

Impact of advances in neonatology on retinopathy of prematurity: Lithuania, Vilnius County, 1995–2003

Rasa Bagdonienė*¹,

Rasa Sirtautienė¹,

Nijolė Drazdienė²,

Nijolė Vezbergienė¹,

Albina Našliūnienė¹

¹ Vilnius University Children's Hospital, Santariškių 7, LT-08661 Vilnius, Lithuania

² Center of Neonatology of Vilnius University, LT-08661 Vilnius, Lithuania

Background: The aim of the study was to report a rapid tendency towards better survival of the premature infants as well as a decrease in mean birth weight (BW) and gestational age (GA) among threshold ROP babies.

Materials and methods: Official data on neonate mortality are taken from Department of Statistics to the Government of the Republic of Lithuania. Neonate survival data are taken from Lithuanian Medical Birth Register.

A retrospective analysis for evaluating the dynamics of BW and GA among threshold ROP infants, based on prospectively collected data from January 1995 to December 2003 was performed by the authors of the paper.

Results: During the study period a remarkable decrease in neonate mortality rate was detected in Lithuania (81.4‰ in 1995 versus 43.1 ‰ in 2003). The survival of very low birth weight (VLBW) infants increased from 62.7% to 88.9%, and the same index among extremely low birth weight (ELBW) infants increased from 18.5% to 56.7%. 2202 infants underwent screening for ROP in 1995–2003. Of them 320 (14.5%) reached the threshold and underwent treatment. The mean BW of threshold infants decreased from 1558.1 g to 1037.3 g, and the mean GA decreased from 30.7 to 27.2 weeks.

Conclusion: remarkable decrease in the mortality and an increase in the survival rates of premature infants is evident in Lithuania. Improvement in neonatal care brought a rapid decrease of mean BW and mean GA of threshold ROP infants.

Key words: retinopathy of prematurity, birth weight, gestational age

INTRODUCTION

Medical care for premature infants has changed dramatically during the last decade in Lithuania. Due to a positive influence of the Perinatal program, perinatal and neonatal mortality has been decreasing in the country since 1992. We should note that deliveries of neonates with birth weight less than 1000 g were not registered at all in our country until 1991 when independence was proclaimed. The increased survival of premature infants brought the new problem to the country – an epidemic wave of retinopathy of prematurity. Screening and treatment for ROP in Lithuania was started in 1994 in Vilnius University Children's Hospital (VUCH). During the soviet ruling, ROP was an unknown disease for our medical society.

The primary objective of our study was to report a rapid tendency towards a better survival of premature infants as well as an evident decrease in mean birth weight (BW) and gestational age (GA) among threshold ROP babies.

MATERIALS AND METHODS

We used the official data from Department of Statistics to the Government of the Republic of Lithuania (Statistics Lithuania) on neonate mortality in Lithuania and in Vilnius Perinatal Centre.

Very low birth weight (VLBW) (< 1500 g) and extremely low birth weight (ELBW) (< 1000 g) neonates' survival data were taken from Lithuanian Medical Birth Register.

All infants in our tertiary level hospital were out-born. Starting from 1995 till 1998, all infants with gestational age (GA) of 36 weeks or less, admitted to intensive care and premature infants' units of Vilnius University Children's Hospital underwent screening for ROP. In 1998 the national guidelines for screening were established (1). From 1999 to 2002, infants with GA ≤ 35 weeks and/or BW ≤ 2500 g were enrolled to screening protocols (national screening limits). From 2003 we have started to screen for ROP infants with GA ≤ 33 weeks and/or BW ≤ 2000 g. Those who reached the threshold were treated by cryo or laser-cryo procedu-

* Corresponding author. E-mail: rbagdoniene@hotmail.com

res. All screening, treatment and postoperative follow-up procedures were performed by the same two ophthalmologists (R. Bagdoniene & R. Sirtautiene). All infants were examined at 1–2 week intervals starting from 2–5 postnatal weeks.

Tropicamide 0.5% solution was used for dilation of the pupils. An all-pupil binocular indirect ophthalmoscope (Keeler, UK) and +20 or +28 D lenses (Nicon, Japan) was used for examinations. Lid speculum was employed in all babies. The strabismus hook was used for rotation and indentation (if necessary) of the globe. ROP staging and criteria for treatment were in concordance with International Classification of ROP (IC ROP) and Cryotherapy for Retinopathy of Prematurity Cooperative Group (CRYO ROP CG) recommendations (2, 3). Data was tabulated and expressed as the mean, median and standard error of mean (SEM) using statistical analysis software on personal computer.

RESULTS

Mature and premature neonates' mortality rates in the whole country are depicted in Fig 1. Mature infants' mortality is almost stable during the period, showing a very slow tendency to decrease below 2‰, but mortality among premature infants is decreasing remarkably, reaching 43.1‰ in 2003.

Figure 1 shows that premature infants' mortality rates in Vilnius Perinatal Centre became even smaller than the average means in Lithuania. At the very beginning of the study period (1995) premature infants mortality rates exceeded 80‰ in Lithuania. At that time the situation in Vilnius PC was much worse. Here premature infants mortality rate exceeded 95‰. The period from 1991 to 1994 was not covered by our study, but we included it for a more proper evaluation of our former status (premature infants' mortality was not recorded at all until 1995).

Very low and extremely low birth weight neonates' survival data are shown in Fig. 2. The survival rate of premature infants weighting less than 1000 g increased more than threefold (18.5% and 56.7% respectively) over the study period. In the group of BW 1500–1000 g, the survival rate is approaching to 90% and is almost stable since 1999.

During the period of 1995–2003, 2202 infants (out of 2297 hospitalized to VUCH) underwent screening for ROP, of them 320 (14.5%) reached the threshold and underwent treatment for ROP. In the period of 1995–1998, threshold ROP was found in 16.2% of all screened infants (all hospitalized to VUCH); during 1999–2002 threshold ROP was found in 11.5% of infants screened according to our screening criteria (11.1% of hospitalized), and in 2003 (after reducing the screening criteria) threshold ROP was found in 28.3% of screened premature infants (15.0% of hospitalized to VUCH).

There were 143 girls (44.7%) and 177 boys (55.3%) among infants who reached the threshold.

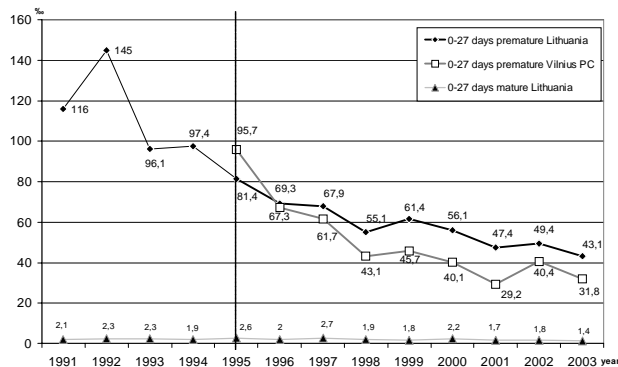


Fig. 1. Mortality rates of mature and premature neonates in Lithuania (per 1000 live births)

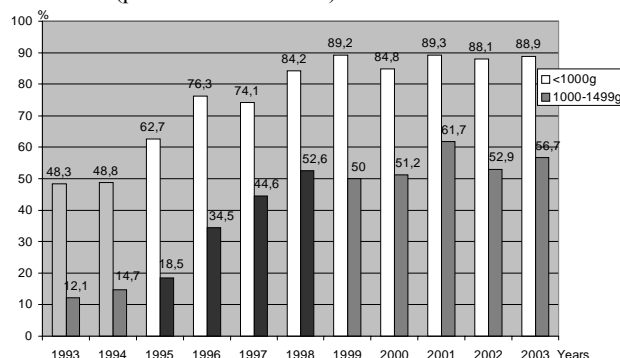


Fig. 2. Survival data on very low and extremely low birth weight neonates (%)

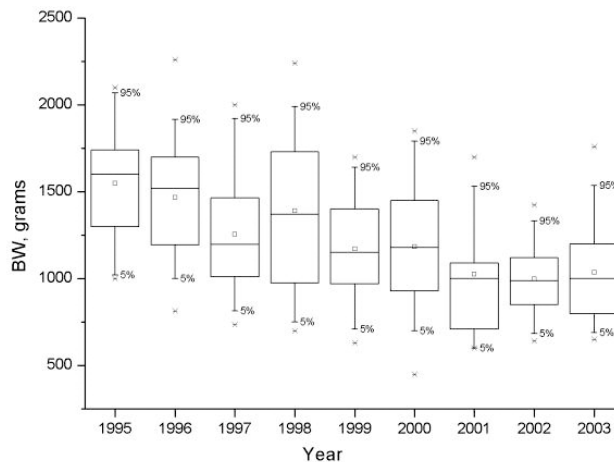


Fig. 3. Distribution of threshold infants by BW

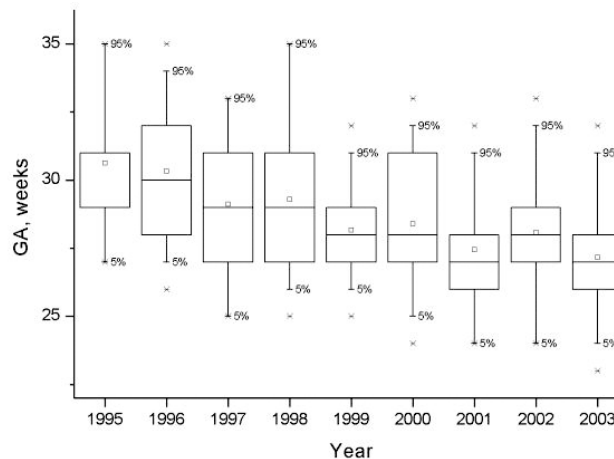


Fig. 4. Distribution of threshold infants by GA

Table 1. BW data on threshold ROP infants in 1995–2003

Year	Mean BW, g	Median BW, g	SE of mean, g
1995	1558.1	1600	49.3
1996	1468.0	1539	47.0
1997	1255.0	1198	44.4
1998	1390.4	1390	36.7
1999	1170.8	1150	43.2
2000	1183.7	1180	72.4
2001	1025.2	1000	67.0
2002	998.5	1009	43.5
2003	1037.3	1005	45.0

The mean BW of these infants was 1558.1 g in 1995 and dropped to 1037.3 g in 2003 (Table 1, Fig. 3).

The smallest infant in 1995 had the birth weight of 1000 g. Until 1998, we had threshold ROP cases among infants with BW exceeding 2000 g (Fig. 3).

The distribution of threshold infants by GA was presented in Table 2 and Fig 4. Mean gestational age was decreasing gradually from 30.7 weeks in 1995 to 27.2 weeks in 2003. The curve of decreasing GA (Fig. 4) is very similar to the premature infants' mortality curve for the same period. Even the small breaks in these curves occur at the same years (2000 and 2002), when mean GA (28.5 and 27.2, respectively) coincided with premature infants' mortality numbers (56.1% and 49.4%, respectively).

DISCUSSION

ROP is a disease of prevention, and the starting step is improvement of prenatal and neonatal care. According to the official statistics and Lithuanian Birth Register data, 5–6% of all newborns in Lithuania are born prematurely. Perinatal and neonatal mortality has decreased in Lithuania since 1992 due to improving the quality of perinatal care. The widespread use of antenatal corticosteroids for women at risk for preterm delivery and surfactant for the prevention and treatment of neonatal respiratory distress syndrome were associated with decreases in mortality and morbidity of low and very low birth weight infants. Better survival of these infants faced the new problem: retinopathy of prematurity, an unknown disease for soviet ophthalmologists, rapidly became one of the sharpest problems in the last decade.

It was impossible to directly introduce up-to-date western screening recommendations for our infants. Our medical system in this field was lagging more than 20 years behind. Only ancient literature data were useful for us. Improvement of neonatal technologies, access to foreign literature, and probations in western ophthalmologic clinics allowed us to catch up with the leaders. In a several years' timeframe we passed through the whole history of ROP. Our personal activity was very important as well. Conferences, teaching courses for ophthalmologists and neonatologists, education literature – books (4, 5) and methodical recommendations (6), articles in local

Table 2. GA data on threshold ROP infants during 1995–2003

Year	Mean GA, weeks	Median GA, weeks	SE of mean, weeks
1995	30.7	31	0.3
1996	30.3	31	0.3
1997	29.1	29	0.3
1998	29.3	29	0.4
1999	28.2	28	0.3
2000	28.4	28	0.5
2001	27.5	27	0.4
2002	28.1	28	0.5
2003	27.2	27	0.4

scientific journals (7–13) stimulated the progress. Within a period of the nine years we established our screening criteria (in 1998) (1), applied them successfully, and ascertained in 2002 that it was time to update the se criteria (14). The shift was 2 weeks in lowering GA and 500 g in lowering BW (35 weeks and 2500 g in 1998 versus 33 weeks and 2000 g in 2003).

Similar data were presented by Holmström et al from Sweden (15, 16). They compared ROP data in two decades (1988–1990 and 1998–2000) and concluded about lowering the screening criteria from 32 to 31 weeks of GA.

One of the burdening issues of ROP was the fact that all our infants were outborn. According to CRYO ROP CG study (17), stage 3 ROP was detected in 16.7% of inborn infants and in 25.5% of outborns.

It would be interesting to compare our data on the mortality of neonates with the data of multicenter study (14 hospitals) performed in 1984–1985 in Japan. The average survival rate of infants weighing less than 1000 g was 60.3% (18). We do not have any statistical data from those years, because deliveries of neonates less than 1000 g were not registered at all in our country until 1991. But at the end of our study period, survival rate is approaching 60% in Lithuania too.

Threshold ROP was detected in 14.5% of all infants screened for ROP. In a CRYO ROP CG study (3), 6% of infants reached threshold. The criteria for screening in our and CRYO ROP CG cohorts were absolutely different. Until 1999, the mean BW of our threshold infants was exceeding 1250 g, the upper screening limit in the CRYO ROP CG study. Nevertheless, during 2001–2003 the mean and median BW decreased remarkably in comparison to 1995–1996 (Table 1). Our data corroborate much better the reports from other developing countries. For example, Sharma et al (19) found 15% threshold ROP among infants weighing less than 2000 g. The authors emphasized that all the patients exceeding 1500 g BW with threshold ROP had a very difficult postnatal course, including complications such as septicemia, asphyxia, hypoglycemia, and intraventricular haemorrhage. The situation was identical in all our babies at the beginning of our study period.

Azad et al. (20) from New Delhi, India presents data on favorable and unfavorable threshold ROP infants with BW $953.2 \pm 2.19 - 1059.57 \pm 2.62$ g and GA $28.63 \pm 2.03 - 28.36 \pm 1.98$ weeks, respectively. We would like to mention data from a middle-income country, Vietnam (21). The study was performed in 2001; a total of 225 infants with BW ranging from 900 to 2000 g (mean, 1512 g) were screened for ROP. Threshold ROP was present in 9.3% of them.

It seems evident that threshold ROP manifests itself in very “heavy” and “old” infants as it was in our study. On the other hand, we all know that ROP is an avoidable disease and given the constant advancements in treatment techniques and broadening of skill sets of doctors, the incidence and severity of ROP will diminish.

Nevertheless, we are approaching high income countries. For example, the recent data from Italy (22) Catholic University Hospital in Roma show that ROP was diagnosed in 67 preterm infants. Their mean BW was 942 ± 245.6 grams and mean GA 27.7 ± 1.83 weeks. Our knowledge and clinical sense suggest that in a reasonably short time we shall achieve a similar level. Based on our experience, current achievements, and field proven results, we strongly believe we will be able to stay in line with Western world practice of successful neonatal care, ROP diagnosis and treatment.

CONCLUSION

A remarkable decrease in the mortality and an increase in the survival rate of premature infants is evident in Lithuania. Improvement in neonatal care brought a rapid decrease of mean BW and mean GA of threshold ROP infants.

Received 12 June 2006

Accepted 31 July 2006

References

- Sirtautiene R, Bagdoniene R. Epidemiology and screening for retinopathy of prematurity in Vilnius County. *Medicinos teorija ir praktika (Theory and practice of medicine)* 1998; 3: 115–7.
- The Committee for the Classification of Retinopathy of Prematurity. An international classification of retinopathy of prematurity. *Arch Ophthalmol* 1984; 102: 1130–4.
- Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity. One-year outcome – structure and function. *Arch Ophthalmol*. 1990; 108: 1408–1.
- Bagdonienė R, Sirtautienė R. Neišnešiotų naujagimių retinopatija (Retinopathy of prematurity). Vilnius, Gilija; 1998: 1–104.
- Bagdonienė R, Sirtautienė R. Akių ligų atlasas (Atlas of eye diseases, in Lithuanian). Vilnius, Alma Littera; 2001: 1–734.
- Bagdoniene R, Sirtautiene R. Neišnešiotų naujagimių retinopatija (Retinopathy of Prematurity, in Lithuanian). Vilnius, 1998: 1–24.
- Bagdoniene R, Sirtautiene R. Cryotherapy for ROP. Two years of experience. In Suveges I, Follmann P, editors. Proceedings of the XIth Congress of the European Society of Ophthalmology, Budapest, (Hungary), June 1–5, 1997. Bologna (Italy): Monduzzi Editore SPA, 1997: 967–71.
- Sirtautiene R, Bagdoniene R, Nasliuniene A. ROP in triplets. In: Reibaldi A, Di Pietro M, Scuderi A, editors. Progress in Retinopathy of Prematurity. Proceedings of the International Symposium on Retinopathy of Prematurity, Taormina. Amsterdam / New York: Kugler Publications, 1997: 89–93.
- Bagdoniene R, Sirtautiene R. Cryotherapy for Zone I retinopathy of prematurity. *Acta medica Lituanica* 1998; 2: 181–7.
- Sirtautiene R, Bagdoniene R. Sexual differentiation and retinopathy of prematurity. *Acta medica Lituanica*, 1998; 3: 270–3.
- Bagdoniene R, Sirtautiene R. Threshold retinopathy of prematurity in Lithuania. Tendencies during three years. In: Reibaldi A, Di Pietro M, Scuderi A, editors. Progress in Retinopathy of Prematurity. Proceedings of the International Symposium on Retinopathy of Prematurity, Taormina. Amsterdam / New York: Kugler Publications, 1997: 31–6.
- Bagdoniene R, Sirtautiene R. Tunica vasculosa lentis and its prognostic value in cryotherapy for ROP. *Acta medica Lituanica*, 1999; 1: 70–3.
- Sirtautienė R, Bagdonienė R. Neišnešiotų naujagimių retinopatija (NNR) – patohistologiniai aspektai (Pathohistological aspects of ROP, in Lithuanian). *Medicinos teorija ir praktika (Theory and practice of medicine)*, 1998; 4(16): 179–81.
- Bagdoniene R, Sirtautiene R. Is it time to change screening limits for retinopathy of prematurity? Abstract book of the XI Forum Ophthalmologicum Balticum, Tallinn 2004: 55.
- Holmström G, el Azazi M, Jacobson L et al. A population-based, prospective study of the development of ROP in prematurely born children in the Stockholm area of Sweden. *Br J Ophthalmol* 1993; 77: 417–23.
- Larson E, Holmström G. Screening for retinopathy of prematurity: evaluation and modification of guidelines. *Br J Ophthalmol*, 2002; 86: 1399–402.
- Palmer EA. What have we learned about retinopathy of prematurity during the past ten years? In: Reibaldi A, Di Pietro M, Scuderi A, editors. Progress in Retinopathy of Prematurity. Proceedings of the International Symposium on Retinopathy of Prematurity, Taormina. Amsterdam / New York: Kugler Publications, 1997:217–25.
- Nagata M, Takeuchi A. When should we start fundus examination of premature infants? In: Shapiro MJ, Biglan AW, Miller MM, editors. Retinopathy of Prematurity. Proceedings of International Conference on Retinopathy of Prematurity. Amsterdam / New York: Kugler Publications, 1993: 49–54.
- Sharma T, Gopal L, Badrinath SS. Retinopathy of prematurity: an Indian experience. In: Shapiro MJ, Biglan AW,

- Miller MM, editors. Retinopathy of Prematurity. Proceedings of International Conference on Retinopathy of Prematurity. Amsterdam/New York: Kugler Publications, 1993: 33–4.
20. Azad RV, Sethi A, Kumar H. Management outcome in prethreshold retinopathy of prematurity. *J Pediatr Ophthalmol Strabismus* 2003; 40: 330–4.
21. Phan MH, Nguyen PN, Reynolds JD. Incidence and severity of retinopathy of prematurity in Vietnam, a developing middle-income country. *J Pediatr Strab* 2003; 40(4): 208–12.
22. Pagliara MM, Lepore D, DeSantis R. The changing face of ROP. *Invest Ophthalmol Vis Sci*, 2002; 43: E-Abstract 1241.