/day of enteral feeding, mean (SD)	40.23 (28.33)	26.38 (20.37)	37.99 (27.89)	33.68 (22.48)	0.006*	
Duration of hospitalization, mean (SD)	115.34 (33.51)	83.82 (27.6)	108.96 (30.45)	101.13 (31.55)	<0.001*	
Postnatal corticosteroids for BPD, n (%)	338 (54.2)	735 (29.3)	234 (49.6)	239 (50.6)	0.697	0.021
Surgically treated PDA, n (%)	188 (31.0)	328 (13.4)	118 (25)	113 (23.9)	0.600	0.025
Moderate-to-severe BPD, n (%)	398 (63.8)	904 (36.0)	267 (56.6)	271 (57.4)	0.766	0.017
Severe brain injury, n (%)	138 (22.1)	316 (12.6)	87 (18.4)	85 (18.0)	0.865	0.011
Sepsis, n (%)	236 (37.8)	610 (24.3)	170 (36.0)	162 (34.3)	0.574	0.036
NEC, n (%)	74 (11.9)	130 (5.2)	43 (9.1)	37 (7.8)	0.460	0.046

Data are presented as mean (SD) or n (%). BPD, bronchopulmonary dysplasia; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; PROM, premature rupture of membranes; ROP, retinopathy of prematurity; SMD, standardized mean difference; GA, gestational age; PSM, propensity score matching; DM, diabetes mellitus; IVF, in vitro fertilization SD, standard deviation. ^aValues are missing for 431 infants in the total population and 131 infants in the PSM cohort. ^bValues are missing for 18 infants in the total study population and 5 infants in the PSM cohort. ^cValues are missing for 25 infants in the total study population and 6 infants in the PSM cohort. ^dValues are missing for 325 infants in the total study population and 97 infants in the PSM cohort. * Paired t test. ** McNemar's test.

Definition

We used only the z-scores of the anthropometric values for GA based on the INTERGROWTH-21st standard, instead of percentile or raw data, at birth and discharge [12]. The z-scores of weight, length, and head circumference at birth were subtracted from those z-scores at discharge. Postnatal growth failure was defined when the change in each anthropometric z-score between birth and discharge was <10th percentile of 3,133 infants enrolled in the study.

GA was determined either through obstetric examination by ultrasound at early pregnancy or based on the obstetric record of the last menstrual period of the mother. Maternal hypertension included hypertension before pregnancy and pregnancy-induced hypertension. Maternal diabetes mellitus (DM) included DM and gestational DM. Chorioamnionitis was based on histologic findings of the presence of acute inflammatory changes in the chorion-decidua, amnion, umbilical cord, and chorionic plate by pathologists at each participating facility based on the criteria of Salafia et al. modified by Yoon et al. [13, 14]. BPD was defined as moderate-to-severe BPD using the criteria from the National Institute of Child Health Workshop [15]. Surgically treated patent ductus arteriosus (PDA) was defined as symptomatic PDA requiring surgical treatment. Severe brain injury included grades 3–4 IVH according to the Papile classification, post-hemorrhagic hydrocephalus, and cystic periventricular leukomalacia using brain sonography or brain magnetic resonance imaging [16]. NEC was defined as stage 2 or higher according to Bell's criteria [17]. ROP treatment was determined by ophthalmologists at each participating facility using Early Treatment for Retinopathy of Prematurity criteria [18]. ROP requiring treatment was defined as an operation (cryotherapy, laser photocoagulation, or vitrectomy) or intravitreal injection with anti-vascular endothelial growth factor (anti-VEGF) [19].

Statistical Analysis

To compare the characteristics of infants with and without ROP requiring treatment in the total population, the continuous variables were analyzed using *t* tests or the Mann-Whitney test and expressed as means and standard deviation (SD). The categorical variables were analyzed by χ^2 tests and expressed as numbers and percentile. To analyze the relationship between each anthropometric value for postnatal growth failure and ROP requiring treatment, 1:1 PSM was performed including GA and the outcomes of postnatal corticosteroids administration for BPD, surgically treated PDA, moderate-to-severe BPD, severe brain injury, sepsis, and NEC using a nearest neighbor approach with a caliper restriction to minimize the effect of other variables confounding the relationship of ROP requiring treatment and growth. To compare the demographics of the groups after PSM, the paired *t* test and McNemar's test were used. Univariable conditional logistic regression analysis was performed separately to identify the risk factors that affected each postnatal growth failure. Multivariable conditional logistic regression was used to adjust for variables (male gender, z-score at birth, in vitro fertilization [IVF], maternal hypertension, premature rupture of membranes [PROM], the duration of invasive ventilation, days to achieve 100 mL/kg/day of enteral feeding, and the duration of hospitalization) that showed statistically significant differences with a *p* value of <0.1 in univariable analysis. A *p* value of <0.05 was considered statistically significant. Statistical analyses were performed by Rex (Version 3.0.3; RexSoft Inc., Seoul, Korea).

Results

A total of 3,133 VLBW infants fulfilled the inclusion criteria, and 624 (19.9%) were diagnosed with ROP requiring treatment. Among 624 infants, 101 (16.2%) received both laser photocoagulation and anti-VEGF therapy, 368 (59.0%) received only laser photocoagulation, and 113 (18.1%) received only anti-VEGF therapy. The remaining 42 infants did not have procedural data.

The characteristics of the VLBW infants enrolled in this study indicated a significant difference in neonatal characteristics and comorbidities between infants requiring and not requiring ROP treatment. Infants requiring ROP treatment had lower GA and birth weight z-scores than infants not requiring ROP treatment. The rate of multiple pregnancies, IVF, the duration of invasive ventilation, days to achieve 100 mL/kg/day of enteral feeding, the duration of hospitalization, postnatal corticosteroids administration for BPD, surgically treated PDA, moderate-to-severe BPD, severe brain injury, sepsis, and NEC were higher in infants requiring ROP treatment than in infants not requiring ROP treatment (Table 1).

In the total study population, postnatal growth was greatly suppressed in the order of length (mean -1.68 SD 1.7), head circumference (-1.28 , SD 1.6), and weight (-1.05 , SD 1.1) ($p < 0.001$, data not shown). All anthropometric values were lower in infants requiring ROP treatment at birth and discharge than in infants not requiring ROP treatment (Table 2). In the propensity score-matched cohort, the order of suppression of postnatal growth was the same, but the degree of suppression was greater than that of the total study population (length, mean -2.06 , SD 1.8 ; head circumference, -1.58 , SD 1.8 ; weight, -1.29 , SD 1.2 ; $p < 0.001$, data not shown). All anthropometric values except length at birth were significantly lower in infants requiring ROP treatment than those not requiring ROP treatment.

In the univariable conditional analysis of the factors not involved in PSM, z-score at birth, the duration of invasive ventilation, the duration of hospitalization, and ROP requiring treatment were shown to be risk factors for postnatal growth failure assessed by weight. In postnatal growth failure assessed by length, IVF, maternal hypertension, the duration of invasive ventilation, days to achieve 100 mL/kg/day of enteral feeding, and the duration of hospitalization were significant risk factors. Male gender, z-score at birth, the duration of invasive ventilation, days to achieve 100 mL/kg/day of enteral feeding, the duration of hospitalization, and ROP requiring treatment were associated with postnatal growth failure assessed by head circumference (Table 3). Multivariable conditional logistic regression

Table 2. Trend of z-score changes in each anthropometric marker over time

z-score	Study population (N = 3,133)			PSM (n = 944)		
	ROP treated (n = 624)	ROP not treated (n = 2,509)	p value*	ROP treated (n = 472)	ROP not treated (n = 472)	p value**
At birth						
Weight	0.02 (1.03)	0.18 (0.88)	<0.001	0.01 (1.06)	0.14 (0.94)	0.047
Length	−0.45 (0.92)	−0.23 (0.89)	<0.001	−0.43 (0.95)	−0.33 (0.88)	0.114
HC	−0.34 (0.88)	−0.11 (0.88)	<0.001	−0.33 (0.92)	−0.17 (0.96)	0.012
At discharge						
Weight	−1.50 (1.37)	−0.75 (1.23)	<0.001	−1.45 (1.37)	−0.99 (1.33)	<0.001
Length	−2.79 (2.01)	−1.75 (1.82)	<0.001	−2.69 (2.01)	−2.19 (1.97)	<0.001
HC	−2.21 (1.91)	−1.24 (1.52)	<0.001	−2.09 (1.97)	−1.57 (1.70)	<0.001
Postnatal growth ^a						
Weight	−1.52 (1.22)	−0.93 (1.02)	<0.001	−1.46 (1.18)	−1.13 (1.17)	<0.001
Length	−2.34 (1.74)	−1.52 (1.60)	<0.001	−2.26 (1.72)	−1.86 (1.74)	<0.001
HC	−1.87 (1.80)	−1.13 (1.45)	<0.001	−1.76 (1.87)	−1.40 (1.67)	0.001

Data are presented as mean (SD). HC, head circumference; ROP, retinopathy of prematurity; PSM, propensity score matching; SD, standard deviation. ^aChange in z-scores from birth to discharge. * Student's *t* test. ** Paired *t* test.

Table 3. Univariable conditional logistic regression for postnatal growth failure in propensity score-matched cohort (n = 944)

	Postnatal growth failure					
	weight		length		head circumference	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Male	1.61 (0.96–2.71)	0.073	1.54 (0.92–2.58)	0.099	2.07 (1.12–3.83)	0.021
z-score at birth ^a	1.40 (1.05–1.88)	0.023	0.85 (0.67–1.08)	0.181	1.46 (1.08–1.98)	0.015
Multiple pregnancies	1.52 (0.88–2.64)	0.134	1.43 (0.82–2.50)	0.210	1.41 (0.76–2.63)	0.277
IVF	1.56 (0.86–2.81)	0.144	2.38 (1.25–4.56)	0.009	1.2 (0.60–2.38)	0.602
Maternal hypertension	0.5 (0.19–1.33)	0.166	2.08 (1.05–4.15)	0.037	1.17 (0.54–2.52)	0.695
Maternal DM	0.89 (0.34–2.30)	0.809	0.45 (0.16–1.31)	0.144	0.6 (0.22–1.65)	0.323
Chorioamnionitis	0.77 (0.43–1.38)	0.378	0.74 (0.43–1.27)	0.278	0.94 (0.48–1.86)	0.862
PROM	1.52 (0.92–2.52)	0.104	0.63 (0.38–1.05)	0.078	0.93 (0.55–1.57)	0.789
No antenatal corticosteroid	0.83 (0.42–1.65)	0.602	0.87 (0.41–1.82)	0.706	1.25 (0.59–2.67)	0.565
Oligohydramnios	0.94 (0.46–1.90)	0.858	0.82 (0.41–1.67)	0.591	1.33 (0.56–3.16)	0.514
Cesarean section	0.69 (0.39–1.22)	0.201	1.16 (0.68–1.98)	0.587	0.85 (0.49–1.49)	0.572
Duration of invasive ventilation	1.01 (1.00–1.03)	0.011	1.03 (1.02–1.04)	<0.001	1.03 (1.01–1.04)	<0.001
Days to achieve 100 mL/kg/day of enteral feeding	1.01 (1.00–1.02)	0.151	1.01 (1.00–1.02)	0.017	1.02 (1.00–1.03)	0.007
Duration of hospitalization	1.02 (1.01–1.03)	0.001	1.02 (1.01–1.04)	<0.001	1.02 (1.00–1.03)	0.010
ROP requiring treatment	1.58 (1.11–2.25)	0.011	1.39 (0.99–1.96)	0.059	2.11 (1.43–3.12)	<0.001

CI, confidence interval; OR, odds ratio; PROM, premature rupture of membranes; DM, diabetes mellitus; IVF, in vitro fertilization. ^az-score at birth in each anthropometric mode.

analysis adjusted for the confounding variables of postnatal growth failure revealed that ROP requiring treatment was associated with postnatal growth failure assessed by head circumference (adjusted odds ratio [aOR] 1.91, 95% confidence interval [CI] 1.18–3.09, *p* = 0.008), but not weight (aOR 1.45, 95% CI 0.97–2.17, *p* = 0.070) or length (aOR 1.21, 95% CI 0.81–1.82, *p* = 0.350; Table 4).

Discussion

This study demonstrated that ROP requiring treatment was associated with postnatal growth failure assessed by head circumference, but not by weight and length, when GA, prematurity-related morbidities, and prenatal factors were controlled in the propensity score-

Table 4. Multivariable conditional logistic regression analysis of the association between ROP requiring treatment and postnatal growth failure

	Postnatal growth failure					
	weight		length		head circumference	
	aOR (95% CI)	<i>p</i> value*	aOR (95% CI)	<i>p</i> value*	aOR (95% CI)	<i>p</i> value*
ROP requiring treatment	1.45 (0.97–2.17)	0.070	1.21 (0.81–1.82)	0.350	1.91 (1.18–3.09)	0.008

aOR, adjusted odds ratio; CI, confidence interval; ROP, retinopathy of prematurity; IVF, in vitro fertilization. * Adjusted for male gender, z-score at birth, IVF, maternal hypertension, premature rupture of membranes, the duration of invasive ventilation, days to achieve 100 mL/kg/day of enteral feeding, and the duration of hospitalization.

matched cohort. The disproportionate growth patterns of preterm infants such as more weight gain relative to length gain [20] or suboptimal head growth [21] during NICU hospitalization, especially in a more immature population [22], were constantly observed even though advanced nutritional support was provided. Thus, interest in the effect of non-nutritional factors such as inflammation and infection on growth is increasing.

Among the risk factors for ROP, prenatal inflammation and infection are known to sensitize the retina to subsequent insults rather than directly triggering ROP [9]. In addition, a study recently reported that postnatal factors related to inflammation such as sepsis, NEC, grades 3–4 IVH, and supplemental oxygen on day 28 were more strongly correlated with severe ROP than prenatal inflammation-related factors [23]. Those morbidities may also adversely affect nutritional support by impaired lipid tolerance, the withholding of enteral feeding, and volume restriction, and can lead to poor growth of prematurity by disrupting metabolic-endocrine homeostasis under these postnatal stress and undernutrition conditions [24]. We conducted PSM to minimize the effect of these comorbidities known to be related to postnatal growth failure to identify the relationship between ROP requiring treatment and postnatal growth.

In this study, the average PMA at discharge was 41.3 ± 4.14 weeks (mean $\pm$ SD). In both the total study population and the propensity score-matched cohort, infants with ROP requiring treatment had significantly lower birth weight and postnatal weight growth than infants not requiring ROP treatment. This is consistent with previous reports that appointed postnatal weight gain as one of the criteria for efficient ROP screening [4–6] and a large cohort study [25]. However, those studies were not intended to search for the independent relationship between postnatal weight gain and ROP and did not control for poten-

tial confounders, especially comorbidities. Our multivariate analysis showed that ROP requiring treatment was not associated with postnatal growth failure assessed by weight or length but with head circumference. Li et al. [26] also showed that low weight velocity from day 7 to day 28 was associated with ROP, but in a multivariable logistic regression analysis adjusting for GA, BPD, and surgical ligation for PDA, it was no longer significant. The results of this study indicated a close relationship between ROP requiring treatment and poor head growth, independent of the comorbidities, suggesting a shared pathogenetic progression between ROP and head growth failure.

Löfqvist et al. [27] reported that head growth decelerated after birth until 30–32 weeks of PMA, and the degree of head growth retardation during those periods corresponded to the severity of ROP and the suppression of serum IGF-1 levels. They suggested that retinal vascular growth retardation that initiates ROP is paralleled by brain growth deceleration. In this study, we could not analyze head circumference growth divided by periods. Nevertheless, the study results showed that the severity of ROP was correlated with head circumference growth during the entire hospitalization period. The results of this national cohort study are consistent with previous studies on the relationship between ROP and head growth [27, 28] by showing that ROP requiring treatment was associated with postnatal head growth failure during NICU hospitalization. This is also consistent with reports that ROP was associated with poor neurodevelopmental outcomes [1, 2, 29] since reduced head growth before term was associated with later suboptimal neurodevelopment in preterm infants [30, 31].

There are several limitations of this study. First, z-scores were measured using the INTERGROWTH-21st standard, which had not previously been validated in Korean preterm infants. However, in a recent study using

KNN data, the association of extrauterine growth restriction defined by INTERGROWTH-21st growth chart with neonatal morbidity was well demonstrated [32]. There was a significant difference in the magnitude of z-score changes between the INTERGROWTH-21st standard and the Fenton chart [32], therefore, we defined postnatal growth failure as a change in z-score of <10th percentile of the 3,133 infants enrolled in the study. Thus, caution is needed when interpreting these results.

Second, since only anthropometric values at birth and discharge were collected in the KNN registry, it was impossible to measure changes in postnatal growth failure within some specific period of PMA. Third, the collection of information on the date of treatment, zone, and plus disease began in 2015 in the KNN, and 65% of the infants in this study lacked these data, which precluded more detailed analyses. Last, postnatal growth failure is known to be affected by nutritional and non-nutritional factors. However, detailed nutritional information was not available in the network database.

Conclusion

ROP requiring treatment was associated with poor head circumference growth, not with weight and length. Our findings suggest that ROP requiring treatment and poor head growth during NICU hospitalization are fundamentally related.

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Statement of Ethics

The study conformed to the ethical guidelines of the World Medical Association Declaration of Helsinki. The registration of data in the KNN was approved by the IRB of each participating center. Informed consent was obtained from the parents of each infant prior to participation in the KNN registry. This study was approved by the IRB of Seoul National University Hospital (IRB No. 1303-092-476).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

S.P.B. and E.K.K. conceptualized and designed the research. S.P.B., Y.M.Y., and S.Y.P. collected and analyzed the data. S.P.B. and J.H.Y. wrote the manuscript. S.H.S assisted with study design and reviewed the manuscript. E.K.K. reviewed and revised the manuscript. All authors read and approved the final manuscript.

Data Availability Statement

The KNN Publication Ethics Policy adheres to the following research data management and access guidelines: all information about patients and participating NICUs is confidential and may be used by individuals for approved research purposes. If an individual or institution that is not affiliated with KNN wants to use the data, it must make an official request to the KNN Publication Ethics Committee and obtain approval from the network.

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