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Factors Affecting the Developmental Outcomes of High-Risk Newborns

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Abstract

Background: Newborns weighing less than 2,500 grams and those with birth asphyxia are particularly vulnerable to multiple complications. This study aimed to evaluate the prevalence and factors related to developmental delays in high-risk newborns. **Methods:** This study included the clinical data of infants with a birth weight of under 2500 grams or an Apgar score of less than 7 at 1 or 5 minutes after birth. Medical records from January 1, 2015 to December 31, 2020 were included. The actual age of the infants was corrected according to gestational age. Participants with genetic abnormalities (trisomy 21, 18, 13) and congenital brain anomalies (hydrocephalus, encephalocele) were excluded. The Developmental Assessment for Intervention Manual (DAIM) was used during follow-up visits. Multivariate logistic regression analysis was used to examine the data. **Results:** Of the 297 patients included, 110 completed the follow-up and 62 infants (56%) had developmental delays. Significant associations with delayed development included maternal age (adjusted odds ratio [AOR] 3.36, 95% confidence interval [CI] 1.19 - 9.46), male sex (AOR 3.23, 95% CI 1.24 - 8.44), gestational age below 32 weeks (AOR 33.35, 95% CI 1.39 - 799.87), and neonatal hypoglycemia (AOR 3.81, 95% CI 1.13 - 12.85). **Conclusion:** Maternal age, male sex, gestational age less than 32 weeks, and neonatal hypoglycemia were all associated risk factors for developmental delays in high-risk infants.

Keywords

Birth Asphyxia, Low Birth Weight, Neurodevelopmental Outcome

1. Introduction

Low birth weight is defined by the World Health Organization (WHO) as a pediatric condition in which a newborn weighs between 1500 and 2499 grams. An

infant born weighing between 1000 and 1499 grams is known as a very low birth weight infant, and a newborn with a birth weight of 999 grams or less is considered an extremely low birth weight infant. An Apgar score of 4 - 7 at 5 minutes after birth indicates mild to moderate birth asphyxia, while an Apgar score of 0 - 3 indicates severe birth asphyxia [1]. Low birth weight and birth asphyxia are common occurrences in newborns worldwide, with a prevalence of 15.5% and 15.9%, respectively [2] [3]. Today, medical technology has advanced to a point where the survival rate of premature infants has improved considerably, particularly those with extremely low birth weight. Lower gestational age, especially below 25 weeks, results in more severe impairment in the infants [4] [5]. Prompt intervention by medical professionals reduces the risk of long-term complications. Respiratory distress syndrome and sepsis are the most common complications in preterm births [6]. Premature infants can develop bronchopulmonary dysplasia, retinopathy of prematurity, developmental delays, and other long-term complications [7]. Furthermore, newborns weighing less than 2500 grams and those with hypoxic-ischemic encephalopathy are particularly vulnerable to developmental delays [8] [9]. In Thailand, the incidence of birth asphyxia is 90.2 - 100.7 per 1000 live births [10]. According to the WHO, neonatal deaths resulting from birth asphyxia account for 29% of all neonatal deaths globally [11]. In Thailand, the Developmental Assessment for Intervention Manual (DAIM) was implemented in 2015, and the development of high-risk newborns was followed up on a regular basis.

This study aimed to determine the prevalence of low birth weight and birth asphyxia in newborns, as well as the correlating factors that contribute to developmental delays.

2. Methods

The Institutional Review Board (IRB No. 0007/63) of Medicine Faculty of Naresuan University approved the study. The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study. De-identified data were collected for this cross-sectional analytical study from inpatient and outpatient records at our hospital. The inclusion criteria were as follows: patients with a birth weight of less than 2500 grams or an Apgar score of less than 7 at 1 or 5 minutes after birth from 1 January 2015 to 31 December 2020. Exclusion criteria included newborns with genetic abnormalities (trisomy 21, 18, 13) and congenital brain anomalies (hydrocephalus, encephalocele). The inpatient data of the newborns came from the prenatal, perinatal, postnatal, and maternal records, and the outpatient data came from their developmental records using the Developmental Assessment for Intervention Manual (DAIM). The DAIM is a nationwide developmental screening tool for high-risk infants and includes advice and videos that parents can use to encourage their child's development. According to DAIM, the high-risk newborns mean the newborn weighs under 2500 grams and Apgar score of less than 7 at 1 or 5 minutes. The

Thai Child Development Integrated Committee developed the DAIM in 2015. It consists of 122 items in five domains: 1) gross motor skills, 2) fine motor skills, 3) receptive language skills, 4) expressive language skills, and 5) personal and social skills. It also consists of five items on neurodevelopment. DAIM was shown to achieve a sensitivity and specificity of 85.7% and 86.3%, respectively for assessment of infant development delay [12]. Corrected age was calculated prior to the developmental assessment if the newborn's gestational age was less than 37 weeks.

A follow-up assessment of the infants was conducted every 2 months in the first 6 months, then every 3 months until 2 years of age, and if their development was abnormal, they were advised to start a program of early stimulation by a caregiver at home for a month. The developmental stimulation program included instructions and videos to encourage development. The infants were then re-evaluated for development. If delayed development persisted, the infants were referred for additional development stimulation from healthcare personnel.

Statistical analysis

Data entry and analyses were performed using Stata12.1 (College Station, Texas 77845 USA). The demographic data are expressed as percentages. Logistic regression was used to calculate the odds ratio (OR) for the association between factors and delayed development. The adjusted OR (AOR) was calculated using multiple logistic regression with a 95% confidence interval (CI) and according to a significance level of $p < 0.05$.

3. Results

The data of 297 newborns were included in this study. The data of 16 newborns were excluded because of Down syndrome, brain anomalies, and referral to other hospitals resulting in incomplete data for the developmental assessment. In addition, 171 newborns had incomplete follow-up data. Thus, the data of 110 newborns were analyzed, of which 62 were found to have developmental delays (56%) (**Figure 1**).

Among the 110 high-risk newborns included in the study, 62 were female (56.4%), 61 had a gestational age between 32 and 37 weeks (55.5%), 86 weighed between 1501 and 2499 grams (78.2%), 2 had an Apgar score less than 7 at 1 and 5 minutes after birth (1.8%), 44 stayed in the hospital for 1 - 7 days (length of stay [LOS]) (40%), and 79 were not intubated (71.8%). Seventy neonates had mothers above 20 years of age (63.1%). Most of the mothers (n = 87, 89.1%) had an uncomplicated delivery (possible complications included gestational diabetes, preeclampsia, and intrauterine infection) (**Table 1**).

Sixty-two of the 110 newborns (56.4%) had developmental delays; 35 of these 62 (56.5%) newborns had only one developmental delay out of the five domains, while the remainder had multiple developmental delays. The most common developmental delays were noted in gross motor skills (n = 52, 47.3%), expressive language skills (n = 24, 21.8%), and receptive language skills (n = 16, 14.5%) (**Table 2**).

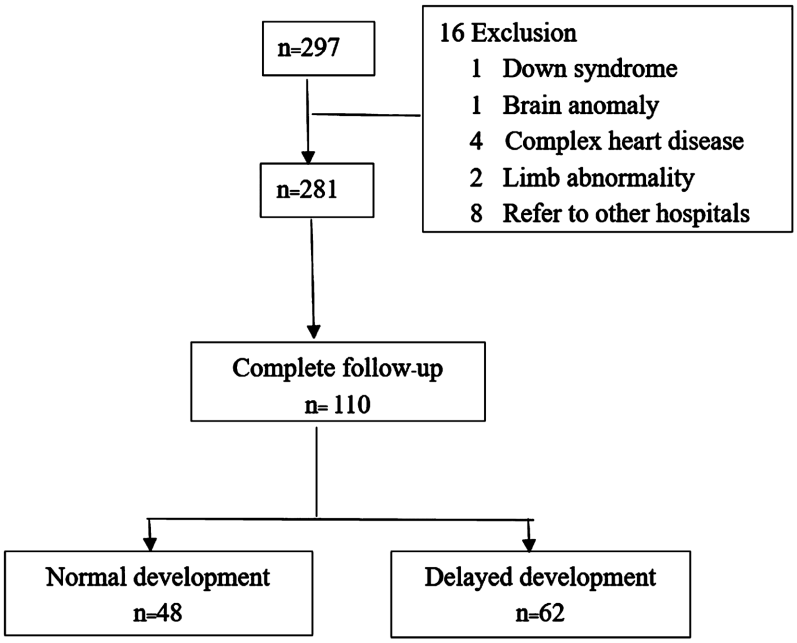

Figure 1. Number of participants.

Table 1. Demographical data of the neonates and mothers.

Data	Number (n = 110)	Percentage (%)
Sex		
Male	48	43.6
Female	62	56.4
Gestational age (weeks)		
<25	2	1.8
25 - 32	17	15.5
32 - 37	61	55.5
37 - 42	30	27.2
Birth weight (g)		
<1000	9	8.2
1000 - 1499	15	13.6
1500 - 2499	86	78.2
2500 - 3799	0	0.0
≥3800	0	0.0
Apgar score at 1 minute < 7	22	20.0
at 1 and 5 minutes < 7	2	1.8
Twin		
Yes	36	32.7
No	74	67.3

Continued

Length of hospital stay		
1 - 7 days	44	40.0
7 days - 1 month	42	38.2
1 - 3 months	12	10.9
Intubation		
No	79	71.8
1 - 7 days	13	11.8
7 days - 1 month	8	7.3
1 - 3 months	10	9.1
Hypoglycemia		
Yes	26	23.6
No	84	76.4
Phototherapy		
Yes	69	62.7
No	41	37.3
Maternal age (years)		
15 - 20	13	11.8
20 - 35	70	63.6
>35	27	24.6
Maternal complication		
No complication	87	79.1
Gestational diabetes	11	10.0
Preeclampsia	12	10.9

Table 2. Characteristics of the developmental delays in the newborns.

Data	Number (n = 110)	Percentage
Normal	48	43.6
Delayed development	62	56.4
Developmental domains:		
• Gross motor skills	52	47.3
• Fine motor skills	15	13.6
• Receptive language skills	16	14.5
• Expressive language skills	24	21.8
• Personal and social skills	14	12.7

Our findings showed that male sex was associated with significant devel-op-mental delays (p = 0.017, AOR = 3.23, 95% CI = 1.24 - 8.44). Gestational age

below 32 weeks was also associated with delayed development (p = 0.031, AOR = 33.35, 95% CI = 1.39 - 799.87), as was hypoglycemia (p = 0.031, AOR = 3.81, 95% CI = 1.13 - 12.85). An analysis of the maternal risk factors revealed that maternal age was associated with significant developmental delays (p = 0.022, AOR = 3.36, 95% CI = 1.19 - 9.46) (**Table 3**).

4. Discussion

In this retrospective study, the prevalence and the associated factors related to the developmental delays in high-risk newborns were analyzed. The findings showed that male sex, lower gestational age, maternal age, and hypoglycemia all contributed to various developmental delays. The prevalence of developmental delays in this study was 56.4% (62/110), with gross motor delay being the most common. In this study, all the infants with developmental delays were born with a birth weight less than 2500 grams and 22.6% (14/62) had Apgar score less than 7 at 1 minute or 5 minutes. But only 2 infants had severe birth asphyxia and developmental delays. The development of some of the newborns started to normalize after the intervention; however, 30.6% (19/62) of the infants still had developmental delays after the intervention. The incidence of developmental delays in this study was 17.2% (19/110) in those who received early intervention. In a previous study, the prevalence of developmental delays ranged from 8.76% to 28% [13] [14].

Preterm birth has a significant impact on brain development, with an increased risk of the less cerebral volume of gray and white matter, and the male sex appears to be particularly vulnerable to the adverse effects of preterm birth on the development of white matter, as revealed in a previous study [15]. Other studies have shown that male preterm infants had more risk of developmental delay than female preterm infants [16] [17]. According to the results of this study, the male sex was associated with a 3.23-times higher risk of delayed development compared to the female sex, which corresponds to the findings in previous studies [9] [16] [17].

The findings of this study revealed that preterm infants with a gestational age under 32 weeks had a significant delay in development compared to those with a gestational age over 32 weeks, which is similar to the findings of a previous study [14]. Studies done over the last three decades have shown that preterm infants with gestational ages ranging from 25 to 31 weeks have a higher rate of survival without neurodevelopmental impairment. However, infants with extremely low gestational age (under 25 weeks) have limited survival and morbidity remains high [4] [5]. None of the newborns analyzed in this study had a gestational age of less than 25 weeks; the minimum gestational age was 25 weeks and 1 day, and the follow-up at corrected age revealed normal development.

Low birth weight infants are commonly associated with teenage pregnancies. Newborns with low birth weight have an increased risk of illness and longer hospital stay [13] [14]. Maternal age of over 35 years also increases the risk of

Table 3. Factors associated with the developmental delays.

Variable	n = 110	Delayed (n = 62)	Crude Odds Ratios	Adjusted Odds Ratios	95%CI	P-value
Sex						
Male	48	32 (66.7)	2.13	3.23	1.24 - 8.44	0.017*
Female	62	30 (48.4)	1	1		
Gestational age (weeks)						
<32	19	14 (73.7)	2.51	33.35	1.39 - 799.87	0.031*
≥32	91	48 (52.7)	1	1		
Birth weight (g)						
<1500	24	17 (70.8)	2.21	1.13	0.12 - 10.54	0.912
1500 - 2499	86	45 (52.3)	1	1		
Apgar score at 1 or 5 minutes						
<7	24	14 (58.3)	1.11	0.39	0.09 - 1.74	0.218
7 - 10	86	48 (55.8)	1	1		
Maternal age (years)						
<20 or >35	40	28 (70.0)	2.47	3.36	1.19 - 9.46	0.022*
20 - 35	70	34 (48.6)	1	1		
Maternal complications						
Gestational diabetes	11	8 (72.7)	2.38	3.20	0.59 - 17.47	0.179
Preeclampsia	12	8 (66.7)	1.78	2.23	0.49 - 10.26	0.302
No complication	87	46 (52.9)	1	1		
Twins						
Yes	36	20 (55.6)	0.95	1.40	0.51 - 3.88	0.516
No	74	42 (56.8)	1	1		
Length of stay						
1 - 7 days	44	21 (47.7)	1	1		
7 days - 1 month	42	24 (57.1)	1.46	0.52	0.13 - 1.99	0.338
>1 month	24	17 (70.8)	2.66	0.07	0.01 - 1.97	0.116
Intubation						
Yes	31	22 (71.0)	2.83	2.53	0.43 - 14.99	0.306
No	79	40 (50.6)	1	1		
Hypoglycemia						
Yes	26	19 (73.1)	2.59	3.81	1.13 - 12.85	0.031*
No	84	43 (51.2)	1	1		
Phototherapy						
Yes	69	45 (65.2)	2.65	2.95	0.80 - 10.94	0.105
No	41	17 (41.5)	1	1		

*$p < 0.05$; CI, confidence interval.

adverse perinatal outcomes, such as preterm birth and low birth weight [18] [19] [20]. Kortekaas *et al.* (2020) linked the maternal age of 20 - 35 years to positive developmental outcomes for infants. Thus, a maternal age of less than 20 years and greater than 35 years was found to be associated with a risk of delayed development in infants [19].

Neonatal hypoglycemia is the most common metabolic challenge in premature and low birth weight infants [21] [22] and has been linked to developmental delays [14] [23] [24] [25], however, no research has been conducted on prevention of neonatal hypoglycemia. Early detection and treatment of neonatal hypoglycemia are therefore critical.

The findings in this study are subject to some limitations. First, only 40% of the total number of newborns included in the study had complete follow-up data; this may have an effect on the interpretation of the results in this study. Moreover, approximately 87.1% (149/171) of the newborns with birth weights between 2000 - 2500 grams were excluded from the study because they were unable to undergo the DAIM assessment in this study or had an assessment done in another healthcare facility. Data regarding this issue is not enough in this area. Every area should have such data to make a better health policy and thus we here attempted to determine factors affecting the developmental outcome in low birth weight and birth asphyxia. Second, the number of infants with Apgar at 5 minutes less than 7 was too small, not enough to interpretation. The third, hypothermia was the common and important problem of preterm infants but this study does not include these factors. Further studies could include more hospitals and long-term follow-up of cognitive development and learning difficulties. In addition, data on children with Apgar scores at 5 minutes less than 7 should be collected for further developmental outcomes. The hypothermia factors should be included in further studies.

5. Conclusion

Our findings indicated that infants with low birth weight and birth asphyxia were at a high risk of developmental delays. Furthermore, the associated risk factors included maternal age, male sex, gestational age below 32 weeks, and neonatal hypoglycemia. Thus, early detection of neonatal hypoglycemia and an early stimulation program supported by occupational therapists or trained caregivers can decrease the risk of developmental delays in these high-risk infants.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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