

<https://doi.org/10.52418/moldovan-med-j.66-1.23.06>
UDC: 617.735-053.32(478)



Retinopathy of prematurity, the prevalence and risk factors in Moldova

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Manuscript received November 30, 2022; revised manuscript February 17, 2023; published online March 10, 2023

Abstract

Background: Retinopathy of prematurity (ROP) is a serious disease that affects premature infants and still represents the leading cause of blindness worldwide that can be prevented if detected earlier in time.

Material and methods: The ROP prospective observational study was performed enrolling all premature infants admitted to the Intensive Neonatal Care (INC) and Premature Care Unit from January 2020 to December 2021 with the gestational age (GA) of 32 weeks and less at birth and body weight (BW) of 2000 g and less. A total of 98 premature infants had retinal evaluation by indirect ophthalmoscopy starting with the five postpartum weeks followed every 7-10 days until 38 weeks and then every 2 weeks until 42-45 weeks. The severity of ROP was graded according to the International classification of ROP. The effects of GA and BW on the prevalence and severity on ROP were evaluated.

Results: Out of studied 98 infants, 36 patients (36.7 %) developed ROP stage 1 and 2, in one or both eyes, 3 (3.07%) infants developed stage 3. Out of these 3 premature infants with stage 3, one underwent avastin intravitreal injection with successful regression, 2 patients underwent laser photocoagulation treatment successfully.

Conclusions: The prevalence of ROP in this unit-based study was 36 patients (36.7 %). The most important risk factors: Low gestational age, and low body weight. Lower gestational age and body weight was a risk factor, as the greatest number (76%) 20 infants out of 26 with GA ≤ 29 weeks and BW ≤ 1000g developed ROP stage 1 and stage 2; 3.06% (3 infants) developed stage 3. Very important in preventing ROP vision loss, screening all infants at risk regardless of GA and BW as well as the duration of staying in INC represents the greatest priority.

Key words: retinopathy of prematurity, newborn, gestational age, risk factors.

Cite this article

Mazur L, Bendelic E, Corduneanu A. Retinopathy of prematurity, the prevalence and risk factors in Moldova. *Mold Med J.* 2023;66(1):35-38. <https://doi.org/10.52418/moldovan-med-j.66-1.23.06>.

Introduction

Retinopathy of prematurity (ROP) represents the leading cause of preventable worldwide blindness in infants. Currently we are facing a tremendous survival premature rate associated with increasing incidence of ROP.

Embryonic retinal arteries start to grow in the third month of the pregnancy and their development ends at birth. Therefore, the stages of the evolution of the eye are defective in prematurity and the growth of normal vessels is stopped. After premature delivery the process is associated with abnormal neovascularization of the retina.

International classification of ROP is a consensus statement that creates a standard nomenclature for classification of ROP [1]. The International Classification describes ROP by location zones and severity stages, as well as plus and preplus disease: Stage 1 – Demarcation line separates avascular retina from vascularized retina; Stage 2 – Ridge from demarcation line; Stage 3 – Extra retinal neovascularization; Stage 4-5 – Partial and total retinal detachment.

Currently the ROP is under constant epidemiological study around the world. GA and BW are the essential factors determining the ROP. According to Moldovan screening guideline all preterm babies with gestational age of 32 weeks and less, and body weight of 2000 g and less should be screened. According to the United Kingdom screening guideline body weight (BW) less 1500 g and gestational age (GA) less 32 weeks require indirect ophthalmoscopy. United States has validated new ROP screening criteria, BW less than 1500 g, and GA less than 30 weeks.

Material and methods

This was an institutional unit-based cohort prospective study of 98 preterm infants admitted to Intensive Neonatal Care and Premature Care Unit of the *Gheorghe Paladi* Municipal Clinical Hospital in Chisinau, the Republic of Moldova, from January 2020 to December 2021.

The examination was carried out according to the ROP guidelines recommended by Moldovan Ophthalmology Society: Preterm infants with GA ≤ 32 weeks, and BW ≤

2000 g, were examined. The severity of ROP was graded according to the International classification of ROP. The first examination was performed at 4-5 weeks postpartum under aseptic precautions in a temperature-controlled room. Infants with no ROP sign were examined every 2 weeks until 45 weeks. If ROP was found (demarcation line), examination was repeated every week until 45 weeks. Pupils were dilated with tropicamide 0.5% and phenylephrine 0.5% eye drops, pediatric eyelid speculum was used. Indirect ophthalmoscopy was performed. The 28D diopter condensing lens was used.

Results

A total of 98 preterm infants enrolled in this study from January 2020 to December 2021 screening data are shown in table 1. A total of 36 infants (36.7%) out of 98 have been detected with ROP. GA and BW show significantly different pattern between infants with and without ROP. In general, the proportion of ROP increased with lower BW and lower GA (fig. 1, 2). Lower gestational age and body weight were a risk factor, as the greatest number 20 infants (76%) out of 26 with GA ≤ 29 weeks and BW ≤ 1000 g developed ROP stage 1-2; 3 infants (3.06%) developed stage 3. While in infants' group with BW 1001 g – 1500 g 16 patients (24.6%) out of 65 developed ROP.

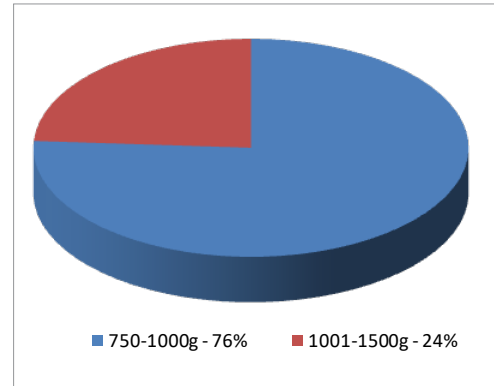


Fig. 1. Correlation BW-ROP

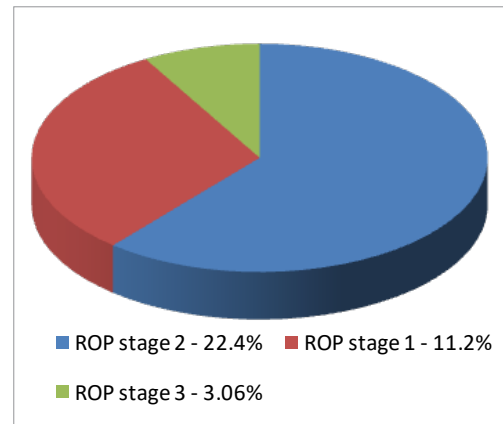


Fig. 2. ROP stage proportion

Table 1. Proportion of infants with different ROP stage

	No ROP	Total ROP	ROP Stage 2	ROP Stage 1	ROP Stage 3	AP-ROP	Number of infants examined
BW, g							
≤ 750		4		3	1	0	4
751-1000	6	16	11	4	1	0	22
1001-1250	25	10	6	3	1	0	35
1251-1500	24	6	5	1	0	0	30
1501-2000	7	0	0	0	0	0	7
Total	62 63.2%	36 36.7%	22 22.4%	11 11.2%	3 3%	0	98 100%
GA, weeks							
GA ≤ 26w		4		3	1	0	4
27-29 w	6	16	11	4	1	0	22
29-30w	27	10	6	3	1	0	37
31-32w	29	6	5	1	0	0	35
Total	62 63.2%	36 36.7%	22 22.4%	11 11.2%	3 3.06%	0	98 100%

Discussion

The control of blindness in children is a priority within the World Health Organization Vision 2020 program. The World Health Organization Vision 2020 program defines ROP as “avoidable disease” [2]. After an improvement in child health care in Moldova, and ROP screening, rate of blindness decreased in our country.

The prevalence and treatment outcome of ROP in the world are affected by social factors, such as economic development, and the healthcare level of premature infants. With the establishment and improvement of ROP screening and treatment schedules in developed countries, the prevalence of ROP has been declining. On the other hand, the survival rate of very low BW premature infants and critically ill infants has been increasing. The prevalence of ROP in the USA increased from 14.70% in 2000 to 19.88% in 2012 [3-5]. The frequency of ROP was 2.4% in newborns weighing more than 2,500g and 30.2% in newborns with birth weight between 750-999g. So, the increasing number of ROP was associated with simultaneous decline in newborn mortality. In a national study in the UK between 1997-1999 the treatment rate was 59% while in 2013-2014 – 62.39% of newborns developed type 1 and 8.26% of infants had aggressive posterior ROP so the treatment rate was 2 times higher than previously estimated [6-9]. In Taiwan between 2002-2011 were reported 36.6% of infants with ROP.

According to recent data India accounts for 10% (about 280.000) of worldwide ROP related blindness due to low screening rate and low health care services of premature babies [10-14]. Five-year demographic profile of ROP in a tertiary institute in North India from 2013-2017 reveals 32.3% of infants with ROP from which 28% were detected with aggressive posterior ROP (AP-ROP). In Turkey, a study revealed during 2020-2022 the prevalence of ROP was about 16% [15-16]. While in China during 2016-2020 the ROP prevalence was 17.9%. As well as in Egypt during 2018-2020 the overall prevalence of ROP was 34.1% [17-18].

Importantly, in Italy in a prospective observational multicenter study between January 2008 – December 2009 there were registered 62.9% of preterm infants with ROP and 34% of infants required surgical treatment [19].

In Romania, according to an institutional publication the prevalence of ROP was estimated to be 40-50% with treatment rate 9%-16%. And at least 100 blind children born from 2002-2017 were attributed to missed screening [20].

Interestingly, for example in Japan, in an institutionally-based study between 2009 and 2011 there were registered 70.6% of ROP in infants born before 28 weeks with mean BW 779g at a neonatal intensive care unit Red Cross Sendai Hospital Japan [21].

Most screening guidelines were drawn up based on GA and BW which are the identified risk factors of ROP. Other factors, such as, long-term fluctuation oxygen therapy,

long intubation period, necrotizing enterocolitis, serious systemic diseases, intraventricular hemorrhage, multiple blood transfusions, and long-term hospitalization were reported to correlate to ROP [22-23].

More published research demonstrates the magnitude of this real public health care problem that persists not only in low-income countries.

The prevalence of ROP in this unit-based study was 36.7% which is relatively higher, and the treatment rate was 3% which involved patients with stage 3, two preterm infants underwent laser photocoagulation therapy, and one underwent intravitreal anti-vessels endothelial growth factor injection with no reactivation. Otherwise, there were 4 infants with stage 3 and there were not detected ROP stage 4 or stage 5 nor aggressive posterior ROP.

This study indicates that the prevalence of ROP increases gradually with the lower GA and BW. GA and BW are still the most important risk factors for ROP.

Conclusions

GA and BW are still the major risk factors in the evolution and severity of ROP. According to this institutional, unit-based study the prevalence of ROP was 36%. The proportion of ROP increased with lower gestational age and lower body weight, as the greatest number as 76% of infants with GA ≤ 29 weeks and BW ≤ 1000 g developed ROP stage 1 and stage 2. There were not registered ROP stage 4 or 5 nor AP-ROP. The treatment rate in this study was 3%.

ROP screening criterion of BW ≤ 2000 g, or GA ≤ 32 weeks proved to be the most effective in Moldova as well.

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Authors' contributions

LM conceptualized the study and drafted the first version of the manuscript, interpreted the data. EB and AC critically revised the manuscript. All the authors revised and approved the final version of the manuscript.

Funding

This study was supported by *Gheorghe Paladi* Municipal Clinical Hospital. The study was the authors' initiative. The authors are independent and take responsibility for the integrity of the data and accuracy of the data analysis.

Ethics approval and consent to participate

The study was approved by the Research Ethics Committee of *Nicolae Testemitanu* State University of Medicine and Pharmacy, proceedings No 01/26.08.2016.

Conflict of interests

No competing interests were disclosed.