

РЕЗУЛЬТАТИ ДИСЕРТАЦІЙНИХ ТА НАУКОВО – ДОСЛІДНИХ РОБІТ

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NEURODEVELOPMENTAL OUTCOMES
IN PRETERM INFANTS WITH
INTRAVENTRICULAR HEMORRHAGE AND
PERIVENTRICULAR LEUKOMALACIA

Summary

Neonates commonly present with multiple insults, which, probably, increase the likelihood of neurological impairment.

The aim of the study was to determine the incidence of brain injuries (IVH and PVL) and the survival due to these conditions in preterm infants, as well as shorter long-term neurodevelopment outcome in these newborns.

Materials and methods. *We have analyzed morbidity with IVH among infants born preterm from statistical forms of MoH and of Mother and Child Institute (MCI) for the period 2000-2014. We also have analyzed the MCI records to determine the IVH incidence in premature babies and the survival rate of children who suffered from IVH. Furthermore, a retrospective study of 99 preterm babies who suffered from IVH and PVL and were followed up by using Bayley-III tool was performed.*

Results. *According to MoH statistics for the 2002-2014 period, an oscillatory incidence of IVH has been observed with two peaks: in 2003 (46,6/1000) and 2009 (48,8/1000). The largest number of children with IVH has been recorded at MCI in 2006 (130 children - 23,55% cases) and in 2008 (134 children – 22,55% cases). An IVH incidence steady decline has been noticed by the year 2012. 90 (22,01%) of 409 followed up children had IVH and 9 (2,20%) – PVL. Newborns with IVH degree 3 and PVL had more often early sepsis and meningitis.*

Conclusions. *During this time period we have found a decrease of 39,8% of IVH incidence in the Republic of Moldova and a decrease of 27,76% in the MCI. At the age of 2 years of life, children who suffered during neonatal period from grade 3 IVH and PVL are suffering mostly from motor neurodevelopmental impairment (in 42,86% and 66,67% cases, respectively) and from severe neurological pathology in 40-60%.*

Keywords: *premature newborn, intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), neurodevelopment, disability, Bayley tool.*

Neurodevelopmental disability in prematurely born infants remains a very significant problem worldwide. While there have been significant improvements in the survival of preterm infants, this has not been matched by improvements in morbidity. Indeed, there is some evidence that disability has increased, with a moderate rise in the childhood prevalence of cerebral palsy (CP). [1] Children born preterm in the early years have high rates of neurodevelopmental impairment including CP, mental retardation and sensory impairments. [2]

Intrauterine and neonatal insults as preterm birth complications, intrapartum-related factors such as hypoxic-ischemic encephalopathy, infections (notably sepsis and meningitis) and other conditions, such as jaundice and congenital TORCH infections substantially affect the global burden of disease, measured in the Disability Adjusted Life Years (DALY). All these insults contribute to both premature mortality and long-term disability. [3]

According to the Global Burden of Disease Study (GBD), neonatal conditions, including preterm birth complications, represent 202 million or 8.1% of all DALY worldwide. [4] GBD report estimates that neonatal causes, mainly preterm birth complications and neonatal encephalopathy, are among the most important causes of intellectual impairment, and that intellectual disability from preterm birth complications increased by 129.6% compared to 1990.

Mwaniki MK et al. [5] reported that the incidence of impairment after preterm birth alone was 28% and that of infants with prematurity complicated by sepsis was 49%. GBD report estimated that in 2010, 2,84 million deaths occurred in the neonatal period and that years of life lost (YLLs) contribute 96% of preterm, 88% of intrapartum-related conditions, and nearly 100% of neonatal sepsis DALYs. [4] The total YLDs are estimated to be increased from 1990 to 2010 by 29,3% on account of preterm births complications due to the increase in number of live births.

Almost half of extremely premature children develop central nervous system organic lesions of hypoxic-ischemic origin in the form of intraventricular hemorrhage (IVH) of different degree of severity, as well as ischemic foci and periventricular leukomalacia (PVL).

The aim of the study was to determine the incidence of brain injuries (IVH and PVL) and the survival due to these conditions in preterm infants, as well as shorter long-term neurodevelopment outcome in these newborns.

Material and methods

We have analyzed morbidity with non-traumatic intracranial hemorrhages among infants born preterm from statistical yearbooks of the Ministry of Health (MoH), as well as from the statistical Form 32a Report on health care provided to pregnant women and young mothers, section "Diseases and causes of newborns

death" in the Republic of Moldova and in the Mother and Child Institute (MCI) for the period 2000-2014. We also have analyzed the MCI neonatal intensive care unit (NICU)'s records for the period 2000-2012 to determine the IVH incidence in premature babies with very low birth weight (VLBW) - less than 1500g and the survival rate of children who suffered from IVH.

Furthermore, the article includes data of retrospective study of 99 preterm babies who suffered from IVH and PVL and were followed up at the Follow up Centre of the MCI during the period 2008-2014. This cohort is part of a larger cohort of 409 children, who have finalized the Follow up program. Data were collected from the Follow up Center database, composed of the following compartments: a) epidemiological data, b) child's condition after birth, c) child's condition in the NICU, d) data on care and treatment in NICU, e) data at discharge and follow-up visits data. After selecting the children who had all visits done up to 2 years of corrected age (c.a.), data were coded and grouped for computer analysis.

Neurodevelopmental evaluation of cognitive functioning, language, motor, social-emotional and adaptive skills has been performed in children by Bayley Scales of Infant and Toddler Development, 3rd Edition (BSID-III) standardized tool [6]. Bayley average score is 100 with a standard deviation of ± 15 . The evaluation was performed by a trained neonatologist according to the scores of development: less than 70 – severe impairment, 70-85 – impairment or area requiring intensive supervision; >85 – normal development. The classical neurological examination

has been performed by a neuro pediatrician and brain ultrasound examination performed with Doppler at Esaote MyLab 50 machine. Neurological pathology was classified in three grades according to its severity: mild (disorders of muscle tone, minimal brain dysfunctions), medium severe and severe (CP, mental retardation, epilepsy, sensorial impairments). IVH was graded 1 to 4 according to the system of Papile et al. [7], and grades 3 and 4 were considered "severe" IVH. PVL was graded 1 to 4 according to the classification of de Vries [8]. According to the national protocol, IVH screening is performed at 1, 7, 14 and 28 day of life, and PVL – at 0-5 days to 2 weeks, at 3rd week, and weekly up to 40 weeks and monthly to monitor ventriculomegaly.

Unifactorial analysis of variance (ANOVA) and calculation of F statistics were performed for quantitative variables. For qualitative results there have been calculated and applied the chi-square statistic (χ^2) or Fisher Exact test with 95% confidence intervals, depending on a case. For analysis there have been used rates (P), standard errors; significance of results obtained was determined by the test of significance (t-student) and significance level (p).

Results

According to data from the MoH Statistical Yearbooks for the period 2002-2014 period, an oscillatory incidence of IVH has been observed with two peaks in 2003 (46,6/1000) and 2009 (48,8/1000). Starting from 2012 there has been a continuous decrease in IVH cases, figure 1.

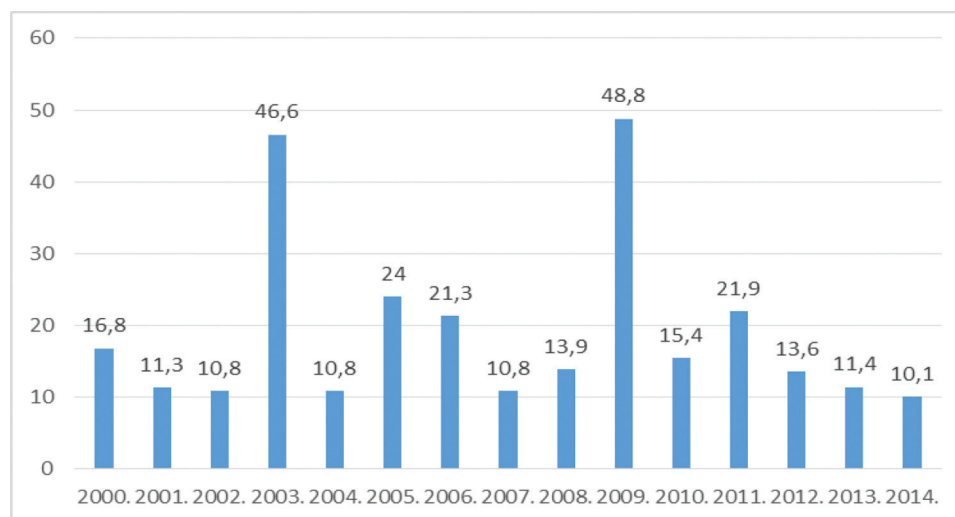


Figure 1. Incidence of IVH per 1000 live born premature babies in maternity hospitals, in the 2000-2014 period, according to data of the MoH

Table 1 shows that along with the improvement of the referral system functioning with the better transfer of mothers with high risk of preterm birth to the 3rd level of care – the Mother and Child Institute – the number of children with VLBW has increased by 34,87%. The largest number of children with IVH has been recorded in two time periods: 2006 (130 children - 23,55% cases) and in 2008 (134 children –

22,55% cases). By the year 2012 there has observed an IVH steady decline (58 – 9,91% children). In the period 2000-2008, when babies born at 28 weeks of gestation and weighing 1000g were cared for, the % of premature babies who suffered from IVH and who have survived is higher than after 2008, making up 2/3 of all children who have suffered from IVH. After 2008, the survival of these children decreases by 50%.

Table 1.

Number and % of premature babies with birth weight below 1500g, born and transported to the MCI between 2000-2012, who have suffered from IVH and who have survived IVH

| | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 |
|-------------------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Number of preterm babies, m<1500g | 204 | 253 | 237 | 281 | 403 | 603 | 552 | 442 | 594 | 596 | 626 | 524 |
| overall IVH, abs. | 28 | 31 | 32 | 38 | 71 | 98 | 130 | 70 | 134 | 113 | 93 | 79 |
| overall IVH, % | 13,72 | 12,25 | 13,5 | 13,52 | 17,61 | 16,25 | 23,55 | 15,83 | 22,55 | 18,95 | 14,85 | 15,07 |
| Number of babies survived after IVH | 20 | 20 | 21 | 25 | 55 | 68 | 90 | 49 | 81 | 63 | 58 | 42 |
| % of babies survived after IVH | 71,42 | 64,51 | 65,62 | 65,78 | 77,46 | 69,38 | 69,23 | 70 | 60,44 | 55,75 | 62,36 | 53,16 |

Number and % of premature babies with birth weight below 1500g, born and transported to the MCI between 2000-2012, who have suffered from IVH and who have survived IVH

In Table 2, children with brain injuries, included in the retrospective study, are presented according to the degrees of prematurity. Thus, 90 (22,01%) of 409 children had IVH and 9 (2,20%) – PVL. 1st and the 2nd degrees IVH have prevailed in extremely preterm (26,76%) and very preterm babies (20,99%) compared to those with

g.a. of 32-37 weeks (7,37%), c2 22,098, p=0,001. A. With statistical difference we have determined the absence of IVH and PVL in babies with gestational age (g.a.) 32-37 weeks in 91,58% cases, compared to the babies with g.a. less than 28 weeks (63,38%) and 28-31 weeks of gestation (73,25%), c2 22,098, p=0,001.

Table 2.

Brain injuries associated with prematurity according to gestational age in 99 out of 409 followed up babies

| Nosologies | Group A, < 28 weeks | | Group B, 28-31 weeks | | Group C, 32-37 weeks | | Total | |
|---------------------|---------------------|----------|----------------------|----------|----------------------|------------|-------|--------|
| Without IVH and PVL | 45 | 63,38 | 178 | 73,25 | 87 | 91,58**A,B | 310 | 75,79 |
| IVH 1+2 degrees | 19 | 26,76**C | 51 | 20,99**C | 7 | 7,37 | 77 | 18,83 |
| IVH 3 degree | 3 | 4,23 | 9 | 3,70 | 1 | 1,05 | 13 | 3,18 |
| PVL | 4 | 5,63 | 5 | 2,06 | 0 | 0,00 | 9 | 2,20 |
| Total | 71 | 100,00 | 243 | 100,00 | 95 | 100,00 | 409 | 100,00 |

** p<0,01 – statistically significant difference between the groups

We have found no statistical difference between pregnancy and birth complications in mothers who gave birth to premature babies who developed PVL and those who gave birth to preterm children without PVL (c2 12,08; p=0.357). We have revealed statistically significant difference between accelerated birth in children with grade 2 IVH (8,86%) compared to children without IVH (1,58%), (c2 36,90; p=0.024, Fisher's Exact Test 0,004). We have additionally analyzed pregnancy and birth complications per ages of gestation in children with IVH of different degree. Mothers of children with 1 and 2 grade IVH with g.a. below 28 weeks have had such complications more frequently than mothers of children with g.a. of 28-31 weeks (70% and 36,8%, (c2 57,47; p=0.0001, Fisher's Exact Test 0,007)).

We have found no statistical difference when comparing steps for resuscitation of children with varying degrees of HIV and PVL (c2 12,55; p=0.403). Statistical tests obtained when comparing Apgar scores of 0-3 points, 4-6 points and 7 and more points at 1, 5 and 10 minutes of life showed statistically significant difference only for the steps B (ventilation) and C (cardiac massage) of resuscitation in the

10th minute of life (c2 10,204; p=0.037) in newborns, who were appreciated by 0-3 points after Apgar.

Children from the study groups have had other comorbidities, which have resulted in a more serious evolution of brain pathology. In most cases no statistical difference was determined regarding the prevalence of other comorbidities in groups of children with IVH of any degree and PVL, except early sepsis, meningitis, sepsis with meningitis and patent ductus arteriosus (PDA), data for these pathologies being included in Table 3. Thus, newborns with the 3rd degree IVH were more frequently diagnosed with early sepsis (53,85%), compared to newborns with IVH degree 1 (9,52%) and IVH degree 2 (14,29%), c2 16,140; p=0.001. The same situation was revealed also for meningitis. In addition, newborns who suffered from PVL had meningitis, sepsis with meningitis more often (33,33%) than newborns with IVH degree 2 (2,86%), c2 27,930; p=0.000 and c2 19,284; p=0.023, respectively. Also, newborns who suffered from PVL (33,33%) were diagnosed with sepsis and meningitis more often than children with IVH degree 2. A similar situation was revealed for PAD.

Table 3.

Comorbidities associated to brain injuries in preterm babies in neonatal period

| | | Group A, IVH 1 degree | | Group B, IVH 2 degree | | Group C, IVH 3 degree | | Group D, PVL | | Total | |
|--------------------|----------------------------|-----------------------|--------|-----------------------|--------|-----------------------|------------|--------------|----------|-------|--------|
| | | n | % | n | % | n | % | n | % | n | % |
| Early onset sepsis | 0 | 38 | 90,48 | 30 | 85,71 | 6 | 46,15 | 5 | 55,56 | 79 | 79,80 |
| | Early onset sepsis | 4 | 9,52 | 5 | 14,29 | 7 | 53,85**A,B | 4 | 44,44 | 20 | 20,20 |
| | Total | 42 | 100,00 | 35 | 100,00 | 13 | 100,00 | 9 | 100,00 | 99 | 100,00 |
| Meningitis | 0 | 40 | 95,24 | 34 | 97,14 | 6 | 46,15 | 6 | 66,67 | 86 | 86,87 |
| | Meningitis | 2 | 4,76 | 1 | 2,86 | 7 | 53,85**A,B | 3 | 33,33**B | 13 | 13,13 |
| | Total | 42 | 100,00 | 35 | 100,00 | 13 | 100,00 | 9 | 100,00 | 99 | 100,00 |
| Sepsis | Without infection | 13 | 30,95 | 9 | 25,71 | 2 | 15,38 | 1 | 11,11 | 25 | 25,25 |
| | Infections (withoutsepsis) | 24 | 57,14 | 20 | 57,14 | 4 | 30,77 | 3 | 33,33 | 51 | 51,52 |
| | Sepsis | 3 | 7,14 | 5 | 14,29 | 4 | 30,77 | 2 | 22,22 | 14 | 14,14 |
| | Sepsis + Meningitis | 2 | 4,76 | 1 | 2,86 | 3 | 23,08 | 3 | 33,33**B | 9 | 9,09 |
| | Total | 42 | 100,00 | 35 | 100,00 | 13 | 100,00 | 9 | 100,00 | 99 | 100,00 |
| PDA | 0 | 40 | 95,24 | 29 | 82,86 | 13 | 100,00 | 6 | 66,67 | 88 | 88,89 |
| | PDA | 2 | 4,76 | 6 | 17,14 | 0 | 0,00 | 3 | 33,33**A | 11 | 11,11 |
| | Total | 42 | 100,00 | 35 | 100,00 | 13 | 100,00 | 9 | 100,00 | 99 | 100,00 |

** $p < 0,01$ – statistically significant difference between the groups

Children who suffered from grade 3 IVH have had at 2 years of life more frequently severe cognitive impairment (in 35,71%), expressive impairment (in 35,71% cases) and, especially, motor impairment (in 42,86% cases) compared to children who did not have IVH. In contrast, children with scores of neurodevelopment higher than 85 or with the development close to normal on three studied functions have not suffered from IVH or had grade 1 IVH, compared to children with IVH of grade 3 (Figure 2). Children, who have been diagnosed with IVH grade 1 and

2, showed neurodevelopmental results similar to those of children without IVH.

PVL, compared to grade 3 IVH, seen in VLBW infants profoundly affects neurological development. In those 9 children, who suffered from PVL, the most deeply was affected the motor function (66,67% cases) compared to cognitive and expressive functions (each in 44,44% cases), figure 2. Vice versa, babies without PVL have had normal cognitive, motor and expressive functions in 8 to 9 cases out of 10 cases.

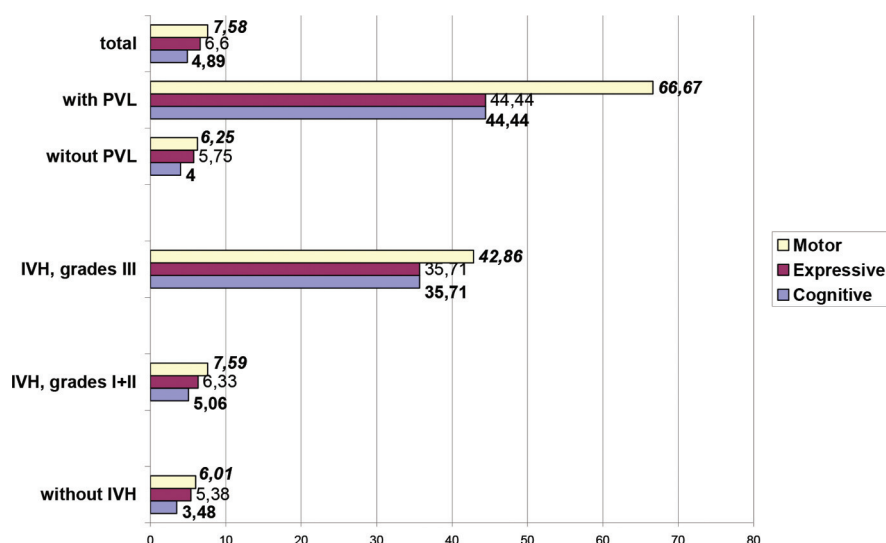


Figure 2. The severe degree of impairment of neurodevelopmental functions (cognitive, expressive and motor) at the age of 2 years in children who suffered from IVH and PVL

In 42,86% of cases, newborns who suffered from grade 3 IVH have developed a severe neurological pathology at the age of 2 years, compared to 35,71% at the age of 12 months and to 35,71% at the age of

18 months. 2/3 (64,87%) of children without IVH were healthy at 12 months of age, with their number increased (79,62%) by 24 months (figure 3). PVL conditions the development of severe neurological pathology in every second (55%) child at 2 years of life (figure 3).

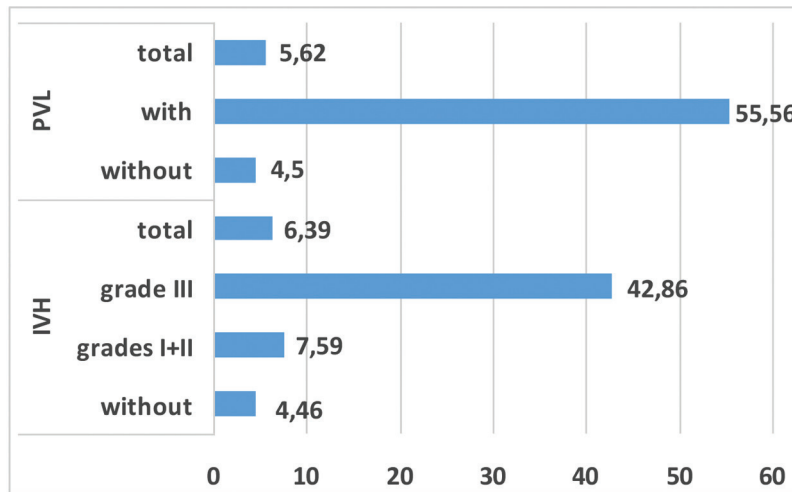


Figure 3. Severe neurological pathology at the age of 2 years in children who suffered from IVH and PVL (%)

Discussion

PVL is a severe brain injury in premature baby, second by incidence (7-22%) after IVH (35-55%), both pathologies being major causes for early death in the neonatal period and later motor and cognitive deficits. The overall IVH incidence has decreased in the last 30 years from 40-70% to fewer than 10% in some European countries. [9,10] In developing countries the IVH incidence was 44,7%. [11] In the last 10 years no decrease in the incidence of grade 4 and 3 IVH has been noticed, a fact that is explained by the use of advanced and invasive treatment technologies and by a lack of antenatal IVH prevention interventions. [12] The short term outcome is closely related to the severity of IVH. [13] The long term outcome of infants who survive of IVH, worsens with increasing severity of IVH and decreasing g.a.. Mortality caused by IVH reaches 27-50%. [14]

PVL is considered today a "disease of periventricular white matter" together with post-hemorrhagic hydrocephalus and periventricular hemorrhagic infarction, being characterized by focal necrosis and diffuse injury. [15] Incidence of PVL reported in some countries was 19,8 to 34,1% for overall PVL [16,17] and 2,5 to 23% for cystic PVL. [18,19,20] Non-cystic diffuse white matter injury is a main pathological type of PVL. [21,22] Most substantial neurodevelopmental impairments occur in 62-100% in cystic forms and 8-17% - in diffuse forms. [23,24]. In the multicenter investigation for brain injury in premature infants at g.a. < 34 weeks conducted in ten big hospitals in China was showed that the number of the overall IVH and severe IVH were 19,7% and 4,6% and the incidence of the overall PVL and cystic PVL were 5,0% and 0,8% [15]. Synnes AR. et al [25] reported an incidence of severe IVH of 2%-20,5% in 17 NICUs. According to the Australian and New Zealand Neonatal Network data the incidence of severe IVH was 2,9%-21,4% [26].

In Moldova, during 2000-2014, according to the official statistics data, the average IVH incidence made up 19,16/1000. There are two peaks of IVH incidence in 2003 and 2009, as a possible explanation for the statistical reporting related to the transition in 2003 from the administrative-territorial structure based on counties (judets) to the one based on rayons, and in 2009, with the adoption of new life birth definition (LBD) and starting to care for extremely preterm babies, and possibly with initial difficulties in using in practice some new methods of ventilation (hFOV).

Peaks of IVH, registered at the MCI, correspond to two time periods: in 2006 (23,55% cases) coincides with practical implementation of new methods of respiratory support (CPAP, mechanical ventilation) and in 2008 (22,55% cases) with the adoption of new LBD, respectively, by starting intensively caring for preterm babies with BW of 500g and g.a. of 22 weeks, who were referred from country maternities "in utero" or postnatal. Average survival of premature babies, who have suffered from IVH in the years 2000-2008 made up 69,17%, and in 2008-2012 – 56,34%, which is explained by the use of the old LBD that dates from the former Soviet Union era and usually by an intensive care for babies with BW ≥1000g and g.a. of 28 weeks in the first period, and in the second period by a care for babies with BW ≥500g and g.a. of 22 weeks.

As a result, for 14 years there has been observed a decrease of 39,8% of IVH incidence in the Republic of Moldova and a decrease of 27,76% in the MCI, with a remark that in 2008 the WHO live birth definition was adopted, which resulted in caring for extremely preterm babies. Similar to the world's development tendency, the incidence of IVH decreases significantly in Moldova. PVL data are not available in the official statistics. Since 2001 and 2007, once with the

endowment of two NICUs from the MCI with cranial ultrasound machines and improvement of ultrasound diagnosis, the diagnostics of IVH and PVL has increased, since 2012 a bedside cranial ultrasound has been used. National protocol regarding neuroimaging examination of premature babies was elaborated with its implementation in practice in 2008.

PVH and IVH mostly affect preterm babies with g.a. below 34 weeks and VLBW. PVL is caused by a series of factors additional to prematurity: infection, respiratory diseases and therapy thereof, asphyxia and hypoxia, hypotension, and IVH – by peculiarities of germinal matrix, lack of self-regulation and fluctuations of cerebral blood flow, maternal infection/exposure to cytokines, perinatal hypoxia, metabolic acidosis, as well as vitamin K deficiency, i.v. rapid boluses, etc. [27] PVL is the main cause of cognitive behavioral, motor and sensory impairments found in children born before 32 weeks of g.a.. [28] IVH has a negative impact on the neurodevelopmental outcome and is due not only to the direct consequences of IVH but also associated lesions, such as posthemorrhagic hydrocephalus (PHH) and PVL. [29]

Posthemorrhage hydrocephalus (PHH), periventricular hemorrhagic infarction (PVHI), and PVL are the most important sequelae of IVH. The first occurs in approximately 25% of infants with IVH and usually it begins within one to three weeks after the brain bleeding. [30]

It is known that preterm delivery is a major risk factor for CP, being a cause of approximately 35% of all cases of PC, and the risk increases the lower the viable g.a.. [31] PVL and IVH are associated with adverse cognitive and motor outcomes. Infants with severe IVH or PVL had lower MDI and PDI scores and a higher incidence of CP. In contrast, infants with grades 1-2 of brain injury had similar neurodevelopmental outcomes at age 2 years to those without brain injury, except for grade 2 PVL, which was associated with an increased risk of CP. [32] Long term prognosis for infants with IVH varies considerably depending on the severity of IVH, complications or other brain lesions such PVL, the most lower birth weight and g.a. add to others significant illness will determinate the outcome. Studies have suggested that preterm infants with grade 1-2 IVH have an increased risk of CP and cognitive impairment compared who those without. [33] Infants with the mayor complications, like PVHI and PHH are at much higher risk of permanent neurologic impairments like CP than dose with IVH alone. [34]

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Our research on neurodevelopment of premature babies is complying with the scientific literature data, which indicate that in addition to gestational age insults from intrauterine and neonatal periods worsen neurological development of such babies. Major brain injuries associated with CP and cognitive impairment in premature infants are presented by the injury of periventricular white matter. PVL causes impairment of motor function in 2/3 (66%) of children and the development of severe neurological pathology in every second baby (55%) at 2 years of life. In case of grade 3 IVH severe neurological pathology and severe impairment of neurodevelopment have been maintained in 42% of cases at the age of 2 years.

Conclusions:

1. Average IVH incidence during 2000-2014, according to official statistics data, made up 19,16/1000. At the MCI, level III of perinatal care, the average % of IVH in the years 2000-2012 made up 15,96%. During this time period we have found a decrease of 39,8% of IVH incidence in the Republic of Moldova and a decrease of 27,76% in the MCI.
2. Peaks of IVH growth both in the republic and in the MCI were related to the caring for extremely premature babies (BW 500g and g.a. of 22 weeks) and the difficulties met by specialists at the beginning of using new methods of respiratory support.
3. At the age of 2 years of life, children who suffered during neonatal period from grade 3 IVH and PVL are suffering mostly from motor neurodevelopmental impairment (in 42,86% and 66,67% cases, respectively) and from severe neurological pathology in 40-60%.
4. Neonates commonly present with multiple insults, which, probably, increase the likelihood of neurological impairment. Such newborns with IVH degree 3 had more often early sepsis and meningitis, and newborns who suffered from PVL – had more frequently sepsis with meningitis, as well as PDA, compared to children who had less severe degrees of IVH.

Perspectives of future research

We plan to follow the neurodevelopmental outcome of preterm babies with different intrauterine and neonatal insults for middle-term period (5-7 years). In this regard we will collaborate with rehabilitation centers within the country. Another area of our scientific interest is the immunohistochemical analysis of brain tissue in babies who suffered from IVH and died before discharge.

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**РЕЗУЛЬТАТЫ НЕВРОЛОГИЧЕСКОГО
РАЗВИТИЯ У НЕДОНОШЕННЫХ
НОВОРОЖДЕННЫХ, ПЕРЕНЕСШИХ
ВНУТРИЖЕЛУДОЧКОВОЕ КРОВОИЗЛИЯНИЕ
И ПЕРИВЕНТРИКУЛЯРНУЮ
ЛЕЙКОМАЛЯЦИЮ**

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Резюме. Новорожденные обычно имеют множественные заболевания, которые, возможно, увеличивают вероятность неврологических нарушений.

Цель исследования состояла в том, чтобы определить частоту повреждений головного мозга (ВЖК и ПВЛ) в общем, в том числе, у выживших недоношенных детей, а также результаты неврологического развития у этих новорожденных в возрасте 2 лет жизни.

Материалы и методы: Мы проанализировали заболеваемость ВЖК среди недоношенных новорожденных из статистических ежегодников Министерства здравоохранения, а также из статистической формы 32а в Республике Молдова и в Институте Матери и Ребенка (ИМР) за период 2000-2014 гг. Мы также проанализировали журналы отделения интенсивной терапии новорожденных ИМР, чтобы определить частоту ВЖК у недоношенных детей и выживаемость детей, которые перенесли эту патологию. Кроме того, было проведено ретроспективное исследование 99 недоношенных детей, которые перенесли ВЖК и ПВЛ и наблюдались в катамнезе.

Результаты. Согласно статистике Министерства Здравоохранения за период 2002-2014 гг., наблюдалось колебание частоты ВЖК с двумя пиками: в 2003 г. (46,6/1000) и 2009 г. (48,8/1000). Наибольшее число детей с ВЖК было зарегистрировано в ИМР в 2006 году (130 детей - 23,55% случаев) и в 2008 году (134 детей - 22,55% случаев). С 2012 года отмечается устойчивое снижение заболеваемости ВЖК. 90 (22,01%) из 409 наблюдаемых в катамнезе новорожденных имели ВЖК и 9 (2,20%) - ПВЛ. Новорожденные с ВЖК 3-й степени и ПВЛ чаще имели сепсис с ранним началом и менингит.

Выводы. За исследованный период времени мы обнаружили снижение на 39,8% заболеваемости ВЖК в республике и на 27,76% в ИМР. В возрасте 2-х лет жизни, дети, которые перенесли в неонатальном периоде 3-ю степень ВЖК и ПВЛ, страдают в основном от двигательных нарушений (в 42,86% и 66,67% случаев, соответственно), а также от тяжелой неврологической патологии в 40-60% случаев.

Ключевые слова: недоношенные новорожденные, внутрижелудочковое кровоизлияние (ВЖК), перивентрикулярная лейкомаляция (ПВЛ), неврологическое развитие, инвалидность, инструмент Бэйли.

**РЕЗУЛЬТАТИ НЕВРОЛОГІЧНОГО РОЗВИТКУ
У НЕДОНОШЕНИХ НОВОНАРОДЖЕНИХ,
ЯКІ ПЕРЕНЕСЛИ ВНУТРІШНЬОШЛУНОЧ-
КОВІ КРОВОВИЛИВИ
І ПЕРИВЕНТРИКУЛЯРНУ
ЛЕЙКОМАЛЯЦИЮ**

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Резюме. Новонароджені зазвичай мають множинні захворювання, які, можливо, збільшують ймовірність неврологічних порушень.

Мета дослідження полягала в тому, щоб визначити частоту ушкоджень головного мозку (ВШК і ПВЛ) в загальному, у тому числі у тих, що вижили, недоношених дітей, а також, оцінити результати неврологічного розвитку в цих новонароджених у віці 2 роки життя.

Матеріали і методи: Ми проаналізували захворюваність ВШК серед недоношених новонароджених на основі статистичних щорічників показників Міністерства охорони здоров'я, а також з статистичної форми 32а в Республіці Молдова і в Інституті Матері і Дитини (ИМР) за період 2000-2014 рр. Ми також проаналізували журнали відділення інтенсивної терапії новонароджених ИМР, щоб визначити частоту ВШК у недоношених дітей і виживання дітей, які перенесли цю патологію. Крім того, було проведено ретроспективне дослідження 99 недоношених дітей, які перенесли ВШК і ПВЛ, і спостерігалися в катамнезі.

Результати. Згідно зі статистикою Міністерства охорони здоров'я, за період 2002-2014 рр., спостерігалось коливання частоти ВШК з двома піками: у 2003 р. (46,6 / 1000) та 2009 р. (48,8 / 1000). Найбільше число дітей, у яких діагностовано ВШК, було зареєстровано в ИМР у 2006 році (130 дітей - 23,55% випадків) і в 2008 році (134 дітей - 22,55% випадків). З 2012 року відзначається стійке зниження захворюваності на ВШК. 90 (22,01%) з 409 спостережуваних в катамнезі новонароджених мали ВШК і 9 (2,20%) - ПВЛ. Новонароджені з ВШК 3-го ступеня і ПВЛ частіше мали сепсис з раннім початком і менингіт.

Висновки. За досліджуваний період часу ми виявили зниження на 39,8% захворюваності на ВШК в республіці і на 27,76% в ИМР. У віці 2-х років життя діти, які перенесли в неонатальному періоді 3-ттю ступінь ВШК і ПВЛ, страждають, в основному, від рухових порушень (у 42,86% і 66,67% випадків відповідно), а також від тяжкої неврологічної патології в 40-60% випадків.

Ключові слова: недоношені новонароджені, внутрішньошлуночкові крововиливи (ВШК), перивентрикулярна лейкомаляція (ПВЛ), неврологічний розвиток, інвалідність, інструмент Бейлі.