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# Threshold retinopathy of prematurity in Vilnius County: nine-year experience

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**Background:** The aim of the study was to present changes of birth weight (BW) and gestational age (GA) among infants who reached threshold ROP and underwent treatment over the period of nine years.

**Materials and methods:** Data were collected prospectively from January 1995 to December 2003. Infants were screened for ROP in Vilnius University Children's Hospital by the same two ophthalmologists (R.B. and R.S). All infants were outborn. BW and GA were recorded in all study subjects.

**Results:** Over the period 1995–2003, 2202 infants were screened for ROP. 320 infants reached threshold (14.5% of all screened) and underwent treatment. The mean BW of threshold ROP infants dropped from 1558.1 g in 1995 to 1037.3 g in 2003 and the mean GA from 30.7 to 27.2 weeks.

**Conclusions:** 1. Insufficient experience in neonatal care was the reason for ROP in "old" and "heavy" infants. 2. BW and GA of threshold ROP cases were decreasing over the study period. 3. With improvement of neonatal care, the incidence of ROP is decreasing but the disease still exists among the most premature infants.

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

## INTRODUCTION

After the crash of the Soviet empire the ophthalmologists from former communistic countries started following Western diagnostic and treatment standards. Because of the lack of knowledge and equipment the earliest stages of retinopathy of prematurity (ROP) were an unknown disease for Soviet specialists. We just knew the "retrolental fibroplasia" – the end stage of ROP.

Nowadays, reviewing the medical documentation of children blind due to "retrolental fibroplasia", we discovered very precise descriptions of the fundus of the eyes, produced while checking them up at the neonatal unit. "Dilated venae", "tortuous arteries" were interpreted as a sequel of intracranial hypertension. In some cases we found descriptions of a "grey retina" in the periphery. Unfortunately, nobody knew the real meaning of these devastating symptoms. These patients were coming back only after the onset of total blindness.

Until the year 1991, only neonates with gestational age (GA) more than 28 weeks and birth weight (BW) more than 1000 grams were registered after delivery in Lithuania. Smaller infants were registered only in cases if they survived more than 7 days.

After proclamation of Lithuanian independence in 1991, the World Health Organization (WHO) recommendations were accepted and all neonates with GA more than 22 weeks and BW more than 500 grams were registered. The new standpoint increased the survival rate of premature infants. But the lack of experience and proper technique determined a new problem – an increasing incidence of ROP.

After learning the disease in Western countries and introducing indirect ophthalmoscopy for infants' examinations in Lithuania we were not able to find babies suitable for screening according to the Western BW and GA recommendations. All our babies were "too old" and "too heavy". It became necessary to elaborate our own screening criteria, so until 1998 year we screened all infants in the neonatal unit.

## MATERIALS AND METHODS

Data were collected prospectively for 9 years – from January 1995 till December 2003. Infants were screened for ROP in the intensive care and premature infant departments of Vilnius University Children's Hospital. All infants were outborn. They were transported to this hospital from three Vilnius hospitals and from several other hospitals located in Vilnius County. Gestation age and birth weight were recorded for all babies. All screening and treatment procedures were performed by the same two ophthalmologists (R. Bagdonienė and R. Sirtautienė). The pupils were dilated with Tropicamide 0.5% solution. A strabismus hook for rotation of the globe and lid speculum was used in the majority of cases. The

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examinations were performed mainly on a weekly or bi-weekly basis and continued until vascularisation of the retina was finished. Infants with ROP were screened at intervals depending on the severity of the disease. Retinopathy of prematurity was staged according to the International Classification of Retinopathy of Prematurity (IC ROP) (1).

Infants who reached threshold ROP as stated by the CRYO ROP CG trial criteria (2) underwent treatment (cryotherapy until June 1998, laser or laser-cryo therapy since July 1998).

**Statistical evaluation**

Analysis of data was performed using confidence intervals for factor means and standard error of mean (SEM) or standard deviation (SD). The t test was used to analyze normally distributed variables. The result was reported as significant whenever the p value was less than 0.01.

## RESULTS

In total, 2297 premature infants were admitted and followed up at Vilnius University Children's Hospital during nine years (1995–2003). The average number per year was 255 ± 44 babies.

2202 infants were screened for ROP over this period. 320 infants reached threshold ROP and underwent treatment for ROP (14.5% of all screened).

The numbers of infants who underwent screening and treatment for ROP are presented in Fig. 1.

The highest number of screened infants was in 1997 year – 324. The highest amount of threshold ROP cases was diagnosed in 1996 and 1997 year (50 and 51 respectively). Since 1999 when national guidelines for screeing were employed, the new group of infants – above screening limits – is arising (3). This group reached 60 infants in 2003.

The lowest percentage of threshold ROP cases was found in 2000 (Table 1). At the end of the study period this number increased to 20% due to the decreasing number of screened infants.

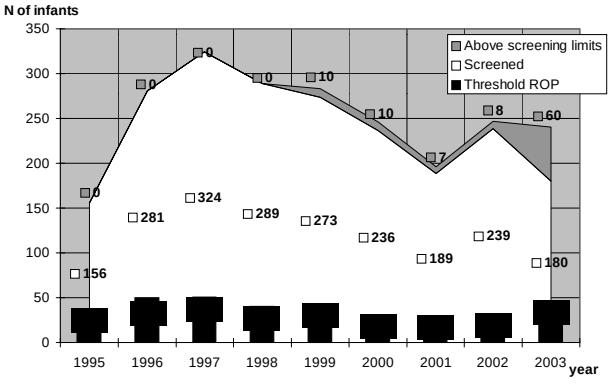


**Fig. 1.** Numbers of infants who underwent screening and treatment for ROP by years

Table 1. **Frequency of threshold ROP by years**

| Year | % of threshold ROP |
|---|---|
| 1995 | 18.3 |
| 1996 | 17.8 |
| 1997 | 15.7 |
| 1998 | 13.8 |
| 1999 | 15.0 |
| 2000 | 9.7 |
| 2001 | 10.6 |
| 2002 | 10.0 |
| 2003 | 20.0 |
| Total | **14.5** |

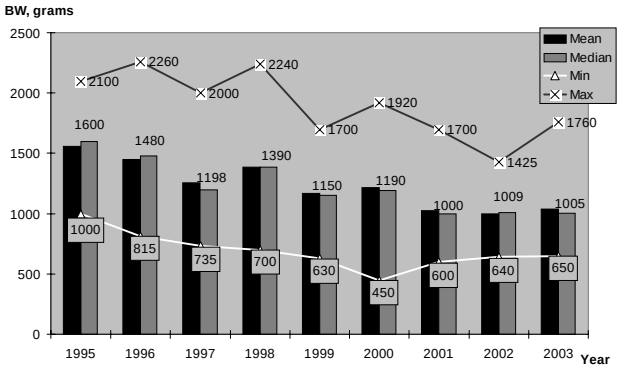


**Fig. 2.** BW data of threshold ROP infants in 1995–2003

The distribution of threshold ROP infants by mean BW is shown in Fig. 2.

The mean BW of all treated infants was 1236.2 g. (SD = 360.0 g).

There was an evident decrease in the mean BW of threshold ROP infants during the nine-year study period. The mean BW dropped from 1558.1 g in 1995 to 1037.3 g in 2003. In 2000, for the first time in Lithuania survived the infant of BW 450 g. In 2.8% of infants treated for ROP, BW exceeded 2000 g in 1995–1998.

For the purpose of a more detailed data analysis, the infants were divided into three subgroups (N1, N2, and N3) of consecutive 3-year periods: 1995–1997, 1998–2000, and 2001–2003. Figure 3 represents an evident shift towards decreasing BW in each 3-year subgroup.

The mean BW of each subgroup was: subgroup N1 – 1408.7 ± 28.9 g, subgroup N2 – 1258.1 ± 35.1 g, and subgroup N3 – 1022.6 ± 29.0 g. The difference was statistically significant between each subgroup ($p < 0.001$).

The distribution of threshold ROP infants by GA is presented in Fig. 4. The mean GA of these infants over the whole period was 28.9 ± 0.2 weeks. The same trend to a decreasing GA is evident: 30.7 weeks in 1995 versus 27.2 weeks in 2003. The same subdivision into three subgroups shows evident and statistically significant differences between each of them: the mean GA of subgroup N1 – 29.9 ± 0.2 weeks, of subgroup N2 – 28.6 ± 0.2 weeks, of subgroup N3 – 27.5 ± 0.2 weeks.

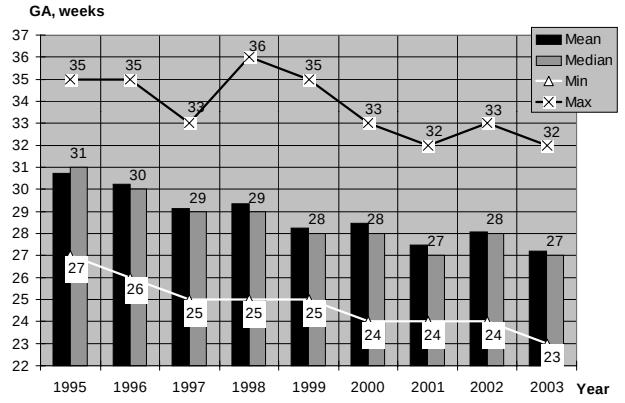


**Fig. 3.** GA data of threshold ROP infants in 1995–2003

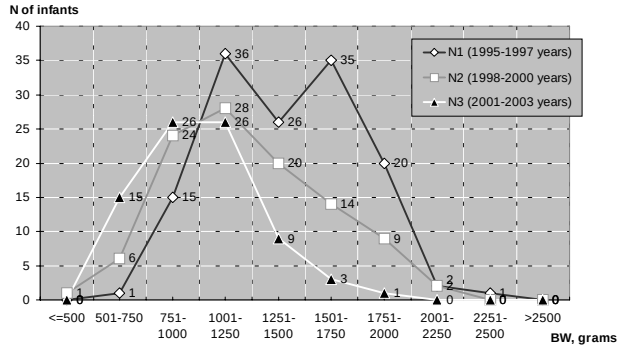


**Fig. 4.** Frequency of threshold ROP by BW in three-year subgroups

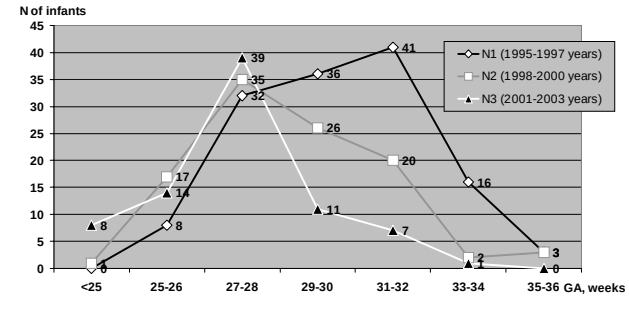


**Fig. 5.** Frequency of threshold ROP by GA in each three-year subgroups

Figure 5 illustrates an evident decrease in GA in each three-year period.

## DISCUSSION

The remarkable improvement in knowledge and technologies determined a sudden reduction in severe ROP cases, especially in the second half of the study period. In 1995, threshold ROP was diagnosed in 18.3% and in 2000 in 9.7% of screened infants. The incidence of threshold ROP decreased almost by half after the first five years of work.

At the very beginning of the study period, improvement in intensive care facilities led to a better survival of neonates, but the "quality" of surviving infants was on the second plan at that moment. First of all neonatologists tried to improve the survival rate of neonates by all available means. Given the fact that there was a severe shortage of modern equipment (old donated incubators, lack of pulsoximeters), insufficient level of experience of the servicing staff, in our opinion, that was the reason for the highest numbers of threshold ROP infants in 1995–1997.

Since 1999 when the national guidelines for screening were employed, the number of screened infants was gradually decreasing. The same trend towards a decrease was observed in the curve of threshold ROP cases. The decrease of threshold ROP among infants with BW >1250 g and GA >30 weeks is evident. Towards the end of the period the incidence of threshold ROP was decreasing, but after the year 2000 it stabilized and even increased in 2003. The introduction of the national guidelines for screening reduced the number of screened babies. This enabled us to cut the number of screening procedures, but on the other hand it was one of the reasons for the growing threshold ROP percentage. Out of 240 infants, only 180 underwent screening thus the increasing percentage of threshold ROP from 15% (if all infants would be screened) to 20%. Another reason is much better survival of the smallest infants and the much higher incidence of ROP among them.

It is difficult compare our data with those reported in the literature from the same period in developed countries. We need to look some time back. For example, Nagata and Takeuchi (4) presented similar data from Japan. In 1984–1985 they screened 600 infants, and 65 of them were treated. The BW of these infants was below 1500 g. Much less threshold ROP cases were in the CRYO ROP study – only 6% (5). On the other hand, the data are very similar to ours in some other low income countries. In one study from India (6), threshold ROP was found in 15% of screened infants below 2000 g. Nowadays, the situation is similar in many developing countries (7–9).

A considerable decrease in the BW of threshold ROP infants was observed over the study period. This tendency is so evident that statistically significant differences are found even between each of the three-year subgroups. As a confirmation of improvement in neonatology, the smallest neonate (450 g) in Lithuania survived in 2000; the infant underwent treatment for threshold ROP and presently is a sighted and normally developing child.

Gestation age shows very similar tendencies to those of BW. Nevertheless, we think that BW is a more reliable factor for evaluation of prematurity in our country. GA is not 100% confirmed by ultrasound examinations on the first trimester of gestation, and some women are inclined to misreport the the last menstrual period because of socioeconomic reasons. The same opinion concerning GA was expressed even by authors from developed countries (10). Nevertheless, even in developing countries there are cases of severe ROP in more mature infants (11). More recently, in 2003, Hutchinson et al. (12) described stage 3

ROP in infants with estimated gestational ages up to and including 32 weeks and birth weights up to and including 1874 g.

Shift to the left is a very obvious tendency in threshold ROP. It means that the incidence of ROP is decreasing among older infants but ROP still exists among smallest preterms. This trend is reflected in ROP incidence in BW and GA groups (Figs. 3, 5). Our experience suggests that now we have reached some kind of plato or temporal stabilization in the number of threshold cases. This is due to a better survival of smallest infants. Unfortunately, the disease still exists among them, and maybe a "new epidemic wave" is approaching us because of the survival of more and more immature infants.

In developed Western countries, ROP underwent two epidemic waves over the period of 60 years (13–15) since Terry has described the disease in 1942 (16). It was concluded that the second epidemic wave was due to increased survival rates of very low BW premature infants weighing 750–999 g and not to the new iatrogenic factors (17–18).

Nowadays in our county the main problem is ROP among 25–32 GA infants as it was in developed countries some 10–15 years ago (18–20). On the other hand, our progress in the newest achievements in this field of medicine so rapid that 9 years of experience brought us through the whole history of sixty years, and now we are going to face the same problem as the one experienced by the developed world – ROP in neonates less than 25 weeks of GA (21).

## CONCLUSIONS

1. Insufficient experience in neonatal care was the reason for ROP in "old" and "heavy" infants.

2. BW and GA of threshold ROP cases were decreasing over the study period.

3. With improvement of neonatal care the incidence of ROP is decreasing but the disease still exists among the most premature infants.

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