

นิพนธ์ต้นฉบับ

ความชุกและปัจจัยที่มีความสัมพันธ์กับพัฒนาการล่าช้ารอบด้านในทารกคลอดก่อนกำหนด
อายุ 6-24 เดือน: การศึกษาภาคตัดขวางในคลินิกทารกความเสี่ยงสูง
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บทคัดย่อ

ความเป็นมา: เนื่องด้วยความก้าวหน้าของเทคโนโลยีทางการแพทย์ในปัจจุบัน ทำให้อัตราการรอดชีวิตของทารกคลอดก่อนกำหนดเพิ่มสูงขึ้น อย่างไรก็ตาม ทารกกลุ่มนี้มักมีพัฒนาการทางระบบประสาทที่ยังไม่สมบูรณ์ และมีความเสี่ยงต่อการเกิดการบาดเจ็บทางสมอง ซึ่งอาจส่งผลกระทบต่อพัฒนาการทางระบบประสาท การเรียนรู้ในระยะยาว และอาจนำไปสู่ปัญหาทางสังคมในอนาคตได้

วัตถุประสงค์: เพื่อศึกษาหาความชุกของพัฒนาการล่าช้ารอบด้านในทารกคลอดก่อนกำหนดอายุ 6 ถึง 24 เดือนที่ได้เข้ารับการรักษาในโรงพยาบาลพระนั่งเกล้า และศึกษาปัจจัยที่สัมพันธ์การพัฒนาการล่าช้ารอบด้านของทารกที่คลอดก่อนกำหนด

วิธีการศึกษา: ศึกษาแบบภาคตัดขวาง ทารกคลอดก่อนกำหนดอายุ 6-24 เดือน ที่มาติดตามอาการที่คลินิกทารกความเสี่ยงสูง โรงพยาบาลพระนั่งเกล้า ตั้งแต่วันที่ 1 มกราคม พ.ศ. 2566 ถึง 31 ธันวาคม พ.ศ. 2567 เข้ารับการตรวจคัดกรองพัฒนาการ โดยเครื่องมือ Denver II โดยกุมารแพทย์พัฒนาการและพฤติกรรม และจะมีการทบทวนเวชระเบียนร่วมกับการสัมภาษณ์ผู้เลี้ยงดูโดยการให้ทำแบบสอบถาม เพื่อเก็บรวบรวมปัจจัยที่มีความสัมพันธ์กับพัฒนาการล่าช้า

ผลการศึกษา: จำนวนกลุ่มตัวอย่างทั้งหมด 32 ราย พบว่ามีทารกคลอดก่อนกำหนดที่มีภาวะพัฒนาการล่าช้ารอบด้านทั้งหมด 9 ราย คิดเป็นร้อยละ 28.1 การได้รับยาสเตียรอยด์ก่อนคลอดของมารดาสัมพันธ์กับการลดภาวะพัฒนาการล่าช้ารอบด้านในทารกคลอดก่อนกำหนดอย่างมีนัยสำคัญ (OR 0.098, 95% CI 0.015-0.646, p value 0.028)

สรุป: ทารกคลอดก่อนกำหนดถือว่าเป็นกลุ่มเสี่ยงต่อการเกิดภาวะพัฒนาการล่าช้า และมีความจำเป็นต้องได้รับการตรวจติดตามพัฒนาการอย่างเป็นระบบและต่อเนื่องมากกว่าทารกกลุ่มเสี่ยงต่ำ พบว่าการไม่ได้รับยาสเตียรอยด์ก่อนคลอดมีความสัมพันธ์อย่างมีนัยสำคัญกับภาวะพัฒนาการล่าช้ารอบด้านในทารกที่คลอดก่อนกำหนด เน้นย้ำถึงความสำคัญของการให้สเตียรอยด์ในมารดาที่มีภาวะคลอดก่อนกำหนดตามมาตรฐานการรักษา

คำสำคัญ: ทารกคลอดก่อนกำหนด, ความชุก, ภาวะพัฒนาการล่าช้ารอบด้าน, ผลลัพธ์ทางพัฒนาการทางระบบประสาท, เครื่องมือคัดกรองพัฒนาการ Denver II, ,มารดาได้ยาสเตียรอยด์, คลินิกทารกความเสี่ยงสูง

**Prevalence and factors associated with global developmental delay in preterm infants
at corrected age 6-24 months: A cross-sectional study at a high-risk newborn clinic**

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Abstract

Background: Advances in neonatal care have improved the survival of preterm infants; however, they remain vulnerable to neurodevelopmental immaturity and brain injury, which may adversely affect long-term developmental and learning outcomes.

Objectives: To determine the prevalence of global developmental delay among preterm infants aged 6–24 months at Pranangklaao Hospital and to identify associated risk factors.

Methods: A cross-sectional study was conducted. Preterm infants aged 6–24 months who attended follow-up at the high-risk newborn clinic, Pranangklaao Hospital, between 1 January 2023 and 31 December 2024, were assessed using the Denver II developmental screening tool by developmental–behavioral pediatricians. Medical records were reviewed, and caregivers were interviewed using structured questionnaires to obtain additional relevant clinical and demographic data.

Results: Thirty-two preterm infants were included in the study; 9 (28.1%) were identified as having global developmental delay. Maternal antenatal corticosteroid exposure appeared to be associated with a protective factor against global developmental delay (OR 0.098, 95% CI 0.015-0.646, p value 0.028).

Conclusion: Preterm infants were at increased risk of developmental delay and required regular systematic developmental monitor. Maternal antenatal corticosteroid exposure appeared to be associated with a protective factor against global developmental delay in preterm infants. These results emphasized the importance of administering antenatal corticosteroids to mothers at risk of preterm birth in accordance with standard treatment guidelines.

Keywords: Preterm infants, Prevalence, Global developmental delay, Neurodevelopmental outcomes, Denver II screening, Antenatal corticosteroids, High-risk newborn clinic

Introduction

A preterm infant is defined as an infant born before 37 completed weeks of gestation. Preterm birth accounts for approximately 10% of all live births worldwide. Compared with term infants, preterm infants have higher rates of impairments in cognition, language, and motor function, approximately 17%, 8%, and 4%, respectively.¹

According to the Department of Health,² the preterm birth rate was 9.9% in Thailand and was slightly lower than the average rate of 13.3% reported among countries with comparable gross national income per capita. Advances in neonatal care have substantially improved the survival of preterm infants. However, due to neurological immaturity and vulnerability to brain injury, preterm infants remain at risk for long-term neurodevelopmental and learning difficulties, which may subsequently lead to behavioral problems and poorer educational outcomes. Therefore, identifying factors associated with developmental outcomes in this population is of considerable importance.

Global developmental delay (GDD) is multifactorial and may result from incomplete neurological maturation in preterm infants. Perinatal and neonatal complications, such as infection and intraventricular hemorrhage, contribute significantly to adverse neurodevelopmental outcomes.³ Infants born at lower gestational ages, particularly those <32 weeks, those with very low birth weight, intraventricular hemorrhage, or periventricular white matter injury, are at especially high risk.

Medical interventions have also been shown to influence neurodevelopmental outcomes. Antenatal corticosteroid and magnesium sulfate administration, along with standard neonatal management including indomethacin and caffeine therapy, have been associated with improved neurodevelopmental outcomes.

In addition to biological and medical factors, socioeconomic status and parental education play crucial roles. Linsell et al.⁴ reported that parental education level, particularly maternal education, was significantly associated with developmental outcomes and school readiness among preterm infants aged 18–21 months. Furthermore, long-term follow-up studies suggested that environmental and parental factors exerted substantial influence on developmental trajectories into adulthood.

Despite growing knowledge, data regarding early childhood developmental outcomes among preterm infants in developing countries remain limited. At Pranangkla Hospital, there has been no systematic collection or analysis of early developmental data among preterm infants. Moreover, national clinical practice guidelines for the management of preterm labor and developmental follow-up in Thailand are largely based on

those from high-income countries, which may differ in population characteristics, socioeconomic context, and caregiving environments. Therefore, this study aimed to determine the prevalence of global developmental delay and identify associated factors among preterm infants aged 6–24 months receiving care at Pranangkla Hospital in a developing country.

Objectives

To determine the prevalence of global developmental delay (GDD) among preterm infants aged 6–24 months attending a high-risk newborn clinic at Pranangkla Hospital and to identify factors associated with GDD in this population.

Methods

A cross-sectional study was conducted in preterm infants aged 6–24 months who attended at high-risk newborn clinic at Pranangkla Hospital. Between January 1, 2023 and December 31, 2024. Data were collected by medical record review and caregiver interviews. Biological parents or guardians were interviewed using a structured questionnaire that had undergone pilot testing before implementation. The questionnaire consisted of three sections: infant demographic information, maternal health information, and socioeconomic and caregiving factors.

Neurodevelopmental screening was conducted between 6 and 24 months of corrected age using the Denver II developmental assessment tool. This instrument evaluates gross motor, fine motor, language, and personal–social skills. These assessments were performed by developmental and behavioral pediatrician who is certified in administering the Denver II at the National Institute for Child and Family Development (NICFD).

This study was approved by the Human Research Ethics Committee of Pranangkla Hospital (Approval No. EC45/2567; amended approval No. EC04/2568). Written informed consents were obtained from all biological parents before data collection.

Definitions

Global developmental delay (GDD) is defined as a significant delay in two or more developmental domains in children younger than 5 years. These domains typically include gross motor, fine motor, speech and language, cognitive development, social and personal development, and activities of daily living (adaptive behavior). A delay is considered significant when performance is approximately 2 standard deviations (≥ 2 SD) below the mean on standardized developmental assessments.

Developmental Quotient (DQ) is a standardized measure used to estimate a child's developmental level relative to their chronological or corrected age until 2 years old.

$$DQ = (\text{Developmental Age} \div \text{Chronological Age or Corrected Age}) \times 100$$

Developmental Age: the age level at which the child is functioning based on standardized developmental assessments

$$\text{Corrected age} = \text{Chronological age} - \text{Weeks (or months) born early} + 40 \text{ weeks}$$

Interpretation

$DQ \geq 85$: Within normal range

$DQ 70-84$: Mild developmental delay/borderline

$DQ < 70$: Significant developmental delay

Sample study and calculation

Infants aged 6–24 months with a history of preterm birth, born between January 2023 and December 2024, were eligible for this study. They were excluded if they had congenital brain malformations, a diagnosis of cerebral palsy according to European guidelines, chromosomal abnormalities or suspected genetic syndromes, visual or hearing impairments, or were unable to attend follow-up visits at the high-risk newborn Clinic, Pranangklae Hospital.

Sample size was calculated using the *Yamane* Formula. Based on the total number of eligible preterm infants attending a high-risk newborn Clinic at Pranangklae Hospital during the study period ($N = 200$), The minimum required sample size was 134 participants.

Statistical analytics

All statistical analyses were performed using JASP statistical software (Version 0.19.1, University of Amsterdam, The Netherlands). A two-tailed p value of <0.05 was considered statistically significant.

Descriptive statistics were used to summarize participants' baseline characteristics. Continuous variables were presented as mean \pm standard deviation (SD) for normally distributed data and as median with quartile range [Q1-Q3] for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. Normality of continuous data distribution was assessed using the Shapiro–Wilk test. For univariate analysis, comparisons between two groups (global developmental delay vs. normal development) were performed using the independent-samples t-test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed variables. Associations between categorical variables were analyzed using Fisher's exact test. Results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). Due to the relatively small sample size, exact methods were applied when appropriate to reduce estimation bias.

Results

A total of 45 preterm infants were assessed for eligibility during the study period. Of these, 13 participants were excluded due to multiple anomalies (1 case), chromosomal abnormalities (7 cases), blindness (1 case), and cerebral palsy (4 cases). Finally, 32 participants were enrolled in the study (Figure 1).

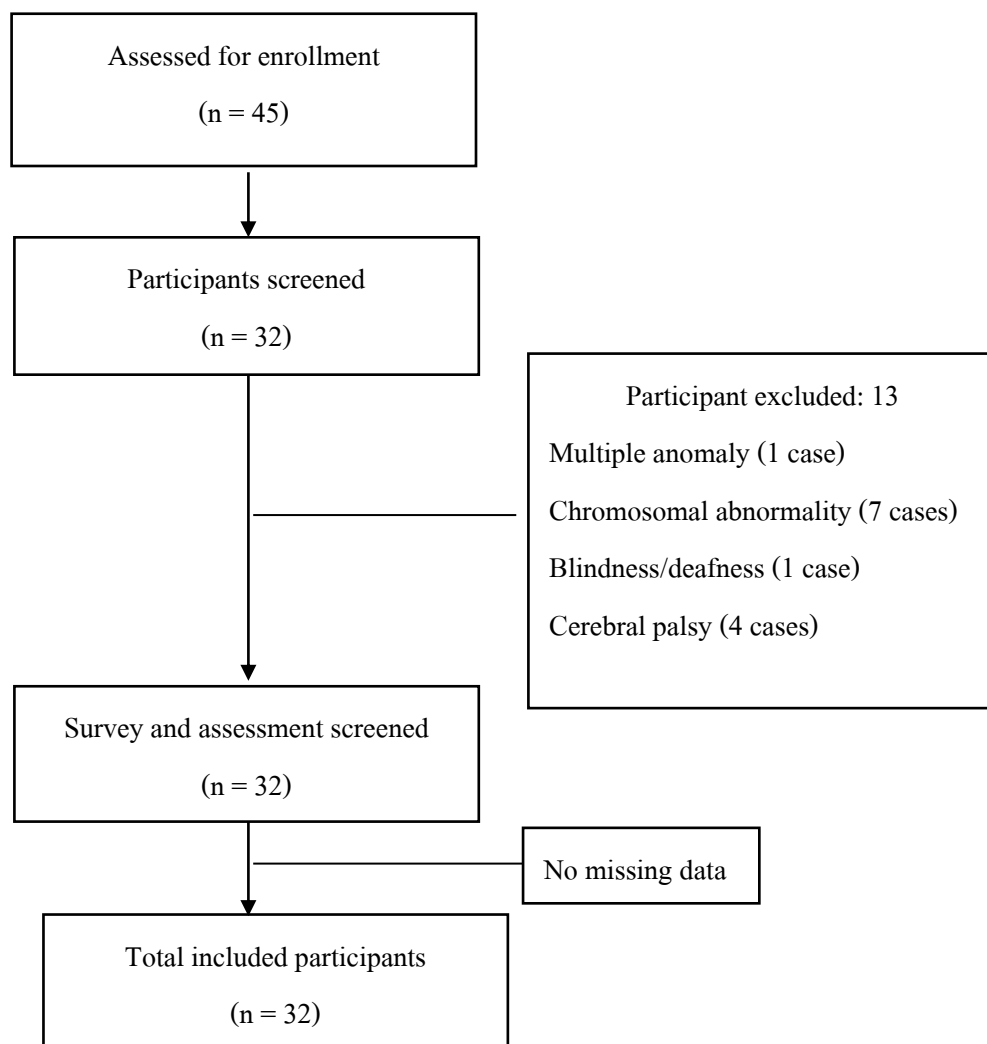


Figure 1 Flow diagram

A total of 32 preterm infants admitted to the NICU between January 1, 2023, and December 31, 2024, and subsequently followed at the high-risk newborn clinic at Pranangkla Hospital were included in the study. Of these, 53.1% were male, and more than 90% were Thai. Median gestational age at birth was 31 weeks [Q1-Q3: 29 – 35], and the median birth weight was 1,434 grams [Q1-Q3: 1047.50 - 1763.50]. The median length of hospital stay was 47 days [Q1-Q3: 25.75 - 68.50]. Mechanical ventilation was required in 53.1 % of infants. Neonatal complications included birth asphyxia 37.5%, respiratory distress syndrome (RDS) 75.0%, shock 31.3%, presumed neonatal sepsis 9 6 .9% , retinopathy of prematurity (ROP) 3 1 .3% , intraventricular

hemorrhage (IVH) 28.1% , bronchopulmonary dysplasia (BPD) 59.3% , and congenital pneumonia 40.6% (Table 1).

Table 1. General characteristics

| Factor | Number | Percentage |
|--|---------------|-------------------|
| Sex | | |
| Male | 17 | 53.1 |
| Nationality | | |
| Thai | 30 | 93.8 |
| Gestational age at birth | | |
| Median [Q1-Q3]: 31.00 [29.00 - 35.00], Min-Max: 25.00 - 36.00 | | |
| < 28 weeks | 3 | 9.4 |
| 28-32 weeks | 18 | 56.3 |
| 33-36 weeks | 11 | 34.4 |
| APGAR at 1-min | | |
| Score ≤ 7 | 12 | 37.6 |
| Fetal distress | 7 | 21.9 |
| Birth weight | | |
| Median [Q1-Q3]: 1434.00 [1047.50-1763.50], Min-Max: 700.00 - 2930.00 | | |
| < 1,000 g | 6 | 18.8 |
| 1,000 - 1,499 g | 11 | 34.4 |
| 1,500 - 2,499 g | 11 | 34.4 |
| $\geq 2,500$ g | 4 | 12.5 |
| Small for gestational age | 9 | 28.1 |
| Hospital length of stay | | |

| Factor | Number | Percentage |
|--|--------|------------|
| Median [Q1-Q3]: 47.00 [25.75 - 68.50], Min-Max: 14.00 - 210.00 | | |
| ≤ 30 days | 10 | 31.3 |
| > 30 days | 22 | 68.8 |
| NICU length of stay | | |
| Median [Q1 - Q3]: 17.50 [6.75 - 43.50], Min - Max: 0.00 - 107.00 | | |
| ≤ 30 days | 17 | 53.1 |
| > 30 days | 15 | 46.9 |
| Neonatal resuscitation | | |
| NIPPV | 30 | 93.8 |
| Intubation | 17 | 53.1 |
| Neonatal complication | | |
| RDS | 24 | 75.0 |
| Shock | 10 | 31.3 |
| Presumed neonatal sepsis | 31 | 96.9 |
| ROP | 10 | 31.3 |
| IVH | 9 | 28.1 |
| BPD lung | 19 | 59.4 |
| Congenital pneumonia | 13 | 40.6 |

Most mothers received antenatal care (90.6%). The median gestational age at the first antenatal visit was 12 weeks (Q1-Q3: 7–17). Complications during pregnancy were observed in several cases. Gestational diabetes mellitus or overt diabetes 28.1%, pregnancy-induced hypertension or preeclampsia 18.8%, infections 9.4%, and others 34.4%. For medication use during pregnancy, dexamethasone was the most frequently

administered (59.4%), followed by other medications (56.3%), while magnesium sulfate was used in 12.5% of cases (Table 2).

Table 2. Antenatal and maternal health

| Factor | Number | Percentage |
|---|--------|------------|
| Antenatal care | 29 | 90.6 |
| First ANC (weeks) | | |
| Median [Q1-Q3]: 12.00 [7.00 - 17.00], Min-Max: 5.00 - 26.00 | | |
| Complication during pregnancy | | |
| GDM/Overt DM | 9 | 28.1 |
| Pregnancy-induced hypertension/ Preeclampsia | 6 | 18.8 |
| Infection | 3 | 9.4 |
| Others | 11 | 34.4 |
| Medication use | | |
| Magnesium sulfate | 4 | 12.5 |
| Dexamethasone | 19 | 59.4 |
| Others | 18 | 56.3 |

Regarding parental and socioeconomic characteristics, both parents were mostly aged between 20–34 years old, with a high school education or lower, and the majority reported a monthly income of ≤20,000 baht. The mother was the primary caregiver in 53.1% of cases, followed by both parents (25.0%), and others (21.9%). Most parents were living together. For developmental promotion and child-rearing, toys were used in 78.1% of cases, and 37.5% of caregivers reported using the DAIM screening tool. No Storytelling in 56.3% of cases. No screen time 59.4%. Exclusive breastfeeding was reported in 31.3% of infants. Nearly all infants received iron supplementation (96.9%), (Table 3).

Table 3. Socioeconomic status and child-rearing

| Factor | Number | Percentage |
|------------------------------------|--------|------------|
| Maternal age | | |
| < 20 | 5 | 15.6 |
| 20 - 34 | 16 | 50.0 |
| ≥ 35 | 11 | 34.4 |
| Maternal education | | |
| High school or lower | 23 | 71.9 |
| Vocational degree | 3 | 9.4 |
| Bachelor's degree or higher | 6 | 18.8 |
| Maternal income (per month) | | |
| ≤ 20,000 baht | 28 | 87.5 |
| > 20,000 baht | 4 | 12.5 |
| Paternal age | | |
| < 20 | 2 | 6.7 |
| 20 - 34 | 22 | 73.3 |
| ≥ 35 | 6 | 20.0 |
| Paternal education | | |
| High school or lower | 23 | 76.7 |
| Vocational degree | 4 | 13.3 |
| Bachelor's degree or higher | 3 | 10.0 |

| Factor | Number | Percentage |
|------------------------------------|---------------|-------------------|
| Paternal income (per month) | | |
| ≤ 20,000 baht | 27 | 90.0 |
| > 20,000 baht | 3 | 10.0 |
| Main caregiver | | |
| Mother | 17 | 53.1 |
| Both parents | 8 | 25.0 |
| Other | 7 | 21.9 |
| Parent's marital status | | |
| Living together | 30 | 93.8 |
| Development promotion | | |
| Toys | 25 | 78.1 |
| Using DAIM screening | 12 | 37.5 |
| Story telling | | |
| None | 18 | 56.3 |
| <3 days/week | 9 | 28.1 |
| ≥3 days/week | 5 | 15.6 |
| Screen time | | |
| none | 19 | 59.4 |
| <2 hours/day | 10 | 31.3 |
| ≥2 hours/day | 1 | 3.1 |
| Milk formula | | |
| Exclusive Breast Feeding | 10 | 31.3 |
| Micronutrient supplement | | |
| Iron supplement | 31 | 96.9 |

Thirteen (40.6%) participants had weight-for-age below the third percentile. Underweight status, defined as a weight-for-height below -2 standard deviations from the WHO reference, was observed in 21.9% of participants. Additionally, 18.8% were classified as having failure to thrive (Table 4).

Table 4. Growth parameter

| Growth assessment | Number | Percentage |
|---------------------------------|--------|------------|
| Weight for age (<percentile 3) | 13 | 40.6 |
| Weight for height (underweight) | 7 | 21.9 |
| Failure to thrive | 6 | 18.8 |

The mean corrected age at the time of Denver II developmental screening was 8.75 months (SD \pm 4.70). The prevalence of global developmental delay (GDD) was 28.1%. Among infants with age-appropriate development, the mean Developmental Quotient (DQ) scores were as follows (Table 5); gross motor 90.0 points; fine motor 100.0 points; language 100.0 points, and personal-social/adaptive 83.3 points. In comparison, infants diagnosed with GDD had lower DQ scores across all domains; gross motor 76.3 points, fine motor 75.0 points, language 72.2 points, and personal-social/adaptive 83.3 points.

Table 5. Developmental assessment

| | Developmental Quotient | | | |
|-------------------------|------------------------|-----------------------|-----------------------|---------------------|
| | Gross motor | Fine motor | Language | Personal-social |
| All participants | 86.1 (16.3) | 90.0 [79.5-100.0] | 87.50 [80.0-100.0] | 83.3 [73.8-87.2] |
| Normal (n=23) | 90.0 (13.2) | 100.0 [90.0-105.6] | 100.0 [83.3-100.0] | 83.3 [75.0-95.8] |
| GDD (n=9) | 76.3 (20.1) | 75.0 [66.7-77.8] | 72.2 [58.3-85.7] | 83.3 [69.2-85.7] |

Normality was assessed using the Shapiro–Wilk test. Data are presented as mean (SD) for normally distributed variables and median [Q1–Q3] for non-normally distributed variables.

A comparison of factors associated with global developmental delay among preterm infants (Table 6) showed that maternal antenatal corticosteroid administration (OR 0.098, 95%CI 0.015-0.646, p value 0.028) was significantly associated with a lower likelihood of global developmental delay.

Table 6. Factors associated with global developmental delay

| Factors | Number | 95%CI | OR | p value |
|---|--------|--------------|-------|---------|
| Child factor | | | | |
| Male | 17 | 0.186-4.106 | 0.873 | 1.000 |
| Gestational age at birth \leq 32 weeks | 21 | 0.707-17.734 | 3.542 | 0.213 |
| APGAR \leq 7 | 12 | 0.616-58.426 | 6.000 | 0.187 |
| Birth weight < 1,500 g | 17 | 0.616-15.709 | 3.111 | 0.243 |
| SGA | 9 | 0.133-3.748 | 0.706 | 0.685 |
| IVH | 9 | 0.267-7.521 | 1.417 | 0.685 |
| Presumed neonatal sepsis | 31 | 0.004-3.254 | 0.121 | 0.281 |
| RDS | 24 | 0.199-7.673 | 1.235 | 1.000 |
| ROP | 10 | 0.089-3.210 | 0.536 | 0.681 |
| Antenatal care and maternal health | | | | |
| Magnesium sulfate use | 4 | 0.012-5.018 | 0.242 | 0.550 |
| Antenatal corticosteroid use | 19 | 0.015-0.646 | 0.098 | 0.028* |
| GDM/Overt DM | 9 | 0.024-2.253 | 0.232 | 0.371 |
| PIH/preeclampsia | 6 | 0.473-19.039 | 3.000 | 0.329 |

| Factors | Number | 95%CI | OR | p value |
|--|--------|-------------------|-------|---------|
| Infection | 3 | 0.014-6.714 | 0.311 | 0.540 |
| Socioeconomic and child-rearing | | | | |
| Maternal education (\geq bachelor degree) | 6 | 0.202-9.126 | 1.357 | 1.000 |
| Paternal education (\geq bachelor degree) | 3 | 0.017-8.086 | 0.371 | 0.557 |
| Maternal income (\geq 20,000 baht) | 4 | 0.108-13.322 | 1.200 | 1.000 |
| Paternal income (\geq 20,000 baht) | 3 | 0.048-8.252 | 0.632 | 1.000 |
| Mother is a main caregiver | 25 | 0.160-6.592 | 1.029 | 1.000 |
| Story telling | 14 | 0.045-1.540 | 0.262 | 0.235 |
| Screen time > 2 hr/day | 11 | 0.250-7.896 | 1.406 | 1.000 |
| Growth assessment | | | | |
| Weight for age (<P3) | 13 | 0.546-18.867 | 3.208 | 0.249 |
| Weight for height (Underweight) | 7 | 0.442- 168.662 | 8.636 | 0.149 |
| Failure to thrive | 6 | 0.202-9.126 | 1.357 | 1.000 |

*p value < 0.05 using Fisher's exact test

** Statistics using Student t-test for normality continuous data, Mann-Whitney U test for non-normality continuous data, Chi-square for nominal data.

*** For the Student's t-test, the effect size is given by Cohen's d. For the Mann-Whitney test, the effect size is given by the rank biserial correlation.

Discussion

Preterm infants were at a higher risk of developing global developmental delay (GDD) than term-born infants.⁵ In this study, the prevalence of GDD among preterm infants followed at a High-Risk newborn clinic of Pranangklaao Hospital was 28.1%, which was comparable to rates reported in previous studies of infants born at similar gestational ages.⁶ No cases of cerebral palsy were identified in this study.

Developmental assessment using the Denver II demonstrated that infants in the GDD group had Developmental Quotient (DQ) scores approximately 2 standard deviations below those of the normally developing group across all domains. The mean differences in DQ scores were 13.7 points in gross motor, 25.0 points in fine motor, and 27.8 points in language, with no difference in the personal–social/adaptive domains. The particularly large differences observed in the fine motor and language domains highlighted that these children were likely to continue demonstrating global developmental delay as they grew older. Given that language and higher-order fine motor abilities typically became more differentiated after the first year of life, longitudinal follow-up might reveal clearer disparities in cognitive and learning outcomes.

However, interpretation should consider that the Denver II was a screening instrument rather than a diagnostic gold standard, such as the Bayley Scales of Infant and Toddler Development or the Mullen Scales of Early Learning. All participants in this study underwent comprehensive history-taking, physical examination, and direct behavioral observation by a developmental–behavioral pediatrician. This rigorous clinical assessment likely enhanced the validity and reliability of both the diagnosis of GDD⁷ and the administration of the Denver II, thereby strengthening the overall accuracy of developmental outcome measurement in this study.

Regarding associated factors, maternal administration of antenatal corticosteroids was the only variable significantly associated with GDD in univariate analysis (OR 0.098, 95% CI 0.015–0.646, p value 0.028). Infants whose mothers received antenatal corticosteroids had lower odds of GDD compared with those who did not. Antenatal corticosteroids were well established for promoting fetal lung maturation⁸ and reducing respiratory morbidity in preterm infants.

Previous studies, including those by Gyamfi-Bannerman et al.⁹, had demonstrated that antenatal corticosteroid exposure was not associated with adverse neurodevelopmental outcomes at long-term follow-up, but did not show a clear direct neurodevelopmental benefit. Similarly, Wei JC, et al.¹⁰ reported associations between antenatal corticosteroid exposure and reduced rates of severe intraventricular hemorrhage, cerebral palsy, and severe neurodevelopmental impairment in early childhood.

Although our findings appeared to suggest a protective association, this result should be interpreted with caution. The sample size was small, and the analysis was limited to univariate comparisons without adjustment for potential confounders. The markedly low odds ratio might reflect residual confounding by factors such as gestational age at birth, birth weight, or severity of neonatal illness. Therefore, our findings did

not establish a causal neuroprotective effect of antenatal corticosteroids but rather indicated a possible association that warranted confirmation in larger, adequately powered studies using multivariable analysis.

In contrast, socioeconomic variables, including household income and parental education, were not significantly associated with GDD in this study. This differs from prior studies, such as those by Patra et al.¹¹ and de Jong et al.,¹² which reported better developmental outcomes among preterm infants from families with higher maternal education and income levels. A plausible explanation for this discrepancy was the limited socioeconomic variability in our study population, as nearly 80% of participating families had come from a disadvantaged background, and a small sample size. This homogeneity might have reduced the ability to detect statistically significant differences in socioeconomic status and had limited power.

Other neonatal and perinatal factors previously reported to increase the risk of developmental delay, such as lower gestational age, low birth weight, birth asphyxia, intraventricular hemorrhage, retinopathy of prematurity, lack of breastfeeding, and malnutrition, were not significantly associated with GDD in this study. This inconsistency with earlier reports might be attributable to the small sample size, limited statistical power, and the relatively young corrected age of most infants at assessment, with the majority being under one year of age. As developmental trajectories, particularly in language and fine motor, which are key domains used in the diagnosis of GDD, become more distinct over time, continued longitudinal follow-up of this study population is essential to better characterize long-term neurodevelopmental outcomes.

Strength and Limitation

To our knowledge, this was the first study conducted at Pranangklaao Hospital to investigate factors associated with global developmental delay and systematically collected developmental outcomes among preterm infants admitted to the NICU.

A limitation of this study was its small sample size, which might have reduced the statistical power and the ability to detect significant associations. Nevertheless, despite the limited number of participants, maternal antenatal corticosteroid exposure appeared to be associated with a protective factor against global developmental delay. A study with a larger sample size may provide sufficient statistical power and yield clearer evidence regarding the outcomes in future research.

Conclusion

Maternal antenatal corticosteroid exposure appeared to be associated with a protective factor against global developmental delay. However, this finding should be interpreted cautiously due to the small sample size and the absence of adjustment for potential confounding factors. Future studies with larger sample sizes may provide clearer evidence regarding the outcomes.

Also, Long-term neurodevelopmental follow-up of preterm infants exposed to antenatal corticosteroids would provide more robust evidence regarding developmental outcomes in this population. Such data could help clarify the benefits and further inform the evidence base supporting corticosteroid administration in mothers in line with established clinical guidelines.

In addition, the standardized protocols for long-term developmental screening and follow-up of preterm infants are critically important. One study had recommended that developmental monitoring for this high-risk population should continue until at least 2 years of age.¹³ However, these guidelines were primarily developed in high-income countries, and developmental follow-up of preterm infants beyond two years of age may be more beneficial and necessary in developing countries.

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