

# Long-term ocular sequelae in preterm Thai infants

## A comprehensive retrospective study

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### Abstract

Prematurity can lead to various ocular conditions, including strabismus, refractive errors, amblyopia, and cataracts. However, comprehensive data on these outcomes in preterm Thai infants is limited. This study aimed to investigate the incidence of retinopathy of prematurity (ROP) and assess long-term ocular sequelae, such as cataracts, refractive errors, strabismus, and amblyopia, among preterm infants at Phramongkutklao Hospital. A retrospective review of medical records was conducted for premature infants screened for ROP between January 2011 and April 2022. Data were collected at birth, and follow-up visits were analyzed at 6 months, 1 year, and 2 years of age. The primary outcomes included the incidence of ROP and the prevalence of long-term ocular sequelae. A total of 308 preterm infants were included in the study. The incidence of ROP was found to be 31.5%. At the 2-year follow-up, the prevalence of cataracts was 0.65%, strabismus 14.4%, and amblyopia 6%. Refractive errors were observed in 51.8% of the infants, with 18.1% showing myopia and 33.7% hyperopia. Logistic regression analysis indicated that delayed growth and development (adjusted odds ratio = 13.28, 95% confidence interval: 1.83–96.68) and amblyopia (adjusted odds ratio = 19.65, 95% confidence interval: 2.85–135.54) were significantly associated with an increased risk of developing strabismus, after adjusting for confounding factors. The study identified an ROP incidence of 31.5% in the preterm cohort. At 2 years, long-term ocular sequelae included a prevalence of cataracts (0.65%), strabismus (14.4%), amblyopia (6%), and refractive errors (51.8%). Delayed growth and development, along with amblyopia, were found to elevate the risk of strabismus development significantly.

**Abbreviations:** BW = birth weight, ROP = retinopathy of prematurity.

**Keywords:** amblyopia, cataract, prematurity, refractive error, retinopathy, strabismus

### 1. Introduction

Retinopathy of prematurity (ROP) primarily affects premature infants and may cause blindness. Although the management of ROP has progressed, its long-term ocular sequelae remain a critical concern. Infants who develop severe ROP are at risk of developing various visual impairments throughout their lives, including refractive error, strabismus, amblyopia, and glaucoma.<sup>[1,2]</sup> Furthermore, structural changes to the retina and blood vessels caused by ROP<sup>[3]</sup> may predispose individuals to retinal detachment and other sight-threatening conditions later in life.

Several studies have contributed valuable insights into the incidence of ROP and its long-term consequences.<sup>[4–15]</sup> These investigations have revealed that the incidence of ROP ranges from 21% to 53%.<sup>[4–10,14]</sup> The involved studies included longitudinally prospective and retrospective data encompassing continuous monitoring for up to 19 years.<sup>[4–14]</sup> Notably, strabismus was observed in 9.5% to 36% of cases,<sup>[4–14]</sup>

whereas myopia was observed in 7.3% to 58.9% of cases.<sup>[4–14]</sup> Moreover, severe visual impairment, defined as vision < 0.9 the Logarithm of the Minimum Angle of Resolution, was observed in up to 56% of patients.<sup>[12]</sup> Cumulatively, these findings underscore the clinical significance of these sequelae and emphasize their pivotal role in prematurity-related visual health.

In Thailand, several reports have contributed to our understanding of the incidence of ROP and its associated factors.<sup>[16–18]</sup> Among these reports, 2 included data from rural areas of Thailand,<sup>[16,18]</sup> with the incidence of ROP ranging from 14% to 31.7%.<sup>[16–18]</sup> The observed variability can be attributed to disparities in the data collection timing, screening criteria, and diagnostic criteria used. Identified factors associated with ROP included a low birth weight (BW),<sup>[16,18]</sup> early gestational age,<sup>[16,17]</sup> positive culture for sepsis,<sup>[17]</sup> male gender,<sup>[18]</sup> and bronchopulmonary dysplasia.<sup>[18]</sup> Notably, the existing literature predominantly concentrated on assessing the incidence of ROP and its correlated risk factors. However,

Written informed consent for publication was waived because of the study's retrospective nature. Participant data were kept anonymous and confidential.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

The study protocol was reviewed and approved by the Institutional Review Board of the Royal Thai Army Medical Department (approval number S089h/64\_Exp).

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a distinctive gap exists in the literature regarding the long-term ocular sequelae of ROP in Thailand. This study provides crucial data from a developing country context, potentially guiding healthcare providers in implementing continuous monitoring strategies for preterm infants to prevent unwanted ocular sequelae.

Our study aimed to assess the incidence of ROP and examine the prevalence of long-term ocular sequelae, including cataracts, strabismus, amblyopia, and refractive errors, among premature Thai infants.

## 2. Methods

### 2.1. Design

This study was a single-center, retrospective analysis.

### 2.2. Participants

A thorough review of patient records was conducted from January 1, 2011, to April 30, 2022. The study included preterm infants born at a gestational age of  $\leq 30$  weeks, with a BW of  $\leq 1500$  grams, as well as those weighing between 1500 and 2000 grams who experienced an unstable clinical course. These infants were screened for retinopathy of prematurity and followed up for long-term ocular sequelae. Inclusion criteria required preterm infants with complete data who attended at least 2 out of 3 scheduled pediatric eye clinic visits at 6 months, 1 year, and 2 years of age. Infants with incomplete data were excluded from the study.

### 2.3. Procedures

We collected basic data for each participant, including date of birth, sex, appearance-pulse-grimace-activity-respiration scores at 1, 5, and 10 minutes, and the presence of comorbidities (sepsis, lung problems, patent ductus arteriosus, intraventricular hemorrhage, necrotizing enterocolitis, hypothermia, jaundice, polycythemia, anemia, and hypoglycemia). Additional data included the duration of hospitalization, fundoscopic findings, and any treatment administered.

A vitreoretinal specialist conducted fundus examinations at every visit, classifying ROP severity based on the International Classification of ROP<sup>[19]</sup> and determining the appropriate treatment. The most severe stages and zones of ROP in both eyes were documented.

Follow-up assessments included:

- Growth and developmental progress, measured using the Centers for Disease Control and Prevention guidelines,<sup>[20]</sup> a standard growth chart, and the Bayley Scales of Infant and Toddler Development, all conducted by pediatricians.
- Visual assessment, amblyopia screening, and ocular alignment evaluation using the Hirschberg technique or cover test, depending on the child's age and cooperation.
- Anterior segment examinations by slit lamp, lens evaluations, and fundoscopic examinations using indirect ophthalmoscopy, all performed by a pediatric ophthalmologist.
- Cycloplegic refraction, performed by an optometrist using standard autorefractometry and manual refraction techniques.

Follow-ups were scheduled at birth, 6 months, 1 year, and 2 years, following our hospital's standard protocol.

### 2.4. Outcome measures

- Cataract: defined as a cloudy lens detected after pupil dilation during fundoscopic examination. A visually significant cataract was defined as a central cataract of 3 mm or more

that obstructs the red reflex and has the potential to impair vision.

- Strabismus: defined as ocular misalignment of more than 8 prism diopters away from orthotropia. The corneal light reflex or cover test was evaluated based on the child's cooperation. Specifically:
  - Esotropia: A convergent eye alignment of more than 8 prism diopters.
  - Exotropia: A divergent eye alignment of more than 8 prism diopters.
- Amblyopia: defined as a reduced vision in 1 or both eyes not attributed to structural abnormalities. In toddlers, abnormal fixation behavior was an indicator of amblyopia.
- Refractive errors: mean refraction of both eyes was recorded. Cycloplegic refraction values were used and calculated as spherical equivalents. Definitions were as follows:
  - Hyperopia: cycloplegic refraction value of greater than + 0.5 diopters.
  - Myopia: cycloplegic refraction value of less than -0.5 diopters.
  - Plano refraction: cycloplegic refraction value between -0.5 diopters and + 0.5 diopters.

### 2.5. Statistical analysis

Descriptive statistics were used to obtain the basic data of the sample group from the general data. Group data were analyzed in terms of the amount and percentage of quantitative data. For normally distributed data, the mean was measured along with the mean and standard deviation. For non-normally distributed data, the average value was summed with the median. Numbers and percentages represent clustered data.

Birth weight, gestational age, ROP stage, and ROP zone were categorized into groups for analysis. Birth weight was classified as very low ( $\leq 1500$  g) and low ( $>1500$  g). Gestational age was categorized as lower ( $\leq 30$  weeks) and higher ( $>30$  weeks). ROP stages were classified as early ( $< \text{stage } 3$ ) and advanced ( $\geq 3$ ). The ROP zone was categorized as posterior ( $< 2$ ) and anterior ( $\geq 2$ ).

Using a significance level of 0.05, logistic regression analysis was conducted to determine the factors independently associated with the incidence of strabismus among premature infants. The logistic regression model accounted for several factors, including sex, gestational age, BW, duration of hospitalization, sepsis, lung problems, patent ductus arteriosus, intraventricular hemorrhage, necrotizing enterocolitis, hypothermia, jaundice, polycythemia, anemia, hypoglycemia, treatment, delayed growth

**Table 1**  
Long-term ocular sequelae at 6, 12, and 24 months.

	6 months	12 months	24 months
Fixation behavior			
Normal	277 (89.9)	192 (96.5)	78 (94)
Abnormal	31 (10.1)	7 (3.5)	5 (6)
Strabismus			
Orthotropia	287 (93.2)	169 (90.9)	71 (85.6)
Esotropia	13 (4.2)	11 (5.9)	7 (8.4)
Exotropia	8 (2.6)	6 (3.2)	5 (6)
Cycloplegic refraction (N [%], average in D)			
Normal	49 (19.4), 0.05	57 (30), 0.13	40 (48.2), 0
Hyperopia	187 (74.2), 1.98	115 (60.5), 1.56	28 (33.7), 1.33
Myopia	16 (6.3), -1.45	18 (9.5), -1.69	15 (18.1), -2.2
Growth and development			
Normal	277 (89.9)	164 (86.3)	62 (75.6)
Delayed	31 (10.1)	26 (13.7)	20 (24.4)

Data are presented as the n (%) of patients or mean.  
D = diopter, N = population size.

and development, amblyopia, cataract, stage, and zone of ROP. Significant factors in the univariate analysis proceeded to the multivariate analysis. Notably, because of its low incidence, logistic analysis was not performed for amblyopia because this could impact the robustness and reliability of the results.

Information was validated and recorded in a data file using the Statistics and Data/Multiprocessor Version 12 program and then analyzed. Statistical Package for the Social Sciences was used for all statistical analyses. A statistical consultant at the Office of Research Development Phramongkutklao Hospital and Phramongkutklao College of Medicine consulted, analyzed, and interpreted data for our project. LLMs do not qualify for authorship.

## 2.6. Ethics approval

The study was approved by the Institutional Review Board of the Royal Thai Army Medical Department (approval number S089h/64\_Exp). Due to its retrospective nature, the Royal Thai Army Medical Department waived the need for informed consent. This study was conducted in accordance with the principles of the Declaration of Helsinki.

## 3. Results

The study collected data from 685 patients using a computerized data system. After excluding 377 cases due to incomplete information, a total of 308 cases were included for analysis. The prevalence of ROP in this cohort was 31.5% (97 out of 308). Male infants constituted 53.9% (166 out of 308) of the study population. The mean BW was  $1501.308 \pm 557.57$  grams, and the mean duration of hospitalization was  $52.79 \pm 42.80$  days. Among the infants, 15.3% (45 out of 308) required treatment; 14% (43 out of 308) underwent indirect laser ophthalmoscopy, and 1.3% (4 out of 308) received intravitreal anti-vascular endothelial growth factor therapy. ROP stages were categorized as follows: 68.5% (211 out of 308) were stage 0, 13% (40 out of 308) were stage 1, 1.9% (6 out of 308) were stage 2, 7.8% (24 out of 308) were stage 3, and 8.8% (27 out of 308) were stage 4, with no cases of stage 5 identified. The distribution of ROP stages by average gestational age was: 31.65 weeks for

stage 0, 30.63 weeks for stage 1, 29.83 weeks for stage 2, 27.25 weeks for stage 3, and 26.15 weeks for stage 4.

Ocular sequelae, including fixation behavior, strabismus, refractive status, and overall growth and development, are shown in Table 1. Notably, attrition of subjects gradually occurred from the follow-up clinic, which may have influenced the comprehensiveness of the long-term assessments and outcomes.

This study observed several ocular conditions in preterm infants, clarifying the prevalence and trends over time. Cataracts developed in 2 infants, with the first case being a congenital cataract and another case being diagnosed at the 6-month follow-up. They did not receive treatment for ROP. This study's overall incidence of cataracts was 0.65% (2/308).

Additionally, strabismus was noted among the participants. Although the number of affected infants decreased over time, data loss resulted in a higher proportional prevalence. At the 2-year follow-up, strabismus was noted in 14.4% (12/83) of the infants; 85.6% (71/83) maintained orthotropic alignment, 6% (5/83) exhibited exotropia, and 8.4% (7/83) exhibited esotropia.

Meanwhile, amblyopia was detected in 10.1% (31/308) of infants at 6 months, but its prevalence gradually decreased to 6% (5/83) by the 2-year mark.

Regarding refractive errors, hyperopia was predominantly observed in 74.2% (187/308) of preterm infants at 6 months, which decreased to 33.7% (28/83) at 2 years. Interestingly, the normal refraction ranges gradually expanded over time, possibly reflecting the emmetropization mechanism. Myopia, which was the least commonly observed refractive error, showed a propensity to increase with time.

We meticulously examined the risk factors linked to the development of strabismus using logistic regression analysis, as shown in Table 2. Analysis revealed 2 notably influential factors that were significantly associated with strabismus development: delayed growth and development (odds ratio = 13.28, 95% confidence interval: 1.83–96.68) and amblyopia (odds ratio = 19.65, 95% confidence interval: 2.85–135.54).

## 4. Discussion

The incidence of ROP in our study was 31.5%, consistent with recent Thai studies, which reported rates between 14% and

**Table 2**  
Associated risk factors for strabismus development.

Variable	Univariate analysis			Multivariate analysis		
	Crude odds ratio	P-value	95% CI	Adjusted odds ratio	P-value	95% CI
Gestational age (weeks)						
<30	1.24	.738	0.36–4.29	2.21	.592	0.12–39.68
≥30	1			1		
Birth weight (grams)						
<1500	1.40	.598	0.40–4.88	0.97	.982	0.10–9.88
≥1500	1			1		
ROP stage						
<3						
≥3	0.98	.979	0.24–4.03	1.34	.901	0.01–145.42
ROP zone						
Posterior (<2)	NA	NA	NA	NA	NA	NA
Anterior (≥2)						
Treatment						
Observe	1			1		
Laser indirect ophthalmoscope	1.20	.802	0.29–5.00	0.15	.482	0.00–28.35
Intravitreal VEGF	16.36	<.001	3.82–70.20	13.28	.011	1.83–96.68
Delayed growth and development						
Amblyopia	31.73	<.001	6.22–161.82	19.65	.003	2.85–135.54
Cataract	0.157	.202	0.01–2.70	10.54	.226	0.23–477.93

Data are presented as median (interquartile range) or n (%) of patients.

CI = confidence interval, IQR = interquartile range, NA = not applicable, ROP = retinopathy of prematurity, SD = standard deviation, VEGF = vascular endothelial growth factor.

Table 3

## Previous literature reporting ocular sequelae from retinopathy of prematurity.

	Page JM et al <sup>[4]</sup> (1993)	Fledertius <sup>[5]</sup> (1996)	Darlow et al <sup>[6]</sup> (1997)	Holmstrom et al <sup>[7,8]</sup> (1999)	Shalij-Delfos et al <sup>[9]</sup> (2000)	O'Connor et al <sup>[10]</sup> (2002)	Donati S. et al <sup>[11]</sup> (2014)	Kulkarni S. et al <sup>[12]</sup> (2019)	Jain S. et al <sup>[13]</sup> (2022)	Sherief ST et al <sup>[14]</sup> (2024)	Our study
Study design	Retrospective	Prospective	Prospective	Prospective	Prospective	Prospective	Retrospective	Retrospective	Prospective cohort	Prospective	Retrospective
Population	190	185	413	260	130	254	261	150	128	222	308
Inclusion criteria	BW < 1251 g	BW < 2000 g GA < 26 weeks	BW < 1500 g	BW < 1501 g	GA < 37 weeks	BW < 1701 g	BW ≤ 1500 g GA ≤ 32 weeks	BW < 2000 g GA ≤ 34 weeks	GA 22–25 weeks	GA < 37 weeks	BW < 1500 g GA < 30 weeks
Incidence of ROP (%) / treatment (%)	53/0	32/0	21/0	40/11	25.4/1.54	50/0	NA	NA	NA	7.2/NA	31.5/15.3
Follow-up/ residual N	2 years/50	7–10 years/88	7–8 years/274	3.5 years/227	5 years/99	10–12 years/169	6 years	1 year	19 years/128	2.62 (2.08–6.28)/222	2 years/88
Primary outcomes	Strabismus Refractive error (myopia)	BCVA Strabismus Refractive error	BCVA Strabismus Refractive error	BCVA Strabismus	Strabismus Amblyopia Refractive error	Visual function (BCVA, contrast, stereopsis, perimetry, and color deficiency)	Refractive error Strabismus	Poor vision Refractive error Structural abnormalities	BCVA Refractive error Contrast Color vision Strabismus Nystagmus	Strabismus Amblyopia Refractive error	Cataract Strabismus Amblyopia Refractive error
Secondary outcomes	Risk factors for primary outcomes = se- verer stage ROP and low birth weight increase myopia/VH grade III and IV/ increase esotropia	Risk factors for poor vision = ear- lier GA and evidence of CNS damage decrease VA score	Comparative data between ROP and non-ROP = BCVA, strabismus, myopia is significantly in the ROP group	Risk factors for primary outcomes = Cryo- therapy treated + neurological problems	Risk factors for primary outcomes = ear- ly GA, duration of supplementary oxygen, and duration of hospital- ization	Refractive error Risk factors for visual impairment and strabismus = lower BW and severe ROP stage increase VA impairment, ROP stage, influence strabismus	Divide into 3 groups: 1. preterm without ROP 2. preterm with mild ROP 3. preterm with severe ROP - At 6 years follow significant hyperopia and strabismus compared with 1 year - Groups 2 and 3 had more myopia and strabismus than Group 1	Comparison between the 3 groups: 1. preterm without ROP 2. preterm with mild ROP 3. preterm with severe ROP Group 3: highest risk of poor vision, refractive error, and structural abnormalities	Comparison with the control group (full term): - BCVA, binocular vision, strabismus, and nystagmus are more significantly related to preterm births - Nonsignificant differences in refractive error, color vision, and contrast sensitivity between the groups	Risk factors for visual impairment = uncorrected refractive errors, strabismus and ROP	Risk factors for primary outcomes = delayed growth development and amblyopia for strabismus
Cataract (%)	NA	1.14	NA	NA	NA	NA	NA	NA	NA	NA	0.65
Strabismus (%)	NA	18	22	13.5 (77.4/22.6)	22	19	1 year: 5.3, 12.5, and 38 6 years: 11.5, 25, and 56.25 (average 15.7)	Group 1 = 25, Group 2 = 21.7, Group 3 = 0 (average 9.5%)	36	11.3	14.4
(esotropia/exotropia)											

(Continued)



**Table 3**  
(Continued)

	Page JM et al <sup>[4]</sup> (1993)	Fledelius <sup>[5]</sup> (1996)	Darlow et al <sup>[6]</sup> (1997)	Holmstrom et al <sup>[7,8]</sup> (1999)	Shalij-Delfos et al <sup>[9]</sup> (2000)	O'Connor et al <sup>[10]</sup> (2002)	Donati S. et al <sup>[11]</sup> (2014)	Kulkarni S. et al <sup>[12]</sup> (2019)	Jain S. et al <sup>[13]</sup> (2022)	Sherief ST et al <sup>[14]</sup> (2024)	Our study
Refractive error (%)	16 (myopia) at 1 year 38 (myopia) at 2 years	13 (myopia < 0 D) 16 (astigmatism > 1 D)	14–21 (myopia < 0 D) 18 (hyperopia > 3 D) 11 (astigmatism > 1 D)	15 (myopia < 0 D) 4.2 (hyperopia > 3 D) 21 (astigmatism > 1 D)	17	22 (myopia < 0 D) 9.3 (hyperopia > 3 D)	Myopia: 1 year: 6.9, 18, and 40.6 6 years: 7.4, 10.8, and 28.4 (average 7.3) Hyperopia: 1 year: 39.2, 28.6, and 22 6 years: 62, 48.3, and 40.5 (average 59.4)	Group 1 = 0, Group 2 = 11, Group 3 = 45 (average 58.9) (Myopia < -2 D)	73	51.8	18.1 (myopia < -0.5 D) 33.7 (hyperopia > 0.5 D)
Poor vision (%)	NA	4.1 (BCVA < 1)	2.9 (BCVA < 1)	1.4 (BCVA < 1) 2.5 (BCVA < 0.3)	NA	3.5 (BCVA < 0.3)	NA	Group 1 = 16, Group 2 = 23, Group 3 = 56 (BCVA < 0.9)	NA	24.8	NA
Amblyopia	NA	NA	NA	NA	17	NA	NA	NA	NA	40.1	6

Data are presented as median (interquartile range) or n (%) of patients.

BCVA = best corrected visual acuity, BW = birth weight, CNS = central nervous system, GA = gestational age, IVH = intraventricular hemorrhage, N = population size, NA = not applicable, ROP = retinopathy of prematurity.

31.7%,<sup>[16–18]</sup> and slightly lower than global data, which ranges from 21% to 53%.<sup>[4–10,14]</sup> It is important to note that our study's inclusion criteria, focusing on preterm infants referred to the pediatric ophthalmology clinic for comprehensive ocular evaluation, may only partially represent the general preterm population within our hospital. This limitation should be considered when interpreting the incidence of ROP.

At the 2-year follow-up, we identified several long-term ocular sequelae among the cohort: cataracts (0.65%), amblyopia (6%), hyperopic refraction (33.7%), myopic refraction (18.1%), exotropia (6%), and esotropia (8.4%). These findings are the first to document such data specific to the Thai preterm population. To place our results in context, we conducted a comprehensive literature review using PubMed with keywords such as “preterm,” “prematurity,” “long-term,” “sequelae,” and “outcome.” We specifically excluded studies involving targeted interventions like laser therapy to maintain a broader perspective on outcomes. The data gathered from the review are presented in Table 3 for comparison.

Our study's cataract incidence of 0.65% is similar to a previous report (1.14%) within the first 6 months.<sup>[5]</sup> However, it is lower than the 1.9% incidence observed in the Early Treatment for ROP study.<sup>[21]</sup> Additionally, the cataract rate in our cohort was higher than that in term infants, as outlined by a large epidemiological study, which reported incidences ranging from 1.2% to 6.0% per 10,000 infants.<sup>[22]</sup> These comparisons underscore the unique risks and considerations for cataracts in preterm infants.

Strabismus was present in 14.4% of our cohort at the 2-year follow-up, with esotropia (8.4%) more common than exotropia (6%). These findings align with prior reports showing strabismus rates ranging from 9.5% to 36%.<sup>[4–14]</sup> However, details on the specific types of strabismus are often not specified in other studies, except for Holmstrom et al,<sup>[7,8]</sup> who similarly found esotropia to be more prevalent than exotropia.

Assessing visual outcomes in our cohort presented challenges due to the young age of participants and limitations in assessment tools, which impacted the recognition of optotypes. We focused on fixation behavior, identifying a 6% incidence of amblyopia. Shalij-Delfos et al<sup>[9]</sup> reported a higher 17% incidence at 5 years, while Sherief et al<sup>[14]</sup> found a 41% rate at 2 years, highlighting variability in amblyopia rates across studies depending on the criteria used. Although preterm infants frequently exhibit delayed growth and cortical visual impairments, our cases predominantly involved poor monocular fixation with normal neurological signs, making such conditions unlikely.

Refractive errors were a notable sequela in our study, affecting 51.8% of preterm infants at the 2-year follow-up. Myopic refraction was observed in 18.1% of cases, while hyperopic refraction was more prevalent at 33.7%. Variability in data collection timing and definitions of myopic refraction has been observed in the literature, with reported incidences ranging from 7.3% to 58.9%,<sup>[4–14]</sup> underscoring refractive errors as a significant long-term outcome in this population. Attempts to correlate refractive error severity with ROP severity yielded no significant association.

Our study also identified delayed growth and amblyopia as significant risk factors for strabismus development. Although these specific factors have not been extensively explored in previous studies,<sup>[4–14]</sup> a strong association between amblyopia and strabismus exists, possibly due to the competitive inhibition theory. Unequal visual stimuli during neural plasticity could cause morphological changes in the lateral geniculate body and visual cortex, contributing to strabismus.<sup>[23]</sup> Additionally, delayed motor development in preterm infants could impact ocular muscle coordination.<sup>[24]</sup> Regression analysis at multiple follow-up points confirmed that these factors significantly influence the development of strabismus, accounting for the potential confounding effects of surgical interventions.

By concluding with a summary of the literature search and positioning our study's findings within the broader research landscape, we aim to provide a clearer context for the observed outcomes and underscore the value of our research in filling knowledge gaps specific to the Thai preterm population.

## 5. Limitations

The strength of our study is that it is a large cohort study with long-term data. This study revealed the incidence of ocular sequelae, including their associated risk factors, in preterm Thai infants, which was a gap in the literature. Nevertheless, this study had some limitations. First, this was a single-center retrospective study; there was no diversity in ethnicity, and data on long-term sequelae of > 2 years needed to be included. Second, visual assessment in this study was only for fixation behavior due to the instrument's limitations. Third, ocular biometry still needs to be performed. Lastly, some patients may have been lost to follow-up during the COVID-19 pandemic. Further studies should provide long-term outcomes for all aspects of the sequelae. Moreover, refractive amblyopia, which may contribute to strabismus development, should be monitored.

## 6. Conclusions

Our study found that the incidence of ROP in this cohort was 31.5%. At the 2-year follow-up, we identified several long-term ocular sequelae: cataracts in 0.65% of cases, strabismus in 14.4%, amblyopia in 6%, and refractive errors in 51.8%. Logistic regression analysis revealed significant associations between delayed growth and development and the occurrence of strabismus, as well as a strong link between amblyopia and strabismus. These findings emphasize the importance of continuous, long-term surveillance to detect and address these treatable ocular conditions early.

Future research should enhance early screening protocols and interventions for ROP, explore its long-term impact on ocular health, and expand the use of telemedicine to increase access to pediatric eye care. Such efforts could improve visual outcomes and quality of life for premature children.

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