

# INCIDENCE AND MAJOR PERINATAL COMPLICATIONS IN EXTREMELY LOW BIRTH WEIGHT

Aniko Manea<sup>1</sup>, Marioara Boia<sup>1</sup>, Daniela Iacob<sup>1</sup>

<sup>1</sup>Dept. Of Neonatology – University of Medicine and Pharmacy Timisoara

## Abstract

**Introduction:** Newborns with extreme prematurity are considered those who have a birth weight under 1000 grams. Morpho-functional plurivisceral immaturity lead to particular diseases, through frequency and gravity.

**Objectives:** The authors aim to study a lot of newborns with extremely low birth weight and to determine the major complications specific for this category.

**Material and method:** the study was carried out in the Premature and Neonatology Department during two years, on a group of 20 premature newborns with birth weight under 1000 grams (800 grams- 1000 grams), with gestational age between 27-32 weeks.

**Results:** In the group studied the distribution by sex showed a number of 11 (55% ) male newborns and 9 (45% ) female newborns.

Respiratory distress syndrome was present in 14 cases (70%), prematurity apnea in 16 cases (80%). It was diagnosed a case of necrotizing enterocolitis. The patent ductus arteriosus was revealed by ultrasound in 8 cases (40%), in 2 cases was associated with septal atrial defect. Intraventricular hemorrhage of several degrees revealed with transfontanelar ultrasound in a ratio of 60%-12 newborns. Within the screening program for prematurity retinopathy the entire group was evaluated, 9 of them (45%) presenting signs of retinopathy in several stages. All the premature presented several degrees of anemia.

**Conclusions:** Extreme prematurity is an important risk factor in increasing neonatal morbidity and mortality, premature with very low birth weight being the most

exposed to all major complications of prematurity both in neonatal period and after this.

**Keywords:** Extreme prematurity, complications.

## Introducion

Plurivisceral morpho-functional immaturity causes some particular diseases through frequency and severity: respiratory distress syndrome, peri- and intraventricular hemorrhage, apnea crisis, patent ductus arteriosus, enterocolitic ulceronecrosis and infections.

Premature newborns have dominant respiratory clinical manifestations but the lesion background is mostly cerebral. By Rusul (1981) the complications of prematurity can be classified as follows:

- Early pathology : idiopathic respiratory distress syndrome, recurrent apnea, intra and periventricular hemorrhage, lung hemorrhage, jaundice, infections
- Late Sechele : at eyes (retinopathy of prematurity-retrolental fibroplasia, myopia, strabismus), auditive (hypoacusis, deafness), neurological (cerebral paralysis, diplegie, choreoathetosis, epilepsy), intelectual (IQ lower than 70), psychic (behavior disturbances).

## Respiratory distress syndrome

By the old statistics respiratory distress syndrome affects 5% of the 1st degree premature, 20% of the 2nd degree premature, 50% of the 3rd degree premature, 70% of the 4th degree premature, and only 0,5% of the term newborn. Related to the gestational age the incidence of the disease is: 20% when gestational age is 34-32 weeks and 40% when gestational age is 32-30 weeks.

The frequency of respiratory distress syndrome related to gestational age and antenatal steroids therapy :

Gestational age	Antenatal steroid therapy	
	without	Yes
<30 weeks	60%	35%
30-34 weeks	25%	10%
>34 weeks	5%	-

**Radiologic examination:** At more then 90% of the patients the radiological image is characteristic since the age of 5 hours and shows characteristic "ground glass image.

**Lab examination** emphasizes hipoxemia (PO<sub>2</sub> arterial <50mmHg) ± hipercapnia (PCO<sub>2</sub> >55-60 mmHg). It was observed that PCO<sub>2</sub> in arterial blood at the beginning of disease can be normal or decreased and, as far as the disease evolves, it increases.

The disesse being characteristic to premature newborn, the treatment will consist of prevention the

premature birth. The antenatal therapy with corticosteroids is indicated for women with risk of premature birth. The treatment will be individualized according to the severity of disease. The therapy aims to maintain, in reasonable limits, the PaO<sub>2</sub> (45-70 mmHg) and the PaCO<sub>2</sub> (34-45 mmHg).

## Peri and intraventricular hemorrhage

Intraventricular hemorrhage is the most frequent form at newborn, more often met at premature than at term newborn. Its' importance comes out not only in the high

incidence of this pathology, while raising the number of small and very small surviving premature, but also in the major impact on the perinatal and postneonatal morbidity and mortality, by secondary neurological sequelae, by lesion associations and complications.

Intraventricular hemorrhage occurs usually at premature with gestational age under 34 weeks. With the support of transfontanelar ultrasound it was established that 50% of the premature under 1500 grams face this type of hemorrhage, and approximately half of them survive. From the survivors 40% develop further normally, 40% remain with minor sequelae and 20% with medium and severe sequelae.

By Perlman and Volpe at premature with birth weight between 500 and 700 grams incidence of intraventricular hemorrhage is 62%, out of which 97% are severe forms (degree III and IV), while at those with birth weight between 700 and 1500 grams the incidence is 25% and only 32% are severe forms. These data are in accordance with data offered by other studies. Gleissner shows, in another study, that incidence of intraventricular hemorrhage is 48,5% at 27 weeks of gestation, 32,4% between 28 and 32 weeks of gestation and goes down at 26% after this gestational age.

The incidence of peri and intraventricular hemorrhage decreased constantly in the last years, from approximately 40% at newborns with birthweight <1500g in initial studies, to approximately 20% in the recent studies.

Although the incidence of the disease went down, its prevalence between the surviving infants is still substantial due to high rate of surviving infants with birth weight under 1000 grams.

#### Patent ductus arteriosus

Definition: abnormal communication between lung and systemic flow at the level of persistent arterial channel, situated between lung and thoracic artery, where it goes up to 5-10mm distal from left subclavicular artery emergence.

The arterial channel is a remaining of the 6th aortic arch identified in the 6th gestational week, having an important role during embriofetal flow, and being the location of pasive shortcut of lung flow. So the blood is lead in a teritory with low vascular resistance (placental flow). This anatomic formation, characteristic to fetal life, is closing, functionally, in the first 12 hours of life and anatomically in the first 3 weeks, through afibrosis process. Remaining fiber belr is known as ligamentum arteriosus. For closing the channel interferes a constrictiv efect of increasing the volume of oxygen in blood, immediatelly postnatal. This effect is directly related with gestational age, being less obvious at large premature bigger than 1000 grams If we want to maintain the arterial channel open immediatelly postnatal we must interfere with prostanglandine infusion.

PDA at premature under 1000 grams, with severe respiratory distress in the first days of life: surfactant administration leads to lung healing, but as the lung disease is healing the lung vascularly resistance decreases, the

volume of blood through PDA increases, identified in 80% of cases. Mechanical ventilation bigger pressures to beat the lung resistance; blood flow through PCA can be so big that the suflul might be not heard. Paralel with lung overloading other organs are less irrigated (during diastolic the diastolic pressure in aorta decreases too much). In these cases it was shown that surgically closing the PDA before the age of 10 days has a positive effect, decreasing the period and pressure for assisted ventilation. In practice, even without major hemodynamic complications, it is tried to close, pharmacologically, the PCA at any premature under 1000 grame, in the 3rd day of life. Only if, after 72 hours of indometacin administration, the left ventricular deficiency is not controlled will be taken in consideration surgical closing of arterial channel.

#### Premature Retinopathy

In the last decade it was described as a new complication which come out at premature, as a multi factor disease. It is characterized by abnormal retinian vascular development, leading to retinal detachment serious visual affection up to blindness. The disease occurs especially at former premature with very low birth weight. The incidence of the disease increases as long as gestation period and birth weight are smaller. International studies show presence of retinopathy at 65% of the premature with birth weight less than 1250 grams and 80% of the newborns with birth weight less than 1000 grams. In SUA, premature retinoathy is the second cause of blindness at the age of 6 years. Those with gestational age <28 weeks present a higher risk of ROP.

Clinical picture:Diagnosis of premature retinopathy is made by ophtalmoscopic examination (an indirect ophthalmoscope). Examination of the retina of a premature infant is performed to determine how far the retinal blood vessels have grown (the zone), and whether or not the vessels are growing flat along the wall of the eye (the stage). Retinal vascularization is judged to be complete when vessels extend to the ora serrata. The stage of ROP refers to the character of the leading edge of growing retinal blood vessels (at the vascular-avascular border). The stages of ROP disease have been defined by the International Classification of Retinopathy of Prematurity (ICROP).

ICROP uses a number of parameters to describe the disease. They are location of the disease into zones (1, 2, and 3), the circumferential extent of the disease based on the clock hours (1-12), the severity of the disease (stage 1-5) and the presence or absence of "Plus Disease". Each aspect of the classification has a technical definition. This classification was used for the major clinical trials. It has been revised in 2005.

The zones are centered on the optic nerve. Zone 1 is the posterior zone of the retina, defined as the circle with a radius extending from the optic nerve to double the distance to the macula. Zone 2 is an annulus with the inner border defined by zone 1 and the outer border defined by the radius defined as the distance from the optic nerve to the nasal ora serrata. Zone 3 is the residual temporal crescent of the retina (fig1).

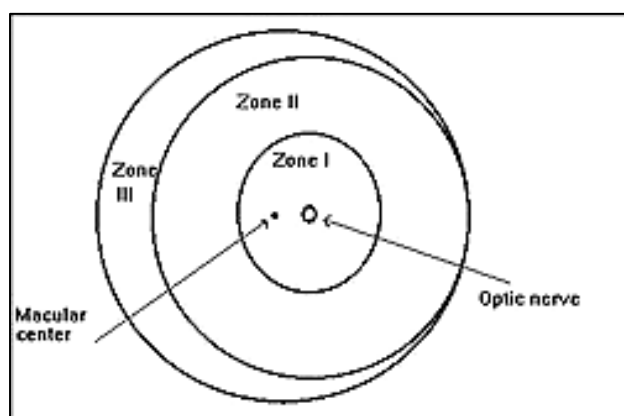


Fig.1 Zones of the retina in ROP.

The circumferential extent of the disease is described in segments as if the top of the eye were 12 on the face of a clock. For example one might report that there is stage 1 disease for 3 clock hours from 4 to 7 o'clock. (The extent is a bit less important since the treatment indications from the Early Treatment for ROP)

The Stages describe the ophthalmoscopic findings at the junction between the vascularized and avascular retina.

- Stage 1 is a faint demarcation line.
- Stage 2 is an elevated ridge.
- Stage 3 is extraretinal fibrovascular tissue.
- Stage 4 is sub-total retinal detachment.
- Stage 5 is total retinal detachment.

Retinal examination with scleral depression is generally recommended for patients born before 30-32 weeks gestation, with birthweight 1500 grams or less, or at the discretion of the treating neonatologist. The initial examination is usually performed at 4-6 weeks of life, and then repeated every 1-3 weeks until vascularization is complete (or until disease progression mandates treatment).

#### Ulceronecrotic enterocolitis

Described in 1960 ulceronecrotic enterocolitis seems to be an affection which belongs to modern intensive care units, where its frequency is 1-15%. The incidence of EUN is variable from one medical center to other and it seem to be 10% amongst the premature with very low birth weight. This variation makes some authors consider EUN as epidemic. Mortality through EUN is 20-30%.

Etiopathogeny. Etiopathogeny of EUN is incompletely cleared. Today it is believed that it has a multifactor determinism. The most important risk factors are prematurity, intestinal ischemia, infection and enteral feeding.

Prematurity. EUN is, first of all, a disease of premature. From the total of ill persons 50% are premature of 3rd și 4th degree, 30% premature of 1st and 2nd degree and only 20% have birth weight over 2500 grams. Morphologic and functional imaturity of intestine and

imunitară imaturity are the base of increased incidence of EUN at premature. Now it is mentioned that EUN incidence is lower at premature with mothers who received glucocorticoids before birth. Glucocorticoids are ahead of lung and gastrointestinal tract development. The imaturity of defense mechanisms of gastrointestinal tract was mentioned as risk factor, bacterial colonisation of premature intestine favorising the agression of bacteria and toxins.

The extremely low birth weight (ELBW) premature infant is an infant born at 1000 grams or less, generally before 28 weeks gestation.

Survivability correlates with gestational age for infants who are appropriate for gestational age (AGA). Infants with extremely low birth weights (ELBW) are more susceptible to all of the possible complications of premature birth, both in the immediate neonatal period and after discharge from the nursery.

#### **Objectives**

The authors aim to study a lot of newborns with extremely low birth weight and to determine the major complications specific for this category.

#### **Material and method**

The study was carried out in the Prematurity and Neonatology Department during two years, on a group of 20 premature newborns with birth weight under 1000 grams (800 grams- 1000 grams), with gestational age between 27-32 weeks. A number of 750 premature newborn were included in the study, hospitalized on anamnestic, clinical and paraclinical criteria.

#### **Results**

Case distribution by prematurity degree was: 1<sup>st</sup> degree 48,27%, 2<sup>nd</sup> degree 30,93%, 3<sup>rd</sup> degree 18,14%, 4<sup>th</sup> degree 2,66% (fig.2).

In the group studied the distribution by sex showed a number of 11 (55%) male newborns and 9 (45%) female newborns (fig.3).

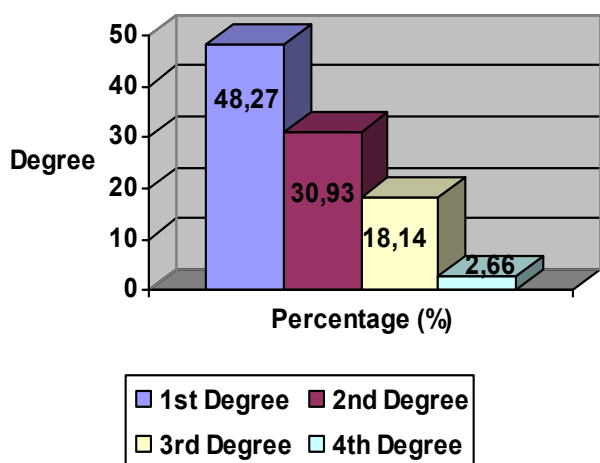


Fig.2 Distribution by prematurity degree.

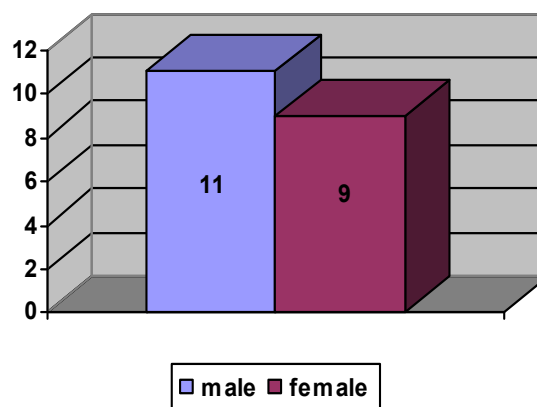


Fig.3 Distribution by sex.

An early complication of extreme prematurity is respiratory distress syndrome (RDS) caused by surfactant deficiency was present in 14 cases (70%). The diagnosis was set clinically and based on the chest x-ray. Apnea of prematurity is common in infants with extremely low birth weights and is defined as cessation of respiratory activity of more than 20 seconds, with or without bradycardia or cyanosis. She was present in 16 cases (80%). It was diagnosed a one case of necrotizing enterocolitis who present the following clinical signs: abdominal distension , hemorrhagic stools, vomiting , edema of the abdominal wall . The patent ductus arteriosus was revealed by cardiac ultrasound in 8 cases (40%), in 2 cases was associated with septal atrial defect (Fig.4)

Babies with extremely low birth weights are at particular risk for IVH because of vulnerability of the germinal matrix and because the protective cerebral

autoregulation present in older babies has not yet developed. Any event that results in disruption of vascular autoregulation can cause IVH, including hypoxia, ischemia, rapid fluid changes, and pneumothorax. Presentation can be asymptomatic or catastrophic, depending on the degree of the hemorrhage. Symptoms include apnea, hypertension or hypotension, sudden anemia, acidosis, changes in muscular tone, and seizures. Intraventricular hemorrhage of several degrees revealed with transfontanelar ultrasound in a ratio of 60%-12 newborns. The neurological exam showed: hypotonia , diminished or abolished primitive reflexes , seizures ,myoclonus.

Within the screening program for prematurity retinopathy the entire group was evaluated, 9 of them (45%) presenting signs of retinopathy in several stages .Two of them needed laser treatment. All the premature presented several degrees of anemia.

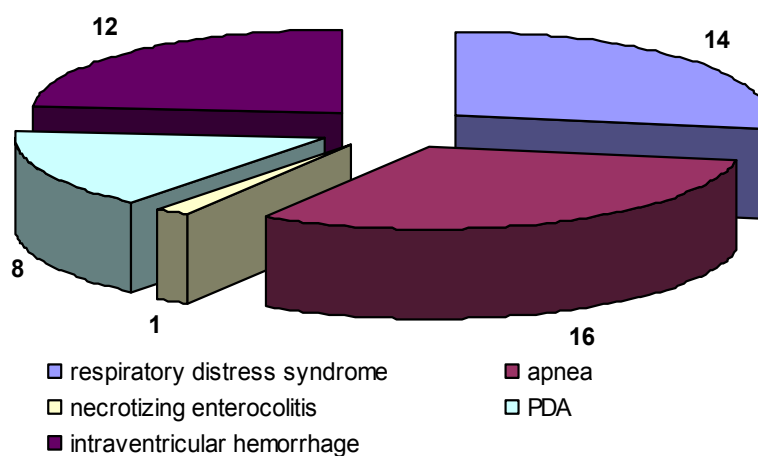


Fig.4 Distribution of complications.

**Conclusions**

Extreme prematurity is an important risk factor in increasing neonatal morbidity and mortality, premature with very low birth weight being the most exposed to all major complications of prematurity both in neonatal period and

after this. Pre term babies with under 32 weeks of gestation period must be investigated in the ROP screening program beginning with the 3<sup>rd</sup> week of life and then every 2 weeks until de age of 44 weeks after birth.

**References**

1. Cloherty J, Stark A, Eichenwald E. Manual of Neonatal Care. 5th ed. Lippincott, Wilkins and Williams; 2003.
2. Cole FS. Defects in surfactant synthesis: clinical implications. *Pediatr Clin North Am.* Oct 2006; 53(5): 911-27.
3. Courtney SE. Continuous positive airway pressure and noninvasive ventilation. *Clin Perinatol.* Mar 2007; 34(1): 73-92.
4. Ilie C. Neonatologie- probleme de baza ale asistentei imediate si precoc a nou-nascutului, Ed. Balcanic, Timisoara 2002
5. Kinsella JP, Inhaled nitric oxide in the premature newborn. *J Pediatr.* Jul 2007; 151(1): 10-5.
6. Lampland AL. The role of high-frequency ventilation in neonates: evidence-based recommendations. *Clin Perinatol.* Mar 2007; 34(1): 129-44.
7. Lupea I. *Tratat de Neonatologie*, Ed Medicala Univ. Iuliu Hatieganu, Cluj Napoca, 2000,82-93.
8. Stevens TP. Surfactant replacement therapy. *Chest.* May 2007; 131(5): 1577-82.
9. Volpe J.J., Hypoxic ischemic encephalopathy; clinical aspects. In Volpe JJ editor, *Neurology of the newborn*, 2nd ed, Philadelphia, WB Saunders, 1987, 236-279
10. Volpe J.J., Intracranial hemorrhage: periventricular-intraventricular hemorrhage of the premature infant, In Volpe JJ editor, *Neurology of the newborn*, 2nd ed, Philadelphia, WB Saunders, 1987, 311-361

Correspondence to:

Aniko Manea  
I. Nemoianu Street, No 2-4  
Timisoara,  
Romania  
E-mail: aniko180798@yahoo.com