Ultrasonography Findings in Eyes With Stage 5 Retinopathy of Prematurity

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BACKGROUND AND OBJECTIVE: To evaluate ultrasonography outcomes in eyes with stage 5 retinopathy of prematurity (ROP).

PATIENTS AND METHODS: Patients with bilateral stage 5 ROP were evaluated retrospectively. Ultrasonography examination was performed in all cases. Patients’ demographic features and ultrasonography findings such as axial eye length, funnel configuration, subretinal hemorrhage, anterior loop traction, retinal cyst, and calcification were assessed, and correlations between variables were analyzed.

RESULTS: Three hundred eyes of 150 patients were included. Sixty-one patients (40.7%) were female. The mean gestational age was 28.8 weeks ± 2.6 weeks, and the mean birth weight was 1,277 g ± 360 g. The mean axial eye length was 14.7 mm ± 1.8 mm. Two hundred forty-five eyes (81.7%) had closed-closed retinal detachment configuration, 32 (10.7%) had open-closed retinal detachment configuration, 17 (5.7%) had open-open retinal detachment configuration, and six (2%) had closed-open retinal detachment configuration. Subretinal hemorrhage (25.7%), anterior loop traction (24%), retinal cyst (2.3%), and calcification (1.3%) were also observed.

CONCLUSION: Closed-closed funnel configuration, reduced axial diameter, and subretinal hemorrhage are associated with poor prognosis, and ocular ultrasonography examination for ascertaining these parameters is very important in cases with stage 5 ROP. In the present study, closed-closed retinal detachment configuration was noted in almost 80% of the cases with stage 5 ROP, which is probably the reason for the surgical failure in these end-stage cases.

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INTRODUCTION

In 2010, an estimated 11.1% of all live births (14.9 million babies) were born preterm worldwide. Improved neonatal care has resulted in improved survival of very premature infants, but the increasing immaturity of these infants has left them at a much higher risk of developing retinopathy of prematurity (ROP).²-⁴

ROP is a vasoproliferative disorder of the retina that may result in significant loss of vision.²,⁵ The disease is characterized by an abnormal retinal vascularization process that depends mainly on the degree of prematurity at birth.⁶ Population-based studies have reported the incidence of severe retinopathy of ROP as between 5% and 35%.⁷,⁸ ROP may regress spontaneously or cause minimal sequelae in mild cases, or it may progress to retinal detachment in more advanced cases.⁹ Timely screening and early retinal ablation in premature infants at risk is the most important step in preventing progression to advanced stages of ROP.¹⁰,¹¹ Despite timely treatment, however, a subset of patients tends to progress to retinal detachment,¹¹,¹² and despite advances in vitreoretinal surgery techniques, anatomical and functional outcomes for stage 5 ROP are worst among all the detachments.¹³ Globally, at least 50,000 children are blind as a result of ROP.¹⁴

Dilated fundus examination using binocular indirect ophthalmoscopy is recommended to ascertain the severity of the disease.¹⁵,¹⁶ Although retinal examination with indirect ophthalmoscopy is sufficient in most cases, ultrasonography examination...
is essential for ascertaining the retinal detachment funnel configuration in cases with stage 5 ROP for deciding upon the surgical approach and identifying the additional findings.\textsuperscript{17-19}

The main purpose of the study was to evaluate the ultrasonography outcomes in eyes with bilateral stage 5 ROP. A secondary aim was to assess the correlation between variables.

**PATIENTS AND METHODS**

The medical records of patients with bilateral stage 5 ROP who underwent ultrasonography imaging at the Istanbul Retina Institute, Istanbul, Turkey, between September 1998 and November 2014 were evaluated retrospectively. Eyes with history of any other diagnosis were not included. Three hundred eyes of 150 patients were eligible for inclusion. The research followed the tenets of the Declaration of Helsinki.

All of the infants were examined after pupillary dilation using binocular indirect ophthalmoscopy and a 28 diopter lens with a lid speculum by ophthalmologists (MK, SA, HO) experienced in examining preterm infants for ROP. All detachments were classified according to the International Classification of ROP.\textsuperscript{15,16}

Ultrasonography imaging was performed in eyes with stage 5 ROP to determine funnel configuration,

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**Figure 1:** (A) Closed anterior and posterior funnel configuration. (B) Open anterior and closed posterior funnel configuration. (C) Open anterior and posterior funnel configuration. (D) Closed anterior and open posterior funnel configuration.
axial length, and other characteristics by a skilled radiologist with experience in ocular ultrasound (CY). A Siemens Sonoline Elegra ultrasound system with a 7.5 L40 linear array probe (Siemens Medical Systems, Erlangen, Germany) was used between September 1998 and December 2005, and Siemens ACUSON Antares ultrasound system with a VFX 13-5 transducer (Multi-D matrix linear array transducer) and a VFX 9-4 transducer (Multi-D matrix linear array transducer; both Siemens Medical Systems, Erlangen, Germany) was used between January 2006 and November 2014.

Data on sex, gestational age, birth weight, and funnel configuration, as well as additional findings such as axial length, subretinal hemorrhage, anterior loop traction, retinal cyst, and calcification, were collected from medical records, and data for all 300 eyes were used for statistical analysis. Descriptive statistical methods (mean, standard deviation) were used for descriptives such as gestational age, birth weight, and axial length, and frequency tables were used for funnel configuration, subretinal hemorrhage, anterior loop traction, cysts, and calcification. One-way analysis of variance with Tamhane post hoc test, Pearson’s chi-square test, and independent sample t test were also used to

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**TABLE 1**

**Patients’ Demographic Characteristics**

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Eyes</td>
<td>300</td>
</tr>
<tr>
<td>Sex (Female/Male)</td>
<td>61/89</td>
</tr>
<tr>
<td>Mean Gestational Age, SD, Weeks</td>
<td>28.8±2.6</td>
</tr>
<tr>
<td>Mean Birth Weight, SD, grams</td>
<td>1,277±360</td>
</tr>
</tbody>
</table>

*SD = standard deviation*

**TABLE 2**

**Patients’ Ultrasonography Findings**

<table>
<thead>
<tr>
<th>Mean Axial Length, SD, mm</th>
<th>14.7±1.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subretinal Hemorrhage, Number (%)</td>
<td>77 (25.7)</td>
</tr>
<tr>
<td>Anterior Loop Traction, Number (%)</td>
<td>72 (24)</td>
</tr>
<tr>
<td>Retinal Cyst, Number (%)</td>
<td>7 (2.3)</td>
</tr>
<tr>
<td>Calcification, Number (%)</td>
<td>4 (1.3)</td>
</tr>
</tbody>
</table>

*SD = standard deviation*
evaluate how funnel configurations were associated with demographic characteristics and additional ultrasonography findings. Statistical analyses used SPSS Version 20.0 (SPSS, Chicago, IL), and a P value of less than .05 was considered statistically significant.

RESULTS

Three hundred eyes of 150 patients were included. There were 61 females (40.7 %) and 89 males (59.3 %), with a mean gestational age of 28.8 weeks ± 2.6 weeks and a mean birth weight of 1,277 g ± 360 g.

Demographic characteristics and ultrasonography findings of patients are summarized in Table 1 and Table 2, respectively. Retinal detachment funnel configurations are shown in Table 3. Doppler ultrasonography images are also presented (Figures 1A-D, Figures 2 and 3).

The study failed to demonstrate a correlation between funnel configuration and sex, gestational age, birth weight, or axial length (P = .45, P = .45, P = .17, and P = .91, respectively). There was a statistically significant correlation between gestational age and birth weight (P = .01). Although there was a statistically significant correlation between birth weight and axial length (Figure 4), the correlation was not strong (P = .018; r = 0.15). No statistically significant correlation between gestational age and axial length was observed (P = .32).

Patients with anterior loop traction had shorter axial length (Figure 5) and higher birth weight, but there was no statistically significant difference (P = .33 and P = .44, respectively). There was also no statistically significant correlation between subretinal hemorrhage and axial length (P = .60). Twenty females (16.4%) and 52 males (29.2%) had anterior loop traction, and there was a statistically significant difference between the two groups (P = .01).

<table>
<thead>
<tr>
<th>Funnel Configuration</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-C</td>
<td>245 (81.7)</td>
</tr>
<tr>
<td>O-C</td>
<td>32 (10.7)</td>
</tr>
<tr>
<td>O-O</td>
<td>17 (5.7)</td>
</tr>
<tr>
<td>C-O</td>
<td>6 (2)</td>
</tr>
</tbody>
</table>

C-C = closed anterior and posterior; O-C = open anterior and closed posterior; O-O = open anterior and posterior C-O = closed anterior and open posterior

Figure 3. Closed anterior and posterior funnel configuration with anterior loop traction.
DISCUSSION

Ultrasonography examination is necessary for ascertaining the retinal detachment funnel configuration in cases with stage 5 ROP in order to determine the surgical approach because funnel configuration is known to be associated with prognosis (19% success in a closed funnel vs. 81% success in an open funnel).17-20 We found 81.7% of eyes had the anterior and posterior closed funnel configuration, in comparison to 28.8% in a study by Jabbour et al.21 and 19% by Maidana et al.17 Similar to the findings in present study, the anterior and posterior closed funnel configuration was found in 81.3% of the eyes in a study by Gobal.20 The open anterior and closed posterior funnel configuration was found in 65% of the eyes in a study by Pulido et al.18 and in 31% of the eyes in the study by Maidana et al.17 In the present study, 10.7% of the eyes had the open anterior and closed posterior funnel configuration. Jabbour et al.21 and De Juan et al.22 found 3% and 12% of the eyes had open posterior and closed anterior retinal detachment configuration, respectively, in comparison to the 2% found in the present study.

Because our clinic is a tertiary referral center for retinal diseases in Turkey, a relatively high proportion of infants had advanced stages of ROP. We observed that referred infants who had inadequate treatment or screening had a higher rate of the closed anterior and posterior funnel configuration than what was found in other studies.17,21

The overall eye size, as shown by in utero ultrasound investigations, increases significantly at 16 to 20 weeks, 28 to 32 weeks, and finally after 37 weeks of gestational age,23 and the average newborn’s eyeball is about 16 mm in diameter from front to back.24 Axial length was inversely related to increasing stage of ROP: the higher the maximum stage of ROP reached, the shorter the axial length.25 In this study, the mean axial length was shorter than for at-term infants, similar to other studies.17,25

Subretinal hemorrhage can arise from the retinal circulation in any vascular abnormality. Released toxins, outer retinal shear forces, and a diffusion barrier created by subretinal hemorrhage all contribute to photoreceptor damage.26 Therefore, patients with subretinal hemorrhage have poor prognosis.17,26 Subretinal hemorrhage has been found in 9% to 47% of eyes.13,18,21,22 In the present study, the percentage of eyes with subretinal hemorrhage was 25.7%. Although patients with subretinal hemorrhage have poor prognosis, patients with anterior loop traction have relatively better prognosis.14 Anterior loop traction has been reported in 16% to 44% of eyes.17,18,21,22 The rate of anterior loop traction in the present study was 24%, similar to the findings of previous studies. The incidence of calcification (1.3%) was lower than that reported by Pulido et al. (4%).18

In conclusion, ROP continues to be a significant problem in premature infants. Because ultrasonography findings such as closed-closed funnel configuration, reduced axial diameter, and subretinal hemorrhage are associated with poor prognosis, a careful ocular ultrasonography examination to determine these prognostic parameters is very important. The largest case series in the literature pointed out that closed-closed retinal detachment configuration compromised almost 80% of the cases, confirming worse anatomical and functional results of surgery for stage 5 ROP patients.
REFERENCES


