Incidence and severity of retinopathy of prematurity in Turkey

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ABSTRACT

Background The purpose of this study was to estimate the current incidence of retinopathy of prematurity (ROP) and the need for treatment in preterm infants in Turkey.

Methods The study included preterm infants who had been screened for ROP between 2011 and 2013 in 49 neonatal intensive care units. Infants with birth weight (BW) ≤1500 g or ≤32 weeks' gestational age and those with BW >1500 g or >32 weeks' GA with an unstable clinical course were included. The incidence of any ROP or severe ROP and treatment modalities were determined.

Results The study population included 15 745 preterm infants: 11 803 (75%) with GA ≤32 weeks, and 3942 (25%) with GA >32 weeks. Overall, 30% were found to have any stage of ROP, and 5% had severe ROP. Severe ROP was diagnosed in 8.2% of infants with BW ≤1500 g and 0.6% of infants with BW >1500 g. Of all infants diagnosed with ROP, 16.5% needed laser photocoagulation, and 20 patients born at >32 weeks' GA required this treatment modality. Vitroretinal surgery was performed in 28 infants with severe ROP: 23 with GA ≤28 weeks and 5 with GA 29–32 weeks.

Conclusions The findings of our study have the important implication that more mature babies are at risk of severe ROP requiring treatment. An effective programme for detecting and treating ROP should be established in Turkey.

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INTRODUCTION

Retinopathy of prematurity (ROP) is a vasoproliferative disorder of the retina resulting from failure of normal progression of retinal vessels in preterm infants.[1] Current advances in neonatal care have improved the survival rate of very preterm infants who are candidates for developing ROP. Early identification of retinal damage and institution of appropriate treatment can prevent blindness and offer the child better overall development.[2] Despite increased awareness of, and improved treatments for, ROP, this disease remains a leading cause of childhood blindness, accounting for up to 10% of cases in developed countries.[3]

The prevalence of ROP varies globally, depending on survival of extremely low birth weight (ELBW) infants, recognition of ROP, and use of guidelines for screening and treatment.[4] In the last decade, the incidence of overall and severe ROP has decreased significantly in developed countries.[5] Studies conducted in high-income countries suggest that severe ROP is mainly detected in infants born at <28 weeks' gestational age (GA); in addition, most infants born at >30 weeks' GA have no or mild ROP. Neonatologists and ophthalmologists in developed countries adjust their screening guidelines to further lower the upper screening limit.[6 7]

Research from several developing countries has shown that the international screening criteria for ROP might not be entirely applicable in developing areas of the world.[8] Infants with severe ROP are larger and of a greater estimated GA than those in developed countries.[9] This is also because the smallest infants tend to die in developing countries.

The incidence of ROP among preterm babies in neonatal intensive care units (NICUs) has been investigated in many different countries. However, there are few studies of ROP incidence in NICUs from Turkey in which 1 300 000 babies are born every year, and those that have been performed are single-centre investigations.

The purpose of this retrospective study was to estimate the incidence and severity of ROP in infants with a birth weight (BW) ≤1500 g or ≤32 weeks' GA in Turkey. We also aimed to determine the incidence of any ROP and severe ROP in infants with BW >1500 g or GA >32 weeks. This is the first multicentre study of the incidence of overall and severe ROP in Turkey; these data can be used to initiate a prospective study and to create a national guideline.

METHODS

This study, supported by the 'Turkish Neonatology Society', involved preterm infants who had been screened for ROP between 1 January 2011 and 31 December 2013 in level III Turkish NICUs. Infants with BW ≤1500 g or ≤32 weeks' GA and those with BW >1500 g or GA >32 weeks requiring cardiorespiratory support and who were determined by the attending clinician to be at risk of ROP were screened.

An electronic questionnaire was sent to all certified neonatologists in Turkey via a special network. Neonatologists working in 49 centres who agreed to participate in this study provided data on ROP in their NICU. The medical records of retinal examinations of preterm infants who met the screening criteria were retrospectively evaluated. Neonates who died before they could be examined or before full vascularisation of the retina and infants who did not complete the follow-up were excluded from the study. A data sheet including GA, BW, presence of any ROP and severe ROP was completed for all infants included in the study. In cases where the retina was not fully vascularised, ophthalmological examination was continued until full vascularisation or 40 weeks of postmenstrual age. The maximum stage of ROP detected for each infant was reported. Severe ROP was defined as

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stage 3 or greater. The study also investigated the need for laser photocoagulation and vitroretinal surgery for ROP.

Data from 49 NICUs were pooled and analysed. The incidence of any ROP or severe ROP and treatment modalities were determined. The study population was also divided into three groups—NICUs of university hospitals, state hospitals and private hospitals—and the incidence of any ROP or severe ROP and laser treatment were compared among the groups.

All infants meeting the screening criteria were scheduled to have their first examination at between 4 and 6 weeks of life. Dilated fundus examinations were carried out in the clinic or NICU under topical anaesthesia by the consultant ophthalmologist. The ophthalmological examinations were repeated weekly or biweekly using the schedule for follow-up recommended by American Academy of Pediatrics until full vascularisation of the retina reached zone 3 (the most peripheral temporal retinal zone). If ROP develops, the eyes are examined more frequently, depending on the severity of the disease and rate of progression.[10] The International Classification of ROP guidelines were used to record stage of disease, location by zone, signs of plus disease, and signs of regression.[11] Criteria for treatment of ROP were based on the Early Treatment for ROP (ETROP) recommendation.[9] Consent forms were also signed by the babies' parents before the initial screening and treatment.

Data analysis was conducted using SPSS V.15.0. The Pearson χ^2 test was used to analyse qualitative variables. A difference with $p<0.05$ was considered significant.

RESULTS

During the study period, data from 49 centres including NICUs of 31 university hospitals (6469 infants), 15 state hospitals (8310 infants) and three private hospitals (966 infants) were obtained. All participating centres had ophthalmology units for ROP screening, but only 34/49 could perform laser photocoagulation and 4/49 could perform vitroretinal surgery. The newborns requiring treatment for ROP in units where there was no possibility of laser photocoagulation or vitroretinal surgery were transferred to other facilities.

The study population included 15 745 preterm infants: 11 803 (75%) with GA ≤32 weeks and 3942 (25%) with GA >32 weeks. Overall, 30% were found to have any stage of ROP, and 5% had severe ROP. The incidence of ROP or severe ROP and treatment according to GA are shown in table 1. The majority (89%) of infants with any ROP were ≤32 weeks of GA, and 71.5% with severe ROP were ≤28 weeks of GA.

ELBW infants had a much higher prevalence of ROP than very low BW (VLBW) infants. Severe ROP was diagnosed in 8.2% of infants with BW ≤1500 g and 0.6% of infants with BW >1500 g. Of all infants diagnosed with ROP, 16.5% needed laser photocoagulation, while the rest regressed spontaneously. This treatment modality was performed in 0.6% of infants with BW 1501–2000 g and in three babies with BW ≥2001 g and GA 33–35 weeks. Severe ROP was diagnosed in 14 babies with BW >1500 g and GA >32 weeks who required treatment. Criteria for treatment of ROP were based on the ETROP recommendation.[9] Table 2 shows ROP and its treatment in relation to BW.

Incidence of any ROP or severe ROP and laser treatment in infants with BW ≤1000 g were found to be significantly higher in NICUs of private hospitals (figure 1).

DISCUSSION

The impact of ROP on vision in the premature infant has been fully appreciated since the early report by Terry.[1] ROP affects a substantial number of premature infants worldwide. As the numbers of infants with ELBW and VLBW who survive increase, more will need screening for ROP. Detection and treatment of ROP are important to prevent poor vision in these infants,[5] so that they will have a better quality of life. However, severe ROP may result in blindness or poor sight even with treatment. The few studies of ROP incidence that have been carried out in Turkish NICUs have been single-centre investigations. The present study is the largest multicentre study performed in Turkey. The overall incidence of ROP in this study was 30%, and the incidence and severity increased with decreasing GA and BW: the frequency of ROP was 35.6% and 13.3% in infants with GA ≤32 weeks and >32 weeks, respectively, and 42% and 13.4% in those with BW ≤1500 g and >1500 g, respectively.

Numbers of babies with ROP in low- and middle-income countries are very different from those in high-income countries. The overall incidence of severe ROP among extremely premature infants born at ≤25 weeks' GA was 15% in a cohort study from Australia.[12] Studies conducted in developed countries suggest that infants born at ≥32 weeks' gestation are not at risk of developing ROP.[9] The percentage of any ROP in infants with BW ≤1500 g observed in our study is comparable to results from other middle-income countries such as Taiwan, Brazil and Iran, where the incidence of ROP ranged between 33% and 45%.[3 13 14] The incidence of any ROP in infants with GA ≤32 weeks has been reported to be 36–50% in our country.[15–18]

Continuous improvements in neonatal care have led to increased rates of survival of very preterm infants in Turkey. As a result, there are more ELBW infants, who are at risk of developing ROP. The frequency of ROP and severe ROP in infants with BW ≤1000 g was reported to be 81.1% and 35.1%, respectively, in a study conducted in 1999–2005 in Turkey.[18] The incidence of any stage of ROP and severe ROP was 55.9% and 18.7%, respectively, in babies with BW ≤1000 g in our study. On the other hand, Chiang *et al*[19] analysed records of

Table 1 Retinopathy of prematurity (ROP) and its treatment in relation to gestational age

Gestational age (weeks)	Screened infants	Infants with ROP	Infants with ≥stage 3 ROP	Infants requiring laser photocoagulation	Infants requiring vitroretinal surgery
≤28	3737	1975 (52.8)	565 (15.1)	574 (15.3)	23
29–32	8066	2228 (27.6)	207 (2.6)	188 (2.3)	5
Subtotal (≤32)	11 803	4203 (35.6)	772 (6.5)	762 (6.5)	28
>32 weeks	3942	526 (13.3)	18 (0.4)	20 (0.5)	–
Total	15 745	4729 (30)	790 (5)	782 (5)	28

Values are number or number (%).

Table 2 Retinopathy of prematurity (ROP) and its treatment in relation to birth weight

Birth weight (g)	Screened infants	Infants with ROP	Infants with ≥stage 3 ROP	Infants requiring laser photocoagulation	Infants requiring vitroretinal surgery
≤1000	2694	1506 (55.9)	503 (18.7)	522 (19.4)	23
1001–1250	3043	1343 (44.1)	163 (5.4)	151 (4.9)	3
1251–1500	3405	997 (29.3)	83 (2.4)	68 (2)	2
Subtotal (≤1500)	9142	3846 (42)	749 (8.2)	741 (8.1)	28
1501–2000	5600	812 (14.5)	37 (0.6)	38 (0.67)	–
≥2001	1003	71 (0.7)	4 (0.4)	3 (0.3)	–
Total	15 745	4729 (30)	790 (5)	782 (5)	28

Values are number or number (%).

15 691 infants from New York and found that the incidence of ROP was 33.2% for infants with BW <1000 g.

In the study reported here, the incidence of treated ROP was 8.1% among VLBW infants and 19.4% among ELBW infants. Liu *et al*[20] reported an incidence of 8.2% for ROP requiring treatment in premature infants weighing <1600 g, and 17.0% of ELBW infants in a Brazilian study were treated.[21] Both findings are comparable to our results. However, the incidence of treated ROP was 28.7% in a study of ELBW infants in the USA.[22] This can be explained by deficiencies in the process of diagnosis or under-recognition of severe ROP in low-income countries and also may be due to differences in treatment criteria.

The incidence of ROP varied among the centres in our study, which reflects the differences in neonatal care between various NICUs. In particular, the rates of any ROP and severe ROP in ELBW infants were significantly higher in private hospital NICUs than in NICUs of university and state hospitals. Standards of neonatal care are likely to be better in university NICUs than in non-university NICUs. Lower rates of ROP in university hospitals can be attributed to several factors: better antenatal and neonatal intensive care; babies receiving supplemental oxygen are monitored and cared for by well-trained neonatal nurses.

The socioeconomic status of the population, reflected in perinatal care, determines the prevalence of ROP. In developing countries, infants who develop ROP are larger and of a greater estimated GA than those in developed countries.[8 23] In a Canadian study, no infant with BW >1250 g developed ≥stage 3 ROP, and no infant born at GA >26 weeks and BW >1000 g developed type 1 ROP.[24] In the present study, 41 neonates with BW >1500 g and three babies with BW >2001 g underwent laser photocoagulation therapy. The rate of laser treatment in infants born at >32 weeks' GA was 0.5% (20 infants), and five infants born at 29–32 weeks' GA needed vitroretinal surgery. The findings of our study have the important implication that bigger and more mature babies are at risk of developing severe ROP that requires treatment in Turkey. Severe ROP was diagnosed in 14 babies with BW >1500 g and GA >32 weeks who needed treatment. Therefore the ROP screening criteria in Turkey should include a risk factor profile for infants born at >32 weeks and/or >1500 g BW.

Our results reveal that there is more surgical ROP compared with severe ROP in the population of infants with GA ≤28 weeks (even in infants born at 33–35 weeks' GA) and in infants with BW ≤1000 g. This might suggest overtreatment of ROP and is a reflection of the reality of a developing country.

ROP is an emerging problem which is due to recent developments in newborn care resulting in more infants eligible for ROP screening in our country. Turkey has been reported to be experiencing a 'third epidemic' of ROP. The population of infants affected have the characteristics of both the 'first epidemic' (inadequately monitored oxygen) and 'second epidemic' (extreme prematurity).[25]

In this study, no risk factors for developing ROP other than BW and GA were evaluated, and this is a limitation of the study. In Turkey, insufficient data on the prevalence of ROP are hindering the establishment of strategies to minimise the occurrence of the disease.

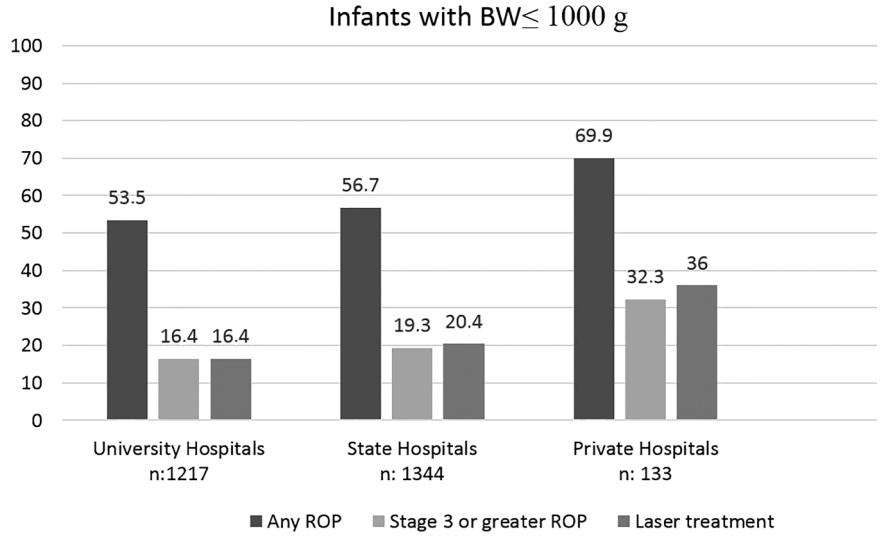

Figure 1 Comparison of the incidence of any retinopathy of prematurity (ROP), severe ROP and laser treatment between university, state and private hospitals in infants with birth weight (BW) ≤1000 g.

Zin *et al*[26] recommended screening infants with BW ≤1500 g or GA ≤35 weeks in NICUs with a high mortality rate (ie, >20% of infants with BW <1500 g).[27] The 2013 report of the Turkish Neonatology Society revealed a mortality rate of 23% for babies with BW <1500 g according to data obtained from 50 NICUs.[28] However, there are great variations in the standard of neonatal care and in mortality rates between different units in Turkey. Ideally, a multicentre, population-based study including epidemiological information and risk factors for ROP should be conducted throughout Turkey to create screening criteria specific to Turkey based on its own population.

In conclusion, the percentage of ROP and severe ROP observed in our study is comparable to the results obtained from other middle-income countries. Turkey is improving access to neonatal intensive care, and more mature babies are also at risk of severe ROP, as neonatal care may be suboptimal in some NICUs. Programmes for improving neonatal care and detecting infants who need treatment and a national guideline for ROP should be established in Turkey.

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Ethics approval The principles outlined in the Declaration of Helsinki were followed in this study.

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