Retinopathy of Prematurity Screening in a Tertiary Hospital in The South-East Region of Turkey: Prevalence and Relation with Multiple Pregnancies

Güneydoğu Anadolu Bölgesindeki 3. Basamak Hastanede Premature Retinopatisi Taraması: Prevalans ve Çoğul Gebelikle İlişkisi

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ABSTRACT

Purpose: To determine the prevalence of retinopathy of prematurity (ROP) and effects of multiple pregnancies on ROP in the southeast region of Turkey.

Materials and Methods: The records of premature infants examined in ophthalmology department of Gaziantep University were included in this retrospective study. Infants with gestational age (GA) ≤32 weeks or birth weight (BW) ≤1500 g were included. Multiple pregnancies were recorded separately.

Results: We included 1396 eyes of 698 preterm infants in our study. The mean BW of the infants without ROP was 1380.44 ± 265.52 g while the mean BW of the patients with any stage ROP was 1221.7 ± 264.97 g (P < 0.001). The mean GA of the infants without ROP was 30.6 ± 1.98 weeks while the mean GA of the patients with any stage ROP was 29.2 ± 2.17 weeks (P < 0.001). Stage of ROP worsened as the BW (P < 0.001) and GA decreased (P < 0.001). Multiple gestation didn't affect the presence of ROP (P = 0.306).

Conclusion: ROP prevalence in the southeast region of Turkey is similar to the western areas. Low BW and low GA are risk factors for the development of ROP. In our study, multiple pregnancy didn't increase the ROP prevalence.

Key words: Retinopathy of prematurity, multiple pregnancy, Retinopathy of prematurity prevalence.

ÖZ

Amaç: Güneydoğu Anadolu bölgesinde prematüre retinopatisi (PR) prevalansının tespit edilmesi ve çoğul gebeliğin PR üzerine etkisinin araştırılması.

Gereç ve Yöntemler: Bu retrospektif çalışmada Gaziantep Üniversitesi Tıp Fakültesi Göz Hastalıkları Bölümü'nde muayene edilen prematüre bebeklerin dosyaları tarandı. Gestasyonel yaşı (GY) ≤32 hafta ve doğum ağırlığı (DA) ≤1500 g olan prematüre bebekler çalışmaya dahil edildi. Çoğul gebelikler ayrıca kayıt edildi.

Bulgular: Çalışmamıza 698 prematüre bebeğin 1396 gözü dahil edildi. Taranan bebeklerin 445 (%63.8)'inde PR tespit edilmezken 253 (%36.2)'ünde herhangi bir evre PR mevcuttu. PR tespit edilmeyen bebeklerin ortalama DA 1380.44 ± 265.52 g iken, herhangi bir evre PR tespit edilen bebeklerin DA 1221.7 ± 264.97 g'dı (p<0.001). PR tespit edilmeyen bebeklerin ortalama GY 30.6 ± 1.98 hafta iken, herhangş bşr evre PR tespit edilen bebeklerin GY 29.2 ± 2.17 haftaydı (p<0.001). DA (p<0.001) ve GY (p<0.001) azaldıkça PR evresinin kötüleştiği görüldü. Çoğul gebeliğin PR prevalansını etkilemediği görüldü (p=0.306).

Sonuç: Güneydoğu Anadolu bölgesinde tespit edilen PR prevalansı batıdaki sonuçlarla benzerlik göstermektedir. Düşük DA ve düşük GY, PR gelişimi için risk faktörleridir. Çalışmamızda çoğul gebelik PR prevalansını etkilememiştir.

Anahtar Kelimeler: Prematüre Retinopatisi, çoğul gebelik, Prematüre Retinopatisi Prevalansı.

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1. INTRODUCTION

Retinopathy of prematurity (ROP) is a proliferative retinal vascular disease which targets premature infants (1). In about 6 - 8% of blind children, ROP is the most common cause and it is a major cause of low vision worldwide. ROP - induced visual loss or blindness significantly impairs the quality of life of preterm infants.[2] Low birth weight (BW) and small gestational age (GA) are the most important risk factors for development of ROP.[3] In recent years the survival rate of very low BW infants is increasing significantly due to the development of perinatal science and technology.[4] Increasing survival rates of premature infants cause an increased ROP incidence in developing countries.[5,6]

Prevalence of ROP has been established in most countries. ROP prevalence was reported 15.6% in USA,[7] 36.4% in Sweden,[8] 36.1% in Germany,[9] 12.5% in England,[10] 18.2% in Brazil[11] and 8.5% in Iran.[12] In Turkey, ROP prevalence has been surveyed mostly in Ankara[13-17] and İstanbul.[18-21] However, Ankara is the capital city and İstanbul is the largest city in Turkey which are socio-economically developed areas of our country. Thus, these studies fail to represent the true prevalence of ROP in Turkey.

Multiple pregnancies have greater risk of premature delivery and lower birth weight than singletons. 42% of twins are born before the end of the 37th week of gestation.[22] Previously ROP prevalence among multiple pregnancies had been studied but there are controversial results (23-27).

In this study, we aimed to determine the prevalence of ROP and the effect of multiple pregnancy on ROP in a tertiary ophthalmology department in Gaziantep which is a city in the southeast region of Turkey.

2. MATERIALS AND METHODS

The medical records of premature infants examined between March 2010 and February 2013 in ophthalmology department of Gaziantep University Faculty of Medicine were included in this retrospective study. Preterm infants with GA ≤32 weeks or BW ≤1500 g were included in this study. Patients with insufficient data were excluded from the study. This study followed the tenets of the Declaration of Helsinki, and ethical clearance was obtained from local Ethics Committee. Parental consent forms were obtained.

2.1. Screening

The first ROP examination took place at 4 weeks postnatally for infants with a GA of more than 27 weeks and at 31 weeks postmenstrual age for infants with a GA of less than 27 weeks. Pupils were dilated using 2 drops of cyclopentolate 0.5%, tropicamide 0.5% and phenylephrine 2.5% at 10 minute intervals. After pupillary dilation, ophthalmological examination was performed with a pediatric eye speculum and pediatric scleral depressor, following instillation of 0.5% proparacaine eye drops for anesthesia. Indirect ophthalmoscopy was performed using a binocular indirect ophthalmoscope with a 20 or 28 diopter lens. Examination was done first in the right eye and then in the left eye. The ROP status of each infant was classified according to the International Classification of ROP, including stage, zone, and extent of disease, and presence or absence of plus disease.[28] If the ROP of both eyes was at different stages, results were recorded independently, patient was evaluated according to the eye with higher stage. Infants with ROP were routinely re-examined every few days to 2 weeks, depending of the zone and severity of ROP.[29] Screenings was done in the presence of a pediatrist who closely monitored the infants. Treatment criteria were based on Early Treatment for Retinopathy of Prematurity Randomized Trial criteria.[30]

2.2. Study Groups

The results in this study were analyzed according to two basic parameters: GA and BW. In terms of BW the infants were divided into the following four patient groups: Group 1 included infants with BW less than 1000 g; Group 2 contained infants with BW between 1000 g and 1250 g, Group 3 included infants with BW between 1250 and 1500 g; and Group 4, included infants with BW more than 1500 g. In terms of GA the infants were also divided into the following four patient groups: infants with GA less than 28 weeks, infants with GA between 29 – 30 weeks, infants with GA between 31 - 32 weeks and infants with GA more than 32 weeks formed group 1, 2, 3 and 4 respectively.

2.3. Statistical Analysis

Statistical analysis was performed using SPSS v.17.0 for Windows (SPSS, Inc. Chicago, IL, USA). The results were evaluated using the chi-square test and Mann Whitney U test as appropriate, with statistical significance level at $P < 0.05$.

3. RESULTS

Of the 726 medical reports of preterm babies, 1396 eyes of 698 cases were included in our study. 28 cases were excluded because of insufficient data. Table 1 shows the demograph-

Table 1. *Demographic characteristics of the screened infants*

	Entire cohort (n=698)
Gender (No.(%))	
Female	342(49.0)
Male	356(51.0)
BW (range) (g)	500-2600
Mean BW (g)	1322,90 ± 275,90
GA (range) (weeks)	24-38
Mean GA (weeks)	30,09 ± 2,16

BW= birth weight.
GA= gestational age.

ic characteristics of the screened infants. Of the screened infants, 445 (63.8%) didn't have ROP while 253 (36.2%) of them had any stage ROP. Of the patients with ROP, 92 (13.2%) had stage 1, 88 (12.6%) had stage 2, 69 (9.9%) had stage 3 and 4 (0.6%) had stage 4 ROP. The mean BW of the infants who didn't have ROP was 1380.44 ± 265.52 g while the mean BW of the patients with any stage ROP was 1221.7 ± 264.97 g ($p < 0.001$). The mean GA of the infants who didn't have ROP was 30.6 ± 1.98 weeks while the mean GA of the patients with any stage ROP was 29.2 ± 2.17 weeks ($p < 0.001$). When the infants were divided according to BW, group 1, 2, 3 and 4 included 110, 162, 353 and 73 cases respectively. 72 out of 110 infants in group 1, 63 infants out of 162 in group 2, 103 out of 353 infants in group 3, 15 out of 73 infants in group 4 developed any stage ROP. When the infants were divided according to GA, group 1, 2, 3 and 4 included 203, 165, 280 and 50 cases respectively. 111 infants out of 203 in group 1, 68 infants out of 165 in group 2, 68 infants out of 280 in group 3, 6 infants out of 50 in group 4 developed any stage ROP. Table 2 and Table 3 shows the distribution of the infants according to birth weight, gestational age groups and stage of ROP. Stage of ROP worsened as the BW ($P < 0.001$) and GA decreased ($P < 0.001$).

Of the 1396 eyes, 76 eyes (5.4%) had plus disease. 1313 eyes (94.0%) were followed up, 76 eyes (5.4%) were lasered using Iridex Oculight® GL laser. Seven of the laser treated eyes (0.5%) developed stage 4 ROP which were sent to Gazi University eye clinic for vitreoretinal surgery. Remaining 71 eyes recovered without any complication.

There were 59 infants with multiple gestation in our study. Of the multiple pregnansies 9 infants were triplets, the rest were twins. Mean BW and mean GA didn't differ between single and multiple gestations. There wasn't any statistically significant difference between single and multiple gestations regarding the presence of ROP ($P = 0.306$).

4. CONCLUSION

Retinopathy of prematurity prevalence has been surveyed in most countries. LAD et al.[7] examined recordings of 34 million live births from 1997 to 2005 in USA. They found a total ROP incidence of 15.6% in premature infants. LARSSON et al.[8] examined 253 preterm infants in Sweden and 36.4% of them had ROP. Gestational age at birth was the most important risk factor in their study. SEIBERTH et al.[9] screened 402 preterm infants and found 36.1% ROP incidence in Germany. PAINTER et al. (10) analysed the data of preterm infants from 1990 to 2011 in England. They found a ROP incidence of 12.5% in 2011. The incidence of ROP increased from 1.28% in 1990 to 12.5% in 2011 according

Table 2: *ROP prevalence in premature infants by BW –differentiated groups, Gaziantep, Turkey, 2010-2013*

ROP stage	Group 1 BW≤1000 g n (%)	Group 2 BW>1000 g/≤1250 g n (%)	Group 3 BW>1250 g/≤1500 g n (%)	Group 4 BW>1500 g n (%)
None	38 (5.44)	99 (14.18)	250 (35.82)	58 (8.31)
1	19 (2.72)	20 (2.87)	48 (6.88)	5 (0.72)
2	24 (3.44)	28 (4.01)	32 (4.58)	4 (0.57)
3	28 (4.01)	13 (1.86)	22 (3.15)	6 (0.86)
4	1 (0.14)	2 (0.29)	1 (0.14)	0
Total	110 (15.76)	162 (23.21)	353 (50.57)	73 (10.46)

ROP: Retinopathy of prematurity, BW: Birth weight, GA: Gestational age

Table 3: *ROP prevalence in premature infants by GA –differentiated groups, Gaziantep, Turkey, 2010-2013*

ROP stage	Group 1 GA≤28 wk n (%)	Group 2 GA≥29 wk/≤30 wk n (%)	Group 3 GA≥31 wk/≤32 wk n (%)	Group 4 GA>32 wk n (%)
None	92 (13.18)	97 (13.90)	212 (30.37)	44 (6.30)
1	31 (4.44)	29 (4.15)	29 (4.15)	3 (0.43)
2	41 (5.87)	23 (3.30)	23 (3.30)	1 (0.14)
3	36 (5.16)	15 (2.15)	16 (2.29)	2 (0.29)
4	3 (0.43)	1 (0.14)	0	0
Total	203 (29.08)	165 (23.64)	280 (40.11)	50 (7.16)

ROP: Retinopathy of prematurity, BW: Birth weight, GA: Gestational age

to their data. They explained this increase with increased neonatal survival, increased awareness of ROP and dissemination of guidence on screening and treatment of ROP. FORTES FILHO et al. (11) screened 352 neonates in Brazil. Incidence of ROP in their study was 18.2%. SAEIDI et al. examined 45 preterm infants for ROP in Iran. They detected that 8.5% of infants had any stage ROP. LIU et al.[31] screened 1864 preterm infants for ROP and incidence was 12.8%. In our study the incidence of ROP was 36.2% which is close to the incidences of Sweden and Germany. Our high ROP incidence may be explained by conducting the screening in a tertiary referral hospital.

In Turkey, the prevalence of ROP has been surveyed mostly in Ankara and Istanbul. CERMAN et al.[18] screened 1252 infants retrospectively. The frequency of any stage ROP in their study was 35.3%. SARIKABADAYI et al.[17] screened 700 neonates with a gestational age < 32 weeks or birth weight < 2000 g, any stage ROP frequency was 32.7% in their study. ALTUNBAŞ et al.[21] evaluated 236 premature infants and 75 (31.8%) of them developed any stage ROP. MUTLU et al.[16] screened 318 neonates and the frequency of any stage ROP in their study was 37.1%. KOCABEYOĞLU et al.[15] screened 405 premature infants and they detected any stage ROP in 88 (21.7%) of them. KÜÇÜKEVCILIOĞLU et al.[14] reported 240 (37.5%) out of 640 neonates had any stage ROP in their study. Prevalence of ROP in our study is similar to the previous studies.

Screening programs for ROP have been proposed mostly from developed countries.[32,33] However, in developing countries these screening programs may miss some more mature infants and they need some modifications. AKMAN et al.[20] screened 801 babies with gestational age less than 37 weeks, they detected 83 ROP cases between 35 - 37 weeks and 11 of them required treatment so they suggested screening infants with a gestational age less than 34 weeks or a birthweight less than 1850 g is a more suitable criteria for our country. Similarly, BAŞMAK et al.[34] detected 54 out of 96 patients with ROP between 32 - 35 weeks and they also suggested that screening protocols must cover more mature babies in developing countries. In our study there were 9 ROP patients with a birth weight more than 1500 g and 6 ROP patients with a gestational age more than 32 weeks. Our numbers are not as high as previous studies but revisioning the screening protocols would decrease the possibility of missed diagnosis.

Low gestational age and low birth weight have been defined as the most important risk factors for ROP in the previous studies.[3,7-9,11,13-20,24,25,27] Our study confirms the earlier studies, as we also found that low birth weight and low gestational age are risk factors for development of ROP. KÜÇÜKEVCILIOĞLU et al.[14] found that gestational age ≤ 32 weeks, birth weight < 1500 g, oxygen therapy, respiratory distress syndrome and sepsis were independent determinants for any stage ROP. KOCABEYOĞLU et al.[15] defined the most important risk factors for ROP development as low birth weight, low gestational age, mechanical ventilation and multiple pregnancy. Our study confirmed the findings of the previous studies as our results also defines low BW and GA as risk factors for the development of ROP.

Effects of multiple gestation on ROP development has been evaluated in previous studies. RIAZI-ESFAHANI et al.[23] screened 99 neonates from multiple gestation pregnancies. They didn't find a significant difference between multiple - birth neonates and matched singletons in terms of frequency and severity of ROP. Similarly R. KRISHNA et al.[24] and M. SARIAYDIN et al.[25] didn't find a significat difference between multiple gestations and singletons regarding any stage ROP. On the other hand, KOCABEYOĞLU et al.,[15] DOS SANTOS MOTTA et al.[26] SABZEHEI et al.[27] defined multiple gestation as a risk factor for ROP. We didn't find a significant relation between ROP and multiple gestation. However stage of ROP was significantly higher in multiple gestations in our study.

In conlusion, the prevalence of ROP in the southeast region of Turkey is similar to the tertiary referral hospitals in the western areas. Low birth weight and low gestational age are risk factors for the development of ROP. According to our findings multiple pregnancy does not affect the presence of ROP. Further studies are needed in the different regions of Turkey to determine the true ROP prevalence in our country.

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