The effect of postnatal weight gain and other risk factors on severe retinopathy of prematurity

Postnatal kilo alımı ve diğer risk faktörlerin şiddetli prematüre retinopatisi üzerindeki etkisi

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Abstract

Aim: To assess the effect of postnatal weight gain characteristics and multiple risk factors on treatment-required retinopathy of prematurity.

Methods: The medical records of preterm infants who were followed up for retinopathy of prematurity in a tertiary referral center were retrospectively reviewed. Infants were grouped as Treatment(-) (retinal maturation without treatment) and Treatment(+) (treatment required). Retinopathy of prematurity findings, weight gain and weight gain rates at the 4th and 6th weeks, and clinical features were noted. The best cut-off points for the weight gain and weight gain rate were assessed with the area under the receiver operating characteristic curve. Risk factors were determined by the logistic regression model.

Results: Twenty-eight of 201 preterm infants (13.5%) were in the treatment (+) group. Birth weight, gestational age, weight gain, and weight gain rate at the 4th and 6th weeks were lower, the duration of oxygen therapy and hospitalization was longer, and a history of bronchopulmonary dysplasia, necrotizing enterocolitis, prolonged mechanical ventilation, and erythrocyte transfusion was more common in the treatment (+) group ($p<0.05$). The best cut-off points (and area under the receiver operating characteristic curve) were calculated as 297.5 g (0.779) and 504.5 g (0.771) for weight gain and 21.02% (0.697) and 54.80% (0.670) for weight gain rates at the 4th and 6th weeks, respectively. History of bronchopulmonary dysplasia and prolonged mechanical ventilation were independently associated with severe retinopathy of prematurity.

Conclusion: Preterm infants with a history of low weight gain profile at the 4th week, bronchopulmonary dysplasia, and prolonged mechanical ventilation should be carefully monitored for the development of the treatment-required retinopathy of prematurity.

Keywords: Birth weight; bronchopulmonary dysplasia; mechanical ventilation; retinopathy of prematurity; weight gain

Öz

Amaç: Postnatal kilo alımı özelliklerinin ve çoklu risk faktörlerinin tedavi gerektiren prematüre retinopatisi üzerindeki etkisinin değerlendirilmesi.

Yöntemler: Üçüncü basamak bir sevk merkezinde prematüre retinopatisi nedeniyle takip edilen preterm infantların tıbbi kayıtları retrospektif olarak incelendi. İnfantlar Tedavi (-) (tedavisiz retinal matürasyon) ve tedavi (+) (tedavi gerekli) olarak gruplandırıldı. Prematüre retinopatisi bulguları, 4. ve 6. haftalardaki kilo alımı, kilo alımı oranları ve klinik özellikler not edildi. Kilo alımı ve kilo alımı oranı için en iyi kesim noktaları alıcı işletim karakteristik eğrisi altı alan ile değerlendirildi. Risk faktörleri lojistik regresyon modeli ile belirlendi.

Bulgular: İki yüz bir preterm infanttan 28'i (%13,5) tedavi (+) grubundaydı. Tedavi (+) grubunda doğum ağırlığı, gebelik yaşı, kilo alımı ile 4. ve 6. haftalardaki kilo alımı oranı daha düşük, oksijen tedavisi ve hastanede yatış süresi daha uzun ve bronkopulmoner displazi, nekrotizan enterokolit, uzamış mekanik ventilasyon ve eritrosit transfüzyonu öyküsü daha yaygındı ($p<0,05$). En iyi kesim noktaları (ve alıcı işletim karakteristik eğrisi altı alan) 4. ve 6. haftalardaki kilo alımı için sırasıyla 297,5 g (0,779) ve 504,5 g (0,771) ve kilo alımı oranları için %21,02 (0,697) ve %54,80 (0,670) olarak hesaplandı. Bronkopulmoner displazi öyküsü ve uzamış mekanik ventilasyon bağımsız olarak tedavi gerektiren prematüre retinopatisi ile ilişkiliydi.

Sonuç: Dördüncü haftada düşük kilo alımı profili, bronkopulmoner displazi ve uzamış mekanik ventilasyon öyküsü olan preterm infantlar tedavi gerektiren prematüre retinopatisi gelişimi açısından dikkatle izlenmelidir.

Anahtar Sözcükler: Ağırlık artışı; bronkopulmoner displazi; doğum ağırlığı; mekanik ventilasyon; prematüre retinopatisi

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INTRODUCTION

Retinopathy of prematurity (ROP) is an abnormal proliferative retinal vasculopathy that results from the relative ischemia of non-vascularized immature retinal areas in premature infants and may cause blindness in the advanced stages (1, 2). Therefore, it is necessary to determine the risk factors of patients carefully, perform their follow-up regularly, apply the appropriate treatment in a timely manner when necessary, and ensure continuous communication between the experienced and specialized ophthalmologist, neonatologist, and the infant's family in terms of ROP.

As a result of the studies conducted, it has been shown that premature birth is not a risk factor by itself, and ROP is a multifactorial disease. Low birth age and weight, application of high-concentration oxygen therapy in the neonatal intensive care unit (NICU), neonatal sepsis, erythrocyte transfusion (ET), history of bronchopulmonary dysplasia (BPD), perinatal asphyxia, intraventricular hemorrhage (IVH), apneic attacks, acidosis, and many other factors have been examined in terms of their role in the etiology of the disease (3-6). Some recent studies have shown that the weight gain of premature infants is effective on the incidence and stage of ROP (6-12). It has been shown that physiological weight gain during the postnatal period is related to serum Insulin-Like Growth Factor-1 (IGF-1) level, and it has been thought that low serum IGF-1 level in premature infants with very low birth weight is a risk factor for the development of ROP (1, 8, 13, 14). Although there have been studies associating weight gain with ROP, there are limited studies in which weight gain has been ratioed to birth weight, and this ratio has been associated with treatment-required ROP (15-18).

This study aims to retrospectively investigate the effects of weight gain characteristics during the neonatal intensive care unit (NICU) period and other risk factors on the development of the treatment-required ROP in premature infants enrolled in a screening and follow-up program for ROP in a tertiary referral center.

MATERIAL AND METHODS

The medical records of 207 infants who were hospitalized in the NICU of a tertiary referral center between September 2010 and September 2014 due to preterm birth and who were screened and followed up for ROP by an experienced ophthalmologist at the same center were retrospectively analyzed. All infants born in the 35th gestational week and/or with a birth weight under 1500 g and infants born after the 35th gestational week, for whom consultation had been requested by neonatologists because of the risk, were included in the study. The study was performed with the approval of the Bakirköy Dr. Sadi Konuk Educational and Research Hospital Clinical Research Ethics Committee (date: 12.12.2014, decision no: 2014-17-16), and the research protocol was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from the parents of the infants included in the study.

All previous ROP screening examinations had been scheduled according to the International ROP Classification, and all examination findings had been recorded according to the American Pediatric Ophthalmology and Strabismus Society criteria (19, 20). Infants were divided into two groups based on previous ROP examination findings: Cases who achieved retinal maturation without treatment were grouped as Treatment(-), whereas cases who required treatment due to the presence of Type 1 ROP or threshold ROP were grouped as Treatment(+).

Gestational age (in weeks), birth weight, duration of the NICU hospitalization, weekly weight gain, and the type and duration of oxygen therapy administered were obtained from medical records. Cases with a duration of mechanical ventilation >21 days were categorized as prolonged mechanical ventilation. Weight gain rates at the 4th and 6th weeks were calculated with the following formula:

*(actual weight at 4th or 6th week – birth weight) * 100 / birth weight*

Medical records of the cases were reviewed, and the history of necrotizing enterocolitis, sepsis, BPD, IVH, and ET were noted. The presence of intrauterine comorbidities such as oligo/polyhydramnios, multiple pregnancy, and maternal conditions were also collected from medical records. Cases with a history of pathologies that prevented weight gain, such as congenital gastrointestinal system anomalies, cases with pathologic weight gain profile, such as hydrocephalus

and massive edema, and cases with no weight gain data during the first postnatal period of 6 weeks, were excluded.

Statistical analyses

Statistical analysis was performed using the Statistical Package for the Social Sciences package program version 22.0 for Windows (SPSS Inc. Chicago, IL, USA). Continuous variables are presented as median and (interquartile range), and categorical variables are presented as numbers and (percentages). Pearson's chi-square test was used to compare categorical data, and continuous variables were compared with the Mann-Whitney U test. Receiver operator characteristic (ROC) curves were constructed for weight gain and weight gain rates in the 4th and 6th week, and the best cut-off values were determined based on specificity and sensitivity. The area under the ROC curve (AUC) was calculated. Binary logistic regression analysis was used to analyze the risk factors. $p<0.05$ was considered statistically significant.

RESULTS

Two hundred and one preterm infants were included in this study. The mean gestational age was 30.00 ± 2.59 weeks, and the mean birth weight was 1419.10 ± 415.61 g. During the follow-up period, 108 (53.7%) infants did not develop ROP, while ROP at any stage was observed in 93 (46.3%) infants. There were 173 infants (86.1%) in the Treatment(-) group and retinal maturation was completed without treatment in this group. The Treatment(+) group included 28 infants (13.9%) who received laser photocoagulation and/or intravitreal anti-vascular endothelial growth factor (anti-VEGF) treatment due to the presence of Type 1 ROP. None of the cases in the follow-up had ROP progression to stage 4 or above. Treatment(+) group had lower birth weight and gestational age compared to Treatment(-) group (p:0.002 and p:0.003, respectively) (Table 1).

The weight gain and weight gain rate in the 4th week were 370.00 (257.50) g and 27.80 (17.36) % in the Treatment (-) group and 222.50 (213.75) g and 19.54 (22.98) % in the Treatment (+) group ($p<0.001$ and p:0.001, respectively). The weight gain and weight gain rate at the 6th week were 760.00 (362.50) g and 55.56 (24.60) % in the Treatment (-) group and 495.00 (379.25) g and 44.25 (24.24) % in the Treatment (+) group ($p<0.001$ and p:0.004, respectively) (Table 1). According to ROC curve analysis, the best cut-off point of the weight gain in the 4th week was 297.5 g (67.6% sensitivity, 77.8% specificity, and the AUC was 0.776), and the best cut-off point of the weight gain in the 6th week was 504.5 g (86.7% sensitivity, 55.6% specificity, and the AUC was 0.771). When the weight gain rates were analyzed, the best cut-off point of the 4th week was 21.02% (70.5% sensitivity, 59.3% specificity, and the AUC was 0.694), while it was 54.80% (53.2% sensitivity, 74.1% specificity, and the AUC was 0.667) in the 6th week (Table 1) (Figure 1).

In terms of other risk factors, the presence of small for gestational age (SGA), IVH, sepsis, and maternal factors did not differ between the groups ($p>0.05$). In the Treatment(+) group, a history of BPD, necrotizing enterocolitis, and ET were more common, and the duration of NICU hospitalization was longer ($p<0.05$) (Table 2). The duration of all types of oxygen therapy was found to be longer in the Treatment(+) group ($p<0.05$), and the frequency of prolonged mechanical ventilation was higher in the Treatment(+) group ($p<0.001$) (Table 3). According to logistic regression analysis, BPD and prolonged mechanical ventilation statistically increased the risk of treatment-required ROP p:0.027 and p:0.047, respectively) (Table 4).

DISCUSSION AND CONCLUSION

Since ROP is one of the most preventable causes of blindness, guidelines have been established for the development of appropriate follow-up and screening programs. Many studies have been conducted to determine the risk factors that may be associated with ROP (5, 6, 21). Studies reporting the prevalence of ROP vary between 10% and 65% according to countries, socioeconomic and demographic characteristics, and inclusion criteria. In this study, the incidence of ROP development at any stage was 45.4%, and the incidence of ROP requiring treatment was 13.5%. In a multicenter study from Türkiye, the incidence was reported to be 30%, and in a recent multicenter study in the USA, this rate was reported to be 65.8% (22, 23).

Table 1. Comparison of the gestational age, birth weight, and weight gain characteristics between the groups.

	Treatment (-) n: 173 *median (IQR)*	**Treatment (+) n: 28** *median (IQR)*	***p****
Gestational age, week	30.00 (3.50)	28.50 (4.00)	**0.002**
Birth weight, g	1480.00 (605.00)	1155.00 (425.00)	**0.003**
4th-week weight gain, g	370.00 (257.50)	222.50 (213.75)	**<0.001**
4th-week weight gain rate, %	27.80 (17.36)	29.54 (22.98)	**0.001**
6th-week weight gain, g	760.00 (362.50)	495.00 (379.25)	**<0.001**
6th-week weight gain rate, %	55.56 (24.60)	44.25 (24.24)	**0.004**

n: Number of cases, IQR: Interquartile range, g: Gram, %: Percentage. *: Mann-Whitney U test. Bold p-values indicate statistical significance (p<0.05)

Table 2. Comparing the frequencies of risk factors between the groups.

	Treatment (-) n: 173	**Treatment (+) n: 28**	***p***
Maternal risk factor, n (%)	75 (43.4%)	12 (42.9%)	0.961*
Multiple gestations, n (%)	29 (16.8%)	3 (10.7%)	0.581**
Gender (female/male)	83/90	12/16	0.615*
Small for gestational age, n (%)	23 (13.3%)	4 (14.3%)	1.000**
Bronchopulmonary dysplasia, n (%)	63 (36.4%)	21 (75.0%)	**<0.001***
Necrotizing enterocolitis, n (%)	25 (14.5%)	11 (39.3%)	**0.001***
Erythrocyte transfusion, n (%)	67 (38.7%)	22 (78.6%)	**0.004***
Sepsis, n (%)	84 (48.6%)	19 (67.9%)	0.091*
Intraventricular hemorrhage, n (%)	36 (20.8%)	8 (28.6%)	0.500*
Prolonged mechanical ventilation, n (%)	15 (8.7%)	12 (42.9%)	**<0.001***

n: Number of cases, %: Percentage. *: Chi-squared test, **: Fisher's exact test. Bold p-values indicate statistical significance (p<0.05)

Table 3. Duration of oxygen therapies according to types and the duration of hospitalization in the groups

	Treatment (-) n: 173 *median (IQR)*	**Treatment (+) n: 28** *median (IQR)*	***p****
Duration of NICU hospitalization, days	38.00 (35.50)	74.00 (57.50)	**<0.001**
Invasive mechanical ventilation, days	1.00 (5.00)	10.50 (54.75)	**<0.001**
Nasal CPAP, days	3.00 (6.00	10.00 (15.00)	**<0.001**
Oxygen hood, days	4.00 (7.00)	9.50 (15.75)	**0.024**
Incubator oxygen, days	1.00 (4.00)	5.00 (9.75)	**0.002**

n: Number of cases, IQR: Interquartile range, NICU: Neonatal intensive care unit, CPAP: Continuous positive airway pressure, IQR: Interquartile range. *: Mann-Whitney U test. Bold p-values indicate statistical significance (p<0.05)

Table 4. Determination of the risk factors for treatment-required retinopathy of prematurity by logistic regression analysis.

	p	**Odds Ratio**	**95% CI**
Bronchopulmonary dysplasia	**0.027**	**3.096**	**1.139 – 8.413**
Necrotizing enterocolitis	0.143	2.314	0.735 – 7.104
Erythrocyte transfusion	0.122	2.204	0.810 – 5.998
Prolonged mechanical ventilation	**0.047**	**2.874**	**1.069 – 8.258**

CI: Confidence interval. Bold p-values indicate statistical significance (p<0.05).

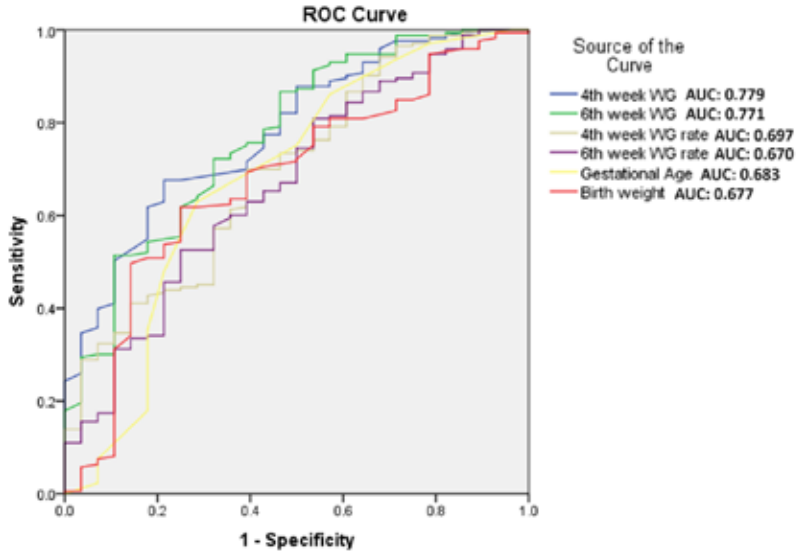

Figure 1. A graph demonstrating the area under the curve with the receiver operator characteristics (ROC) curves analysis of weight gain characteristics at 4th and 6th weeks, gestational age, and birth weight. WG: Weight gain, AUC: Area under the ROC curve

In this study, it is thought that a difference in incidence may have been detected because patients whose weight gain records could be obtained until the 6th week were included.

Many studies have been conducted to determine the risk factors of ROP, which is a multifactorial disease. Especially in the last two decades, studies have shown that birth weight and gestational age, as well as postnatal weight gain and serum IGF-1 levels, are effective on ROP development (8, 10, 13, 24-27). In addition, many prediction algorithms have been developed that include postnatal weight gain and/or IGF-1 level (6, 8, 27, 28). The IGF-1 production of preterm infants born before the 33rd gestational week is very slow until the 44th gestational week, and postnatal serum levels are regulated by total protein and caloric intake (10, 25). The WINROP (weight, IGF, neonatal ROP) algorithm described in 2006 aims to reduce the number of patients' examinations using weekly weight gain, IGF-1, IGFBP-3, birth weight, gestational age, and to detect the ROP development earlier (8). In another study conducted with the WINROP algorithm, it was observed that the algorithm gave the alarm in 319 of 407 patients, and it covered 45 of 47 (95.7%) patients who developed Type 1 ROP in the follow-up, and also by using the WINROP algorithm, it was thought that the number of painful and stressful examinations for preterm infants could be reduced by approximately 53% (29). In this study, the predictive efficacy of weight gain and weight gain rates at the 4th and 6th weeks were evaluated in terms of treatment-required ROP. However, recently published validation studies in various populations have reported controversial results regarding the ROP prediction of these algorithms (12, 17, 30-33). In the current study, weight gain and weight gain rates at both weeks 4 and 6 had statistically significant predictive efficacy. However, the accuracy of the weight gain and weight gain rate for the 4th week was higher than that for the 6th week. Furthermore, no superiority of weight gain rates compared to cumulative weight gain rates in terms of predicting ROP development was demonstrated. Filho et al. determined the best cut-off point for the weight gain proportion at the 6th week for the development of severe ROP in very low birth weight preterm infants as 51.2% and calculated the AUC for this proportion as 0.63 (34). This finding is consistent with the results found in the current study, and unlike the previous study, the rate of weight gain in the 4th week was also evaluated.

Low birth weight and low gestational age have been described as the primary risk factors for the development of ROP. In this study, lower birth weight and lower gestational age were observed in the Treat-

ment (+) group in accordance with previous studies. In addition to these risk factors, many studies have been conducted to define various risk factors for ROP, which is a multifactorial disease (6). However, controversial results have been reported in terms of other maternal and postnatal conditions. Considering clinical features of the preterm infants, although the history of ET, BPD, NEC, and prolonged mechanical ventilation were more frequent in the Treatment(+) group, only BPD and prolonged mechanical ventilation were associated with increased treatment requirement, as revealed by a logistic regression model with binary data showing statistical differences between the two groups. According to the results of a previous meta-analysis evaluating maternal blood pressure status, no evidence was found linking ROP to preeclampsia or eclampsia (35). Controversial results have also been reported in various studies examining the relationship between maternal glycemic status and ROP (36, 37). In the current study, the presence of both gestational diabetes and pre-eclampsia or eclampsia was defined as a "maternal risk factor", and no association of maternal blood pressure and/or glycemic status with severe ROP could be demonstrated. Prolonged oxygen therapy and the presence of BPD have been shown to be risk factors for ROP in previous studies (6). Consistent with previous findings, both BPD and mechanical ventilation for more than 21 days were found to be risk factors for ROP requiring treatment in the current study.

This study has some limitations. Since it was a single center, the number of cases, especially in the severe ROP group, was relatively small. However, it is thought that by including cases from a single center in the study, a standard intensive care process was obtained, and the effect of confounding factors originating from the NICU was minimized. In addition, a large series could not be reached due to the exclusion of cases without weight gain data until the 6th week and the exclusion of cases consulted for ROP follow-up from different NICU centers. Therefore, some of the cases with treatment-requiring ROP were excluded from the study. Although many of the cases included in the study had a history of oxygen therapy such as mechanical ventilation, nasal CPAP, etc., detailed information about the applied therapy (such as peak inspiratory pressure, respiratory rate, fraction of inspired oxygen level, target oxygen saturation) were not presented and analyzed in this study. The lack of information about the oxygen therapy administered can be considered a limitation of this study. However, as mentioned before, since the data were obtained from a single NICU, it can be considered that the oxygen therapy applied has certain standards. Another limitation of this study is that the data on weight gain were limited to postnatal 4th and 6th weeks. It was assumed that the death or NICU discharge of some cases would limit the sample size, especially the number of cases in the Treatment(+) group. Therefore, only the weight gain profiles of the first 6 weeks postpartum were evaluated in this study. Furthermore, the absence of an evaluation of blood levels of IGF-1, which is associated with postnatal weight gain, and the lack of specification of the components of oral or parenteral nutritional support can be considered additional limitations of this study.

In conclusion, the present study, which evaluated the weight gain and weight gain rates at the postnatal 4th and 6th weeks, demonstrated that the weight gain profile at the 4th week had a higher diagnostic efficiency in predicting treatment-requiring ROP compared to the 6th-week data. Moreover, the superiority of weight gain ratios over cumulative weight gain was not shown. In the evaluation of risk factors, it was revealed that prolonged mechanical ventilation and the history of BPD caused an independent increased risk for ROP requiring treatment. Future studies evaluating multiple risk factors and long-term weight gain profiles are needed.

Conflict-of-interest and financial disclosure

The authors declare that they have no conflict of interest to disclose. The authors also declare that they did not receive any financial support for the study.

REFERENCES

1. Hellström A, Smith LE, Dammann O. Retinopathy of prematurity. Lancet. 2013;382(9902):1445-57.
2. Sabri K, Ells AL, Lee EY, Dutta S, Vinekar A. Retinopathy of Prematurity: A Global Perspective and Recent Developments. Pediatrics. 2022;150(3):e2021053924.
3. Hardy RJ, Palmer EA, Dobson V, et al. Risk analysis of

prethreshold retinopathy of prematurity. Arch Ophthalmol. 2003;121(12):1697-701.
4. Bas AY, Demirel N, Koc E, et al. Incidence, risk factors and severity of retinopathy of prematurity in Turkey (TR-ROP study): a prospective, multicentre study in 69 neonatal intensive care units. Br J Ophthalmol. 2018;102(12):1711-6.
5. Darlow BA, Hutchinson JL, Henderson-Smart DJ, et al. Prenatal risk factors for severe retinopathy of prematurity among very preterm infants of the Australian and New Zealand Neonatal Network. Pediatrics. 2005;115(4):990-6.
6. Kim SJ, Port AD, Swan R, Campbell JP, Chan RVP, Chiang MF. Retinopathy of prematurity: a review of risk factors and their clinical significance. Surv Ophthalmol. 2018;63(5):618-37.
7. Hellström A, Ley D, Hansen-Pupp I, et al. New insights into the development of retinopathy of prematurity--importance of early weight gain. Acta Paediatr. 2010;99(4):502-8.
8. Löfqvist C, Andersson E, Sigurdsson J, et al. Longitudinal postnatal weight and insulin-like growth factor I measurements in the prediction of retinopathy of prematurity. Arch Ophthalmol. 2006;124(12):1711-8.
9. Wu C, Löfqvist C, Smith LE, VanderVeen DK, Hellström A; WINROP Consortium. Importance of early postnatal weight gain for normal retinal angiogenesis in very preterm infants: a multicenter study analyzing weight velocity deviations for the prediction of retinopathy of prematurity. Arch Ophthalmol. 2012;130(8):992-9.
10. Anuk İnce D, Gülcan H, Hanta D, et al. Poor postnatal weight gain predicts stage 3+ retinopathy of prematurity in very low birth weight infants. Turk J Pediatr. 2013;55(3):304-8.
11. Chaves-Samaniego MJ, Gómez Cabrera C, Chaves-Samaniego MC, et al. Multicenter validation study of the WINROP algorithm as a method for detecting retinopathy of prematurity. J Matern Fetal Neonatal Med. 2020;33(8):1302-6.
12. Thomas D, Madathil S, Thukral A, et al. Diagnostic Accuracy of WINROP, CHOP-ROP and ROPScore in Detecting Type 1 Retinopathy of Prematurity. Indian Pediatr. 2021;58(10):915-21.
13. Hellström A, Engström E, Hård AL, et al. Postnatal serum insulin-like growth factor I deficiency is associated with retinopathy of prematurity and other complications of premature birth. Pediatrics. 2003;112(5):1016-20.
14. Fu Y, Lei C, Qibo R, et al. Insulin-like growth factor-1 and retinopathy of prematurity: A systemic review and meta-analysis. Surv Ophthalmol. 2023;68(6):1153-65.
15. Sethi NK, Jain B, Gupta NR, Singh SP, Sethi G, Chadha C. Study to evaluate the relation between weight gain in infants and occurrence of retinopathy of prematurity. Indian J Ophthalmol. 2023;71(3):890-4.
16. VanderVeen DK, Martin CR, Mehendale R, et al. Early nutrition and weight gain in preterm newborns and the risk of retinopathy of prematurity. PLoS One. 2013;8(5):e64325.
17. Athikarisamy S, Desai S, Patole S, Rao S, Simmer K, Lam GC. The Use of Postnatal Weight Gain Algorithms to Predict Severe or Type 1 Retinopathy of Prematurity: A Systematic Review and Meta-analysis. JAMA Netw Open. 2021;4(11):e2135879.
18. Akın MŞ, Yiğit Ş. The effects of early nutritional contents in premature infants on the development and severity of retinopathy. Trends in Pediatrics. 2023;4:238-6.
19. Fierson WM; American Academy of Pediatrics Section on Ophthalmology; American Academy of Ophthalmology; American Association for Pediatric Ophthalmology and Strabismus; American Association of Certified Orthoptists. Screening Examination of Premature Infants for Retinopathy of Prematurity. Pediatrics. 2018;142(6):e20183061.
20. International Committee for the Classification of Retinopathy of Prematurity. The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol. 2005;123(7):991-9.
21. Kavurt S, Yücel H, Hekimoğlu H, Baş AY, Demirel N, Türkbay D. Prematüre retinopatisi gelişen olgularda risk faktörlerinin değerlendirilmesi. Çocuk Sağlığı ve Hastalıkları Dergisi. 2012;55(3):125-31.
22. Bas AY, Koc E, Dilmen U; ROP Neonatal Study Group. Incidence and severity of retinopathy of prematurity in Turkey. Br J Ophthalmol. 2015;99(10):1311-4.
23. Palmer EA, Flynn JT, Hardy RJ, et al. Incidence and Early Course of Retinopathy of Prematurity. Ophthalmology. 2020;127(4S):S84-96.
24. Wallace DK, Kylstra JA, Phillips SJ, Hall JG. Poor postnatal weight gain: a risk factor for severe retinopathy of prematurity. J AAPOS. 2000;4(6):343-7.
25. Engström E, Niklasson A, Wikland KA, Ewald U, Hellström A. The role of maternal factors, postnatal nutrition, weight gain, and gender in regulation of serum IGF-I among preterm infants. Pediatr Res. 2005;57(4):605-10.
26. Çetinkaya M, Köksal N, Özkan H, Özmen AT. Prematüre Retinopatisi ile Serum İnsülin Benzeri Büyüme Faktörü-1 Düzeyleri Arasındaki İlişki. Güncel Pediatri. 2008;6(4):47-52.

27. Binenbaum G, Ying GS, Quinn GE, et al. The CHOP postnatal weight gain, birth weight, and gestational age retinopathy of prematurity risk model. Arch Ophthalmol. 2012;130(12):1560-5.
28. Binenbaum G. Algorithms for the prediction of retinopathy of prematurity based on postnatal weight gain. Clin Perinatol. 2013;40(2):261-70.
29. Sun CS. Relation of target SpO2 levels and clinical outcome in ELBW infants on supplemental oxygen. Pediatr Res. 2002;51:305A.
30. Fares A, Abdelmonaim S, Sayed D, et al. Validation of WINROP algorithm as screening tool of retinopathy of prematurity among Egyptian preterm neonates. Eye (Lond). 2024;38(8):1562-6.
31. Desai S, Athikarisamy SE, Lundgren P, Simmer K, Lam GC. Validation of WINROP (online prediction model) to identify severe retinopathy of prematurity (ROP) in an Australian preterm population: a retrospective study. Eye (Lond). 2021;35(5):1334-9.
32. Bai YC, Wu R, Chen SZ, et al. Efficacy of the WINROP algorithm for retinopathy of prematurity screening in Southern China. Int J Ophthalmol. 2021;14(1):127-32.
33. Ekinci DY, Bayraktar H, Sero OL, Okur N. Retrospective validation of the postnatal growth and retinopathy of prematurity (G-ROP) and Colorado retinopathy of prematurity (CO-ROP) models in a Turkish cohort. Turk J Pediatr. 2023;65(3):398-405.
34. Fortes Filho JB, Bonomo PP, Maia M, Procianoy RS. Weight gain measured at 6 weeks after birth as a predictor for severe retinopathy of prematurity: study with 317 very low birth weight preterm babies. Graefes Arch Clin Exp Ophthalmol. 2009;247(6):831-6.
35. Zhu T, Zhang L, Zhao F, Qu Y, Mu D. Association of maternal hypertensive disorders with retinopathy of prematurity: A systematic review and meta-analysis. PLoS One. 2017;12(4):e0175374.
36. Bental Y, Reichman B, Shiff Y, et al. Impact of maternal diabetes mellitus on mortality and morbidity of preterm infants (24-33 weeks' gestation). Pediatrics. 2011;128(4):e848-55.
37. Tunay ZÖ, Özdemir Ö, Acar DE, Öztuna D, Uraş N. Maternal Diabetes as an Independent Risk Factor for Retinopathy of Prematurity in Infants With Birth Weight of 1500 g or More. Am J Ophthalmol. 2016;168:201-6.