

The Effect of Prematurity on Refraction and Keratometric Measurements: Observational Research

Prematüritenin Kıırma Kusurları ve Keratometrik Ölçümler Üzerine Etkisi: Tanımlayıcı Araştırma

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ABSTRACT Objective: To compare refraction and keratometry measurements between preterm and full-term infants and to evaluate the possible effect of postmenstrual age (PMA) and birth weight (BW) on these parameters. **Material and Methods:** Fifty eight preterm infants (Group I) and 57 term infants (Group II) were enrolled. Each subject underwent ophthalmic examination and the results were recorded. **Results:** The study included 115 infants with a mean birth week of 35.17±3.96 weeks and a BW of 2510.70±896.72 g. Examination was performed at a mean PMA of 42.17±4.21 weeks in Group I and 46.18±3.12 weeks in Group II. The keratometry values of the groups were 47.88±3.19 diopters (D) in Group I and 45.70±3.38 D in Group II, respectively. Corneal refractive power of preterm infants was found to be significantly higher than full-term infants ($p=0.001$). Inverse relationship was found between PMA and keratometry value in preterm infants ($p<0.001$, $\beta=-0.63$), and between PMA and BW and keratometry values in term infants ($p=0.03$, $\beta=-0.28$ for PMA, $p=0.02$, $\beta=-0.30$ for BW). In addition, preterm infants were significantly more myopic than full-term infants ($p=0.009$). **Conclusion:** In conclusion, this study supports that myopic shift, as well as the steep and refractive corneas, are significantly associated with the prematurity.

Keywords: Retinopathy of prematurity; keratometry; refractive outcome; myopia; term birth

ÖZET Amaç: Bu çalışmanın amacı, preterm ve term yenidoğanların refraksiyon ve keratometri ölçümlerini karşılaştırmak ve postmenstrüel yaş (PMY) ve doğum ağırlığının (DA) bu parametreler üzerindeki olası etkisini değerlendirmektir. **Gereç ve Yöntemler:** Elli sekiz prematüre (Grup I) ve 57 term (Grup II) yenidoğan çalışmaya dâhil edildi. Tüm yenidoğanlara detaylı göz muayenesi yapılarak sonuçlar kaydedildi. **Bulgular:** Çalışmaya ortalama doğum haftası 35,17±3,96 hafta ve doğum ağırlığı 2510,70±896,72 g olan 115 yenidoğan dâhil edildi. Ortalama postmenstrüel muayene haftası Grup I'de 42,17±4,21 hafta, Grup II'de ise 46,18±3,12 hafta idi. Grupların keratometri değerleri sırasıyla Grup I'de 47,88±3,19 diyoptri (D) ve Grup II'de 45,70±3,38 D idi. Prematüre yenidoğanların korneal kıırma gücü, term yenidoğanlardan anlamlı olarak yüksek bulundu ($p=0.001$). Prematüre yenidoğanlarda PMY ile keratometri değeri arasında ($p<0.001$, $\beta=-0.63$), term yenidoğanlarda PMY ile DA ve keratometri değerleri arasında ters yönlü ilişki tespit edildi (PMY için $p=0.03$, $\beta=-0.28$, $p=0.02$, DA için $\beta=-0.30$). Ek olarak prematüre yenidoğanlar, term yenidoğanlara göre anlamlı olarak daha miyop idi ($p=0.009$). **Sonuç:** Sonuç olarak bu çalışma, dik ve kıırıcı korneaların yanı sıra miyopik kıırma kusurunun prematürite ile önemli ölçüde ilişkili olduğunu desteklemektedir.

Anahtar Kelimeler: Prematüre retinopatisi; keratometri; kıırma kusuru; miyop; term doğum

Premature infants have more refractive errors and other ocular problems than full-term infants regardless of prior retinopathy of prematurity (ROP).^{1,2} In addition, the risk of myopia and other refractive errors is seen more frequently in baby who had se-

vere ROP that require treatment compared to baby born premature, which increases the risk of amblyopia.³⁻⁵ Although studies investigating refractive errors in premature infants show a predisposition to childhood myopia early in life, the mechanisms un-

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Peer review under responsibility of Türkiye Klinikleri Journal of Ophthalmology.

Received: 04 Jul 2023

Received in revised form: 13 Sep 2023

Accepted: 14 Sep 2023

Available online: 20 Sep 2023

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derlying myopia are not clearly understood.⁶ Several risk factors including increased corneal refractive power, axial elongation, decreased anterior chamber depth and high refractive power of the lens can be listed among the underlying mechanisms in the development of myopia.⁷⁻⁹ Most studies in the literature comparing refractive status and keratometric values in preterm and term infants have pointed out the possible role of corneal refractive power in the development of refractive errors.¹⁰⁻¹² The purpose of this study was to compare refraction and keratometry measurements between preterm and full-term infants and to evaluate the possible association of postmenstrual age (PMA) and birth weight (BW) on these parameters.

MATERIAL AND METHODS

The cross-sectional study approved by Etlik Zübeyde Hanım Maternity and Women's Health Training and Research Ethical Review Committee (date: August 6, 2022; no: 11), and adhered to the tenets of the Declaration of Helsinki for research involving human subjects. Informed consent was obtained from all parents. Preterm and full-term infants who underwent ophthalmic examination at the hospital or referred to us from external centers for ROP examination between April 2022 to May 2022 were evaluated. Neonates with severe systemic or syndromic disease, anterior segment pathology that will affect fundus examination and inadequate data were excluded from the study.

According to the gestational age (GA), preterm infants between 26-36 weeks classified as Group I (n=58), and full-term infants between 37-41 weeks were classified as Group II (n=57). The infants' GA, BW, ROP stages and zones and type of treatment in infants requiring treatment were recorded.

According to the national screening guideline, premature infants with $GA < 34$ weeks and $BW \leq 1,700$ g or $GA \geq 34$ weeks and $BW > 1,700$ g, whose clinical condition was unstable, were screened for ROP. The first ROP screening was performed 4 to 6 weeks after birth with dilated pupils. At one hour before examination, the pupils were dilated using 0.5% tropicamide (Tropamid, Bilim İlaç, Türkiye) and 2.5% phenylephrine (Mydfrin, Alcon, USA), which were

administered every 5 min, 2 or 3 times until the pupils were dilated. Topical anesthesia was performed by applying 0.5% proparacaine hydrochloride (Alcaine, Alcon, USA) just before the examination. First, refractive errors and keratometry measurements were evaluated with automated refractometer/keratometer (Handy-Ref-K, Nidek Inc, Aichi, Japan) in the supine position. Considering the effect of the lid speculum on the measurements, the measurements were made by gently opening the lids. All patients' spherical and cylinder power as well as spherical equivalent (SE) and keratometry values were recorded as diopters (D). Then, posterior pole (optic disc and macula) and peripheral retina examination were performed using a binocular indirect ophthalmoscope and a 20-diopter lens using a pediatric eye speculum and scleral depressor. During or after any of the examination sessions, no ocular or systemic complication occurred. The frequency of seeing premature infants during follow-up was planned according to the presence and severity of ROP.

ROP stages of each subject were decided according to the criteria of the International ROP Classification Committee.¹³ According to the ETROP study, laser photocoagulation (LPC) was performed in infants with type I ROP and intravitreal bevacizumab (IVB) therapy was performed in infants with A-ROP.¹⁴

Statistical analysis were performed with SPSS (SPSS Inc., Chicago, Illionis, USA) version 25.0. Data from the right eye were used in the analysis, as the Pearson coefficients showed strong correlations between eyes. Categorical data were presented as numbers (n) and percentage (%) and descriptive data as mean±standard deviation. Chi-square test was used in the analysis of categorical data. The Kolmogorov-Smirnov test was used to test the normality of the distribution of continuous variables. The t test was used for pairwise comparisons of normally distributed data, and the Mann-Whitney U test was used for pairwise comparisons of non-normally distributed data. The relationship between keratometry values and demographic and clinical characteristics was evaluated using linear regression analysis. p values of 0.05 or less were considered statistically significance.

RESULTS

The study included 115 infants with a mean birth week of 35.17 ± 3.96 weeks (26 to 41 weeks) and a BW of 2510 ± 896 g (770-44,500 g). Examination was performed at a mean PMA of 42.17 ± 4.21 weeks (36-53 weeks) in Group I and 46.18 ± 3.12 weeks (41-55 weeks) in Group II. There was a statistically significant difference between the groups for GA, BW and PMA at examination ($p < 0.001$, $p < 0.001$ and $p = 0.000$, respectively).

ROP was detected in 24 of 58 patients (41.3%) in the preterm group. Fourteen of them (58.3%) had Stage 1 ROP and 10 (41.7%) had Stage 2 ROP. There were no patients with Stage 3 ROP. There were no

patients treated with IVB and LPC. Table 1 shows the demographic data and ROP findings of the infants.

Spherical, cylindrical and SE values were 1.18 ± 2.56 D; -2.44 ± 1.46 D and -0.04 ± 2.84 D in Group I and 2.36 ± 2.15 D; -2.13 ± 1.04 D and 1.30 ± 2.21 D in Group II, respectively ($p = 0.009$, $p = 0.379$ and $p = 0.006$). Preterm infants were significantly less hyperopic than full-term infants ($p = 0.009$) (Table 2).

The mean keratometry values of the groups were 47.88 ± 3.19 D (40.75-54.50 D) in Group I and 45.70 ± 3.38 D (39.25-54.25 D) in Group II, respectively. Corneal refractive power of preterm infants was found to be significantly higher than full-term

TABLE 1: Demographic data and ROP findings of infants.

		Group 1 (n=58)	Group 2 (n=57)	p value
Gender	Female (n, %)	36 (62.1)	25 (43.9)	0.05*
	Male (n, %)	22 (37.9)	32 (56.1)	
Gestational age (weeks)	$\bar{X} \pm SD$ (Range)	31.79 ± 2.46 (26-36)	38.60 ± 1.39 (37-41)	<0.001**
Birth weight (g)	$\bar{X} \pm SD$ (Range)	1796.98 ± 617.02 (770-3800)	3236.93 ± 430.11 (2480-4450)	<0.001**
PMA at examination (weeks)	$\bar{X} \pm SD$ (Range)	42.17 ± 4.21 (36-53)	46.18 ± 3.12 (41-55)	0.000**
ROP (n, %)	ROP (+)	24 (41.3)	-	
	ROP (-)	34 (58.7)	-	
Zone (n, %)	Zone II	18 (75)	-	
	Zone III	6 (25)	-	
Stage (n, %)	Stage I	14 (58.3)	-	
	Stage II	10 (41.7)	-	

*Chi-square test; **Mann-Whitney U test; ROP: Retinopathy of prematurity; PMA: Postmenstrual age; SD: Standard deviation.

TABLE 2: Keratometry and refraction values of groups.

		Group 1 (n=58)	Group 2 (n=57)	p value
Spherical (D)	$\bar{X} \pm SD$ (Range)	1.18 ± 2.56 (-6.50 to 5.50)	2.36 ± 2.15 (-1.50 to 7.75)	0.009*
Cylindrical (D)	$\bar{X} \pm SD$ (Range)	-2.44 ± 1.46 (-6.75 to 0.25)	-2.13 ± 1.04 (-4.50 to -5.50)	0.379*
SE (D)	$\bar{X} \pm SD$ (Range)	-0.04 ± 2.84 (-9.88 to 4.38)	1.30 ± 2.21 (-2.63 to 7.00)	0.006*
Keratometry value (D)	$\bar{X} \pm SD$ (Range)	47.88 ± 3.19 (40.75 to 54.50)	45.70 ± 3.38 (39.25 to 54.25)	0.001*

*Student-t test; SE: Spherical equivalent; SD: Standard deviation; D: Diopter.

infants ($p=0.001$). Keratometry and refraction values are presented in Table 2.

According to the development of ROP, there was no significant difference between the groups with and without ROP in terms of keratometry ($p=0.557$). According to the location of the ROP, the keratometry values in Zone II and Zone III infants were 47.54 ± 3.49 D (40.75-53.00) and 47.61 ± 4.58 D (42.75-54.50), respectively. According to the stage of the disease, the keratometry values in Stage I and Stage II infants were 47.14 ± 3.65 D (42.50-54.50) and 48.15 ± 3.97 D (40.75-53.00), respectively. No significant difference was found in preterm infants with ROP in terms of keratometry according to the location of ROP and the stage of the disease ($p>0.05$).

In univariate analysis, there was a significant association between PMA on examination and keratometric value ($p<0.001$, $\beta=-0.63$) in preterm infants, while a significant association was found between PMA ($p<0.001$, $\beta=-0.33$) and BW ($p<0.009$, $\beta=-0.34$) and keratometric values in term infants. No other correlation was detected between other variables and keratometry values for both groups. In the multivariate regression analysis performed in term newborns, it was observed that the relationship between PMA, BW and keratometry values continued significantly ($p=0.03$, $\beta=-0.28$ for PMA, $p=0.02$, $\beta=-0.30$ for BW). The relationship between PMA, BW and keratometry values of the groups is shown in Figure 1.

DISCUSSION

The increase in survival rates of premature infants due to developments in neonatal care causes an increase ROP and ROP-related refractive errors, strabismus and amblyopia.

Several studies in the literature show that myopia is more common in premature infants and is associated with lower BW, GA and ROP severity.^{7,8,15-18} Holmström et al. reported that the incidence of myopia and anisometropia was higher in premature infants compared to term infants, and this rate increased in infants with ROP.¹⁹ Choi et al. evaluated the long-term refraction results of premature infants with and without ROP and reported that 67.2% of the infants had myopia and 26.2% had severe myopia.⁷ In addition, it was reported that myopia in the premature group started to appear at the 6th month and gradually increased until the age of 3, and that eyes with ROP were more sensitive to these changes. Quinn et al. reported that myopic changes in premature infants started between 3 months and 1 year of age, but there was no significant change in the following period.²⁰ Therefore, they hypothesized that 3-month refraction values may be helpful in predicting the development of myopia in premature infants. Refractive errors in eyes with spontaneous regression of ROP are still controversial, and studies report that the frequency and severity of myopia are no different from eyes without ROP.^{21,22}

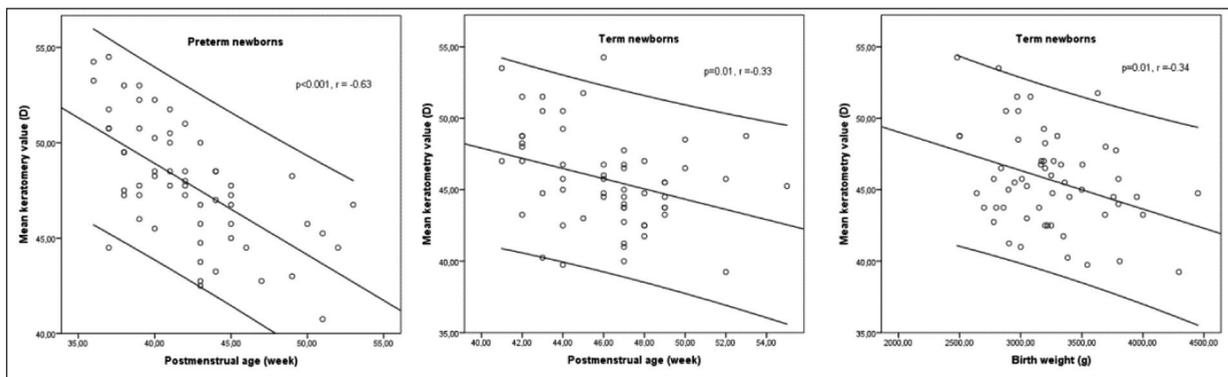


FIGURE 1: The relationship between PMA, BW and keratometry values of the groups.

PMA: Postmenstrual age; BW: Birth weight.

In the present study, significant lower SE values were observed in premature infants (-0.04 ± 2.84 D) compared to full-term infants (1.30 ± 2.21 D). Preterm infants were significantly more myopic than full-term infants ($p=0.006$). Although the ROP group was more myopic, there was no significant difference in myopic refraction between the groups ($p=0.088$). There were only infants with Stage I and Stage II ROP without plus disease in our study. Therefore, we may not have found a relationship between the development of ROP and myopic refraction.

The curvature of the cornea, which can be observed steep in full-term infants and steeper in premature infants, is a factor that affects refractive errors and visual acuity.^{9,12,23} In term babies, the flattening of the cornea after birth compensates for the axial elongation that occurs after birth. In their study on infants with ROP, Gallo and Fagerholm stated that there was a relationship between ROP and keratometry values and that high corneal refractive power played an important role in the development of myopia.²⁴

Although handheld keratometry is a device with high reproducibility and accuracy, difficulties experienced in the use of keratometers due to the movement of infants during the neonatal period have led to different results in studies.²⁵⁻²⁷ Ehlers et al. in their study comparing keratometry values, they found that the keratometry values of premature infants (53.13 D) were higher than those of full-term infants (47.50 D) and children aged 2-4 years (43.69 D).¹² Friling et al. reported that there was a relationship between BW, GA and keratometry values, and keratometry values were higher in preterm infants than in full-term infants.¹⁰ Snir et al. reported that 40-week-old infants with mild ROP were less hyperopic than term infants and their keratometry values were higher and steeper ($p=0.02$).¹¹ They stated that large corneal curvature in infants may affect the development of myopia. Inagaki et al. compared the keratometry values of premature and full-term infants with a mean GA of 36 weeks and found that the mean keratometric values of premature infants (49.5 D) were significantly higher than those of term infants (47.0 D) ($p<0.01$).⁹ Donzis et al. reported that corneal curvature was around 60 D in preterm infants and around 51 D in

term infants, with a decrease starting in the last months of gestation.²⁸

In our study, in accordance with the literature, the corneal refractive power of preterm infants (47.88 ± 3.19 D) was found to be significantly higher than that of full-term infants (45.70 ± 3.38 D). Additionally, there was no significant difference in terms of keratometry between the groups according to the presence of ROP. Similar to the study of Friling et al., there were only infants with Stage I and Stage II ROP without plus disease in our study, and no significant difference was shown in terms of keratometry values in preterm infants according to the location of ROP and the stage of the disease.¹⁰ On the other hand, inverse relationship was found between PMA and keratometry ($p<0.001$, $\beta=-0.63$) in preterm infants, while a significant association was found between PMA ($p<0.001$, $\beta=-0.33$) and BW ($p<0.009$, $\beta=-0.34$) and keratometry in term infants. The lower the PMA, the higher the keratometry values of the infants.

However, there are some limitations in our study. First, the number of infants included in our study was small. Second, ocular biometric values such as axial length, lenticular thickness, and anterior chamber depth were not available. Third, we did not have long-term data. Only refractive error and keratometry measurements were evaluated. Evaluating the development of myopia in premature infants using these parameters may be interesting. In addition the small number of advanced stages infants among the patients included in the study may have affected the measurement results.

CONCLUSION

In conclusion, this study supports that myopic shift, as well as the steep and refractive corneas, are significantly associated with the prematurity. Therefore, regular follow-up may be required in terms of myopic refractive error as the emmetropization process is affected in preterm infants.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that pro-

vides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Eşay Kıran Yenice; **Design:** Eşay Kıran Yenice, Caner Kara; **Control/Supervision:** Eşay Kıran Yenice, Caner Kara; **Data Collection and/or Processing:** Eşay Kıran Yenice; **Analysis and/or Interpretation:** Eşay Kıran Yenice, Caner Kara; **Literature Review:** Eşay Kıran Yenice; **Writing the Article:** Eşay Kıran Yenice; **Critical Review:** Eşay Kıran Yenice, Caner Kara; **References and Fundings:** Eşay Kıran Yenice, Caner Kara; **Materials:** Eşay Kıran Yenice, Caner Kara.

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