

Comparison of retinopathy of prematurity incidence between Turkish citizens and Syrian refugees

Sabit Kimyon, Pelin Çelemler¹, Alper Mete, Krvanç Güngör

Purpose: More than 3.5 million Syrians came to Turkey seeking refuge and over 470,000 Syrian infants were born since the start of the civil war in 2011. Our aim is to compare the incidence of retinopathy of prematurity (ROP) between Syrian refugees and Turkish citizens. **Methods:** This multicenter, retrospective study was conducted in Gaziantep University, Faculty of Medicine and Gaziantep Children's Hospital in Turkey. We included the data of patients who were screened for ROP between July 2015 and June 2017. **Results:** The above-mentioned data of 906 Turkish infants and 199 Syrian infants were included in this study. Mean gestational ages (GAs) were (32.9 ± 2.7) and (32.1 ± 2.8) weeks as well as mean birth weights (BWs) were (1937.5 ± 582.9) and (1696.8 ± 485.5) g, in Turkish and Syrian infants, respectively. GA and BW were significantly lower in Syrian infants while time spent in neonatal intensive care unit was significantly higher. The zone of ROP was lower in the Syrian infants in the first examination and for the most advanced ROP ($P = 0.001$). Any stage ROP was present in 392 (43.3%) and 81 (40.7%) patients in Turkish and Syrian population, respectively ($P = 0.490$). The number of patients who required treatment for ROP were 95 (10.5%) and 20 (10.1%) in Turkish and Syrian groups, respectively ($P = 0.882$). **Conclusion:** Our findings showed that refugee infants had lower BW and GA than native population but the incidence of ROP did not differ between them. Psychosocial stress is an important risk factor for women at reproductive age as it increases the incidence of prematurity. Additional care and psychological support must be given to refugees during perinatal period to decrease the risk of premature birth.

Key words: Incidence, refugees, retinopathy of prematurity, stress, Syrian war

The health care of refugees has become a major problem in the world. United Nations refugee agency reported that there were 22.5 million refugees in the world at the end of 2016 and Turkey hosts the greatest number of refugees worldwide.^[1] The primary reason for refugees to leave their homes is war.^[2] Syrian civil war resulted in migration of millions of people. Turkey is one of the neighboring countries of Syria and accepted a large number of Syrian refugees for temporary protection. More than 3.5 million Syrians came to Turkey seeking refuge as the civil war was started in 2011. Over 750,000 of these refugees are women at reproductive age and 470,000 Syrian babies were born in Turkey.^[3] Most of these refugees live near the Syrian border and since it is a major city close to the border, Syrian population is one of the highest in Gaziantep.

Retinopathy of prematurity (ROP) is a proliferative vascular disease, which can cause poor vision and blindness.^[4] It affects preterm infants and is one of the leading causes of preventable blindness in children.^[5] Low vision resulting from ROP can be prevented by high-quality neonatal care from immediately after birth with appropriate screening and treatment. The most important risk factors for ROP development are small gestational age (GA) and low birth weight (BW).^[6] The survival rate of very low-BW infants is increasing significantly due to the development of perinatal science and technology in recent

Department of Ophthalmology, Faculty of Medicine, Gaziantep University, Gaziantep, ¹Department of Ophthalmology, Gaziantep Children's Hospital, Gaziantep, Turkey

Correspondence to: Dr. Sabit Kimyon, Department of Ophthalmology, Gaziantep University Hospital, Gaziantep, Turkey. E-mail: sabitkimyon@gmail.com

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years, which in turn causes an increased ROP incidence in developing countries like Turkey.^[5,7]

Less than 10% of the Syrian refugees in Turkey live in camps whereas over 3.3 million live in cities.^[3] The Turkish government provide the same healthcare, including screening and treatment for ROP, for all Syrian refugees if they seek it, as for Turkish citizens. To the best of our knowledge, no study has compared the incidence of ROP between refugees and the native population. Our aim in this study is to compare the incidence and severity of ROP between Turkish citizens and Syrian refugees.

Methods

This multicenter, retrospective study was conducted in Gaziantep University, Faculty of Medicine Department of Ophthalmology and Gaziantep Children's Hospital in Gaziantep, Turkey, near the Syrian border. Both hospitals have a neonatal intensive care unit (NICU), and ROP screening was performed in each one by two experienced ophthalmologists. All treatments were delivered in the university hospital. The study was approved by the ethics committee and research

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adhered to the tenets of the Declaration of Helsinki. We included the data of infants screened for ROP between July 2015 and June 2017. Screening criteria were infants with GA \leq 32 weeks, BW \leq 1,500 g, or any disease requiring follow up in newborn intensive care unit. Infants with insufficient data were excluded from the study.

Infants with GA more than 27 weeks were examined at fourth week of birth; infants with a GA less than 27 weeks were examined at 31st week postmenstrually. Pupils were dilated with cyclopentolate 0.5%, tropicamide 0.5%, and phenylephrine 2.5%, which were instilled twice at 10 minute intervals. After installation of 0.5% proparacaine, ROP screening was performed by a binocular indirect ophthalmoscope (Keeler Digital Vantage Plus LED, Keeler Ltd., Windsor, UK) with a 20- or 28-diopter lens using a pediatric eye speculum and a scleral depressor. First the right then the left eye was examined. 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.^[8] If the ROP of both eyes were at different stages, patient was evaluated according to the eye with higher stage. Infants with ROP were followed up depending of the zone and severity of ROP.^[9] Examinations were done in the presence of a pediatricist who closely monitored the infants. Patients were treated according to the criteria defined by Early Treatment for Retinopathy of Prematurity Randomized Trial.^[10] GA, BW, ROP findings at the first examination, requirement for treatment, treatment type, time of complete vascularization, and any complications were noted. Data from Turkish citizens and Syrian refugees were analyzed and compared.

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 independent samples t-test as appropriate, with statistical significance level at $P < 0.05$.

Results

Data of 906 Turkish infants and 199 Syrian infants were included in this study. GA, BW, and time spent in the NICU were significantly different between the two groups of infants screened [Table 1]. Any stage of ROP was present in 392 (43.3%) and 81 (40.7%) Turkish and Syrian infants, respectively ($P = 0.490$). Zone, stage, and plus disease at first examination and the most advanced ROP identified during follow up were compared between Turkish and Syrian infants. *Post hoc* analysis revealed a significantly higher rate of infants with zone 2 ROP in Syrian and zone 3 ROP in Turkish patients, in both the first examination and most advanced ROP [Table 2].

There were no differences between groups regarding the stage of ROP and presence of plus disease [Table 2]. The number of patients who required treatment for ROP were 95 (10.5%) and 20 (10.1%) in Turkish and Syrian groups, respectively ($P = 0.882$). Types of treatments are shown in Table 3. BW and GA differed significantly between treated and untreated infants in both groups [Table 4]. There was no significant difference between groups regarding BW, GA, and time spent in NICU among the treated population [Table 5]. Vascularization was completed by (43.1 \pm 6.1) weeks in Turkish infants and by (42.4 \pm 6.2) weeks in Syrian infants ($P = 0.237$). The numbers of infants with incomplete vascularization at postmenstrual 45 weeks of age were 35 and 11 in Turkish and Syrian infants, respectively. Macular traction was observed in five Turkish patients and one Syrian patient who received laser photocoagulation treatment. One Turkish patient developed strabismus. Three Turkish infants progressed to stage 4 and were referred for vitreoretinal surgery. One Turkish infant and two Syrians developed retinal hemorrhage. One Turkish and two Syrian infants died from cardiorespiratory complications, none of whom were treated for ROP. There were 304 twin Turkish infants and 50 twin Syrian infants, and 34 and 10 triplets in Turkish and Syrian populations, respectively. No significant difference was observed between groups regarding the number of multiple pregnancies ($P = 0.060$). There was no significant difference between singletons and multiple birth infants regarding the presence of any stage ROP ($P = 0.594$) or type 1 ROP ($P = 0.922$).

Discussion

Wars mostly affect the health of women and children because of their dependence on a functioning health care system and they are more susceptible to economic and social disruption resulting from conflicts.^[11,12] Millions of Syrians escape from war to Turkey. Over 750,000 of these refugees are women of reproductive age, and 470,000 Syrian babies were born in Turkey between 2012 and 2018.^[3] Psychosocial stress is shown to increase the risk of preterm delivery.^[13] Rich-Edwards *et al.* thought that women who were exposed to chronic psychological stress may have an increased risk of preterm delivery as a result of increased placental corticotropin-releasing hormone.^[14] Wadhwa *et al.* showed that maternal perinatal stress is significantly associated with GA and BW.^[15] Supporting these studies, Büyüktiryaki *et al.* reported that 26% of the Syrian infants born in their hospital were preterm and the neonatal mortality rate was 1.8% which is higher than Turkish infants (0.97% in 2016).^[16,17] There are similar reports from all over the world regarding minority groups. Michaan *et al.* reported perinatal outcomes of Eritrean

Table 1: Comparison of GA, BW, and time spent in NICU between Turkish citizens and Syrian refugees

	Turkish citizens	Syrian refugees	P
Sex			0.548*
Male, n (%)	475 (52.4)	109 (54.8)	
Female, n (%)	431 (47.6)	90 (45.2)	
GA (weeks) $n \pm SD$	32.9 \pm 2.7	32.1 \pm 2.8	<0.001†
BW (g) $n \pm SD$	1937.5 \pm 582.9	1696.8 \pm 485.5	<0.001†
Time spent in NICU (days) $n \pm SD$	35.8 \pm 24.1	43.4 \pm 15.5	0.040†

GA, gestational age; n, number; SD, standard deviation; BW, birth weight; NICU, neonatal intensive care unit, †Independent samples t-test was used,

*Chi-square test was used

Table 2: Comparison of ROP zones, stages, and plus disease presence at the first examination and the most advanced ROP between Turkish and Syrian population

	First examination			Most advanced ROP		
	Turkish citizens n (%) n=392	Syrian refugees n (%) n=81	P	Turkish citizens n (%) n=392	Syrian refugees n (%) n=81	P
ROP zone						
Zone 1	58 (14.8)	16 (19.8)	0.271*	54 (13.8)	17 (20.9)	0.099*
Zone 2	145 (37.0)	44 (54.3)	0.004*	145 (37.0)	46 (56.8)	0.001*
Zone 3	189 (48.2)	21 (25.9)	<0.001*	193 (49.2)	18 (22.2)	<0.001*
ROP stage						
No ROP	59 (15.1)	17 (21.0)	0.304†	-	-	0.626†
Stage 1	225 (57.4)	50 (61.7)		213 (54.3)	42 (51.9)	
Stage 2	46 (11.7)	5 (6.2)		102 (26.0)	26 (32.1)	
Stage 3	60 (15.3)	9 (11.1)		75 (19.1)	13 (16.0)	
Stage 4	2 (0.5)	0 (0)		2 (0.5)	0 (0)	
Plus disease						
Absent	304 (77.6)	63 (77.8)	0.964†	297	62	0.882†
Present	88 (22.4)	18 (22.2)		95	19	

n, number; ROP, Retinopathy of prematurity. *P values were calculated by *post hoc* analysis with an adjusted significance value of 0.008. †Chi-square test was used

Table 3: Treatments for retinopathy of prematurity in Turkish and Syrian population

	Turkish citizens	Syrian refugees	P*
LP, n	33	8	0.244
IVA, n	50	12	
LP and IVA, n	12	0	

LP, laser photocoagulation; IVA, intravitreal anti-vascular endothelial growth factor; n, number. *Chi-square test was used

Table 4: BWs and GAs of Turkish citizens and Syrian refugees among treated and untreated infants

	Treated infants	Untreated infants	P*
Turkish citizens			
BW (g) n±SD	1383.8±421.0	2001.9±564.9	<0.001
GA (weeks) n±SD	29.5±2.7	33.3±2.4	<0.001
Syrian refugees			
BW (g) n±SD	1336.8±291.2	1735.0±486.8	<0.001
GA (weeks) n±SD	30.3±3.1	32.3±2.7	0.003

BW, birth weight; n, number; SD, standard deviation; GA, gestational age. *Independent samples t-test was used

Table 5: Comparison of GA, BW, and time spent in NICU between Turkish citizens and Syrian refugees treated for retinopathy of prematurity

	Turkish citizens	Syrian refugees	P
GA (weeks) n±SD	29.5±2.7	30.3±3.1	0.293†
BW (g) n±SD	1383.8±421.0	1336.8±291.2	0.560†
Time spent in NICU (days) n±SD	48.9±24.1	67.5±17.7	0.729†

GA, gestational age; n, number; SD, standard deviation; BW, birth weight; NICU, neonatal intensive care unit. †Independent samples t-test was used

and Sudanese refugees in Tel Aviv and they found that refugees had significantly more premature deliveries than the Israeli population.^[18] Similarly, Cacciani *et al.* showed that immigrants have a higher risk of preterm delivery, low Apgar scores, and respiratory diseases in Italy.^[19] In our study, BW and GA of Syrian infants were significantly lower than Turkish infants, supporting previous studies. The zone of ROP was also lower in the Syrian infants at the first examination and for the most advanced ROP. These findings suggest that the Syrian population in Turkey might have a higher incidence of ROP than Turkish citizens but this was not the case in our study. Moreover, the proportion developing type 1 ROP was not significantly different between groups. The lack of difference despite the fact that the Syrian infants screened had significantly lower GAs and BWs and were inpatients for longer might be due to the effect of glucocorticoids on maturation of lungs^[20] as a response to maternal stress which might have decreased the oxygen requirement, a major risk factor for ROP development.

The incidence of any ROP in our study was 43.3% and 40.7% in Turkish and Syrian infants, respectively, which was not significantly different. The incidence of any ROP in Turkey has been reported in several studies and ranged from 31.8% to 37.5%.^[21-25] The higher ROP incidence in our study may be caused by one of the study hospitals being a ROP referral center.

There is conflicting evidence on whether multiple pregnancy increases the risk of ROP^[26] with some studies finding no difference^[27,28] whereas others have reported an increased risk.^[29,30] We did not find a significant difference in our study.

Conclusion

Our findings showed that refugee infants have lower BW and GA than the native population but there was no difference in the incidence of ROP. This might be due to the effect of glucocorticoids on maturation of lungs as a response to maternal stress which might have decreased the oxygen requirement.^[31] Running away from war to a foreign country

and living as a refugee leads to major stress which mainly affects women and children. Psychosocial stress is an important risk factor for women at reproductive age as it increases the incidence of prematurity.^[13] Additional care and psychological support must be given to refugees during perinatal period to decrease the risk of premature birth. Further studies are required to fully understand the effects of maternal stress on the development of the retinal vasculature.

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Conflicts of interest

There are no conflicts of interest.

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