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Accuracy of the postnatal growth and retinopathy of prematurity screening criteria in predicting prethreshold retinopathy of prematurity in the tertiary hospital, Bangkok, Thailand

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Abstract:

PURPOSE: The postnatal growth and retinopathy of prematurity (G-ROP), retinopathy of prematurity (ROP) predictive model, was developed in North America with high sensitivity and fewer infants examined. This study aimed to validate this model in Thai infants by assessing sensitivity and comparing it to the current American Academy of Ophthalmology (AAO) screening guideline.

MATERIALS AND METHODS: The records of infants screened for ROP were retrospectively reviewed from 2015 to 2020. G-ROP model was applied to calculate sensitivity for prethreshold type 1 and 2 ROP and the reduction of the number of infants examined.

RESULTS: Of 129 infants screened, there were 102 infants who met G-ROP criteria. The mean gestational age at birth was 29.7 ± 2.7 weeks. The mean birth weight was 1177.8 ± 401.3 g. Both G-ROP and AAO detected prethreshold type 1 ROP in 24 of 24 infants (sensitivity, 100%; 95% confidence interval [CI], 85.8%–100%). Furthermore, they detected all four infants prethreshold type 2 ROP with 100% of sensitivity (95% CI, 39.8–100.0). The reduction in infants receiving examinations using G-ROP was 20.9%.

CONCLUSIONS: G-ROP model provided high sensitivity and lessen unnecessary examinations for ROP screening in Thai infants.

Keywords:

Postnatal weight gain, retinopathy of prematurity, screening sensitivity, Thai infants

Introduction

Retinopathy of prematurity (ROP) is a common ocular disease in premature infants. To detect ROP, a screening protocol is applied to selected preterm infants. Vajira hospital, Navamindradhiraj University, the tertiary center in Bangkok,Thailand has applied the American Academy of Ophthalmology (AAO) ROP screening policy[1] to a current ROP screening protocol. According to the hospital database, since 2015, prethreshold type 1 ROP, a treatment-requiring form, was found in 17% of all screened infants. Hence, we considered a new, more restricted screening protocol to exclude unnecessary examinations without missing critical cases.

Vascular endothelial growth factor (VEGF) and insulin-like growth factor-1 (IGF-1) play essential roles in the pathophysiology of ROP.[2] In phase 1 after birth, both VEGF and IGF-1 are markedly decreased, and in phase 2, when retina is hypoxia, both VEGF and IGF-1 become increasing. However, monitoring serum IGF-1 levels is not

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practical. Therefore, postnatal weight gain, known as a surrogate marker for IGF-1 status, is used instead.[3]

Postnatal growth and ROP (G-ROP), one of the latest ROP predictive models, integrated gestational age (GA) at birth, birth weight (BW), and postnatal weight gain into screening criteria.[4] It had six steps of criteria. First, infants who were born with GA at birth < 28 weeks or BW < 1051 g would be included in the screening examination. If they were above GA and BW criteria, there were three weight gain criteria to be considered– postnatal weight gain between days 10–19, days 20–29, and days 30–39. If infants gained weight less than the criteria, they would be included. Finally, if infants had nonphysiologic weight gain such as hydrocephalus, they would be included as this weight gain did not reflect their true growth. Our current AAO guideline used only GA and BW criteria. Hence, the additional postnatal weight gain criteria helped reduce the number of infants examined. Furthermore, the G-ROP sensitivity of detecting type 1 ROP was still 100%. Therefore, it is interesting to adapt these new criteria to our practice.

However, the G-ROP model was performed initially in North America, where the patient's characters and hospital environment differed greatly from Thailand. The study aims to evaluate the sensitivity of G-ROP screening criteria based on a database of Thai premature infants in our tertiary hospital.

Materials and Methods

This is a retrospective study done at Vajira hospital, Navamindradhiraj University, Bangkok,Thailand, and approved by Vajira institutional review board (COA 128/2563), the patient consent is waived by Institutional Review Board. Medical records of preterm infants screened for ROP from January 1st, 2015 to December 31st, 2020, were reviewed. ROP screening criteria at Vajira hospital were based on the AAO ROP screening policy.[1] All infants born with GA at birth < 30 weeks, or BW < 1500 g, or BW between 1500 and 2000 g or GA at birth more than 30 weeks who were at risk for ROP evaluated by attending neonatologists would receive ROP examination. Screening examinations were done by an attending pediatric ophthalmologist (CB) or a retina specialist (KH) using an indirect ophthalmoscope with scleral indentation. ROP staging, zoning, and plus assessment were classified according to the International Classification of ROP[5] and the early treatment of ROP study.[6] In addition to the established definition of prethreshold type 1 ROP, we also treated any ROP in zone 1 with preplus disease and stage 2, 3 ROP in zone 2 with preplus disease as type 1 ROP. The screening and follow-up visit timing were based on the AAO ROP screening policy[1] until retinal vascularization reached zone 3 or ROP was regressed. Infants with incomplete medical records and infants who lost to follow-up examinations before the 35-week postmenstrual age were excluded from the study.

Baseline infant characteristics such as gender, ethnicity, GA at birth, BW, ROP findings, age at examination, any treatment, and the number of examinations were collected from ROP charts. Daily weight measurement was collected from nursing flow sheets. Sources of nonphysiologic weight, such as hydrocephalus, were also recorded.

We applied G-ROP predicting model,[4] which included infants with one of the following

1. GA at birth lower than 28 weeks OR
2. BW <1051 g
3. If infants were older than 28 weeks or BW more than 1051 g, then infants would receive an ROP examination, if postnatal weight gain was under the following criteria.
    - Weight gain between postnatal days 10 and 19 <120 g OR
    - Weight gain between postnatal days 20 and 29 <180 g OR
    - Weight gain between postnatal days 30 and 39 <170 g OR
    - Had nonphysiologic weight gain from hydrocephalus.

This study was designed as diagnostic research that studied the performance of G-ROP screening criteria compared to AAO criteria if applied to Thai infants. The primary outcome was sensitivity for prethreshold type 1 ROP using the G-ROP predicting model. The secondary outcomes were sensitivity for prethreshold type 2 ROP, specificity for both type 1 and type 2 ROP, and the reduction of the number of infants screened for ROP using the G-ROP predicting model compared to the AAO screening guideline. Infants' demographics that met G-ROP criteria were summarized as proportion. The sensitivity (95% and 99% confidence intervals [CIs]) and specificity from a 2 × 2 table were analyzed using STATA version 13.0 (StataCorp LLC,Texas, USA). The data are described as a number, proportion, and mean ± standard deviation.

Results

Of 162 eligible infants, 129 infants were included in this study. Thirty-three infants were excluded due to unknown ROP outcomes and lost medical records. The mean GA at birth was 29.7 ± 2.7 weeks (range, 24–37 weeks). The mean BW was 1177.8 ± 401.3 g (range, 500–3040 g). The mean postmenstrual age at the first examination was 33.9 ± 2.4 weeks (range, 29–42 weeks).

ROP developed in 52 infants (40.3%). Prethreshold type 1 ROP was found in 26 infants (18.6%), and prethreshold type 2 ROP was found in 4 infants (3.1%). Twenty-six infants received treatment with either laser or intravitreal bevacizumab, and four of them progressed to ROP stage 4 or 5. The mean postmenstrual age at the last visit was 44.7 ± 5.1 weeks, and the average number of examinations was 6.4 ± 4.3 times per infant.

There were 102 infants who met the G-ROP screening criteria, as shown in Table 1. The G-ROP model predicted prethreshold type 1 ROP in 24 of 24 infants (sensitivity, 100%; 95% CI, 85.8–100) as same as AAO criteria of GA and BW shown in Table 2.

Furthermore, the G-ROP model detected all four prethreshold type 2 ROP infants with 100% sensitivity (95% CI, 39.8–100.0).

Of 27 infants who were not included in the G-ROP criteria, 25 of them did not have any retinopathy. Two infants had ROP (stage 1 zone 2 without plus disease and stage 2 zone 2 without plus disease), and they were all spontaneously regressed. The risk factor in both infants was apnea of prematurity. The reduction in infants receiving examinations according to the G-ROP protocol was 20.9%.

There were 22 infants screened due to the neonatologist's concern despite GA >30 weeks and BW >1500 g. None of them had type 1 or type 2 ROP. When applying postnatal weight gain G-ROP criteria to these infants, there were only 11 infants who met G-ROP as demonstrated in Table 3, and none of them had prethreshold type 1 or ROP.

Table 1: Demographic data of infants who met growth and retinopathy of prematurity criteria

	n (%)
GA <28 weeks	26 (25.5)
BW <1051 g	27 (26.5)
GA >28 weeks and birthweight>1051 g with	
Postnatal weight gain between days 10–19<120 g	24 (23.5)
Postnatal weight gain between days 20–29<180 g	21 (20.6)
Postnatal weight gain between days 30–39<170 g	3 (2.9)
Hydrocephalus	1 (1)
Total	102 (100)

G-ROP=Postnatal growth and retinopathy of prematurity, GA=Gestational age, BW=Birth weight

Discussion

This study was the first to validate the G-ROP prediction model in Thai infants and found 100% sensitivity in detecting presthreshold type 1 and 2 ROP, similar to the original G-ROP study.[4]

Apart from G-ROP, there are other weight gain-based ROP predictive models, such as Win-ROP,[7] Colorado ROP (CO-ROP),[8] and Children's Hospital of Philadelphia ROP (CHOP).[9] A major difference in each model is postnatal weight gain. Each model has its own alarming weight gain for screening. Win-ROP set an alarm at a weekly weight gain of <450 g/week whereas CO-ROP set an alarm at a weight gain in the first 28 weeks of <650 g. The CHOP algorithm used a daily weight gain, GA, and BW to plot on its nomogram to calculate risk. G-ROP had postnatal weight gain criteria that were different in number each week. The G-ROP model was recently

Table 2: Sensitivity, specificity, and reduction in the number of infants examined in each screening criteria

	G-ROP	GA ≤30 or BW ≤1500 g (AAO)
Type 1 ROP (*n*=24)		
Sensitivity		
95% CI	100.0 (85.8–100.0)	100.0 (85.8–100)
99% CI	100.0 (80.2–100)	100.0 (80.2–100)
Specificity (95% CI)	25.7 (17.7–35.2)	21.0 (13.6–30.0)
Type 2 ROP (*n*=4)		
Sensitivity		
95% CI	100.0 (39.8–100.0)	100.0 (39.8–100.0)
99% CI	100.0 (26.6–100)	100.0 (26.6–100)
Specificity (95% CI)	21.6 (14.7–29.8)	17.6 (11.4–25.4)
Reduction in infants receiving examinations (95% CI)	20.9 (14.3–29.0)	17.0 (11.0–24.7)

ROP=Retinopathy of prematurity, G-ROP=Postnatal growth and ROP, GA=Gestational age, BW=Birth weight, AAO=American Academy of Ophthalmology, CI=Confidence interval

Table 3: Infants who were not included American Academy of Ophthalmology's gestational age and birth weight criteria but met postnatal weight gain postnatal growth and retinopathy of prematurity criteria

	Total (*n*)	No ROP (*n*)	ROP (*n*)
Postnatal weight gain between days 10–19<120 g	8	7	1*
Postnatal weight gain between days 20–29<180 g	2	2	0
Postnatal weight gain between days 30–39<170 g	1	1	0

*Zone 2 stage 2 ROP without plus disease. ROP=Retinopathy of prematurity

developed and had 100% sensitivity in detecting ROP type 1, so we chose this model to apply to our patients. Nevertheless, there were some differences between the original G-ROP cohort study and ours. First, the original research was performed in North America where most subjects were Non-Hispanic White (49.4%), and postnatal weight gain may differ from Thai infants. Second, our overall incidence of ROP was similar to the G-ROP's but the proportion of presthreshold type 1 ROP infants in our study was triple as many as the original study (18.6% vs. 6.6%). Despite different subject characteristics, the G-ROP model could detect all presthreshold type 1 and 2 ROP in Thai infants.

There were several retrospective studies on G-ROP performed outside North America. Only a Japanese study[10] showed 100% sensitivity while studies from China (Lu 2023),[11] Saudi Arabia,[12] and Turkey[13] reported 96%, 96.7%, and 91.2% sensitivity, respectively. Nevertheless, G-ROP was considered a high-sensitivity test, this reflected the necessity of the validation of G-ROP before applying it to each population.

There were two missing ROP cases that did not meet G-ROP. Both of them were nontype 1 or 2 ROP which was spontaneously regressed. The G-ROP predicting model worked best in detecting type 1 and 2 ROP, but extended use to detect all ROP infants may require a clinician to consider risk factors in each patient.

Reducing unnecessary examinations is also essential, as dilated fundus examination can cause changes in vital signs and some adverse events such as apnea and hypoxia.[14,15] The benefit of adding postnatal weight gain criteria will help limit some cases that may not need screening. In this study, G-ROP criteria excluded 27 infants who did not meet its criteria, and none had prethreshold ROP. This criterion reduced approximately 50% of infants sent for screening due to the neonatologist's concern despite high GA and BW.

The major limitation of this study was the number of subjects that may affect some statistical interpretations. Furthermore, as it is a retrospective study, it may contain some selection bias, recall bias, and confounding factors. In the future, we plan to do prospective studies in these infants to avoid unnecessary examinations without missing any sight-threatening cases.

Conclusion

G-ROP model provided high sensitivity and lessen unnecessary examinations for ROP screening in Thai infants.

Data availability statement

The datasets generated during and/or analyzed during the current study are not publicly available due to the privacy of participants but are available from the corresponding author on reasonable request.

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Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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