ORIGINAL ARTICLE

CONTENTS

Clinical manifestation, laboratory and instrumental characteristics of infants born to mothers with a complicated anamnesis

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ABSTRACT

Aim: To improve early diagnosis by analyzing the pathological pattern of «mother-newborn» in newborns.

Materials and Methods: The study group included newborns with a diagnosis of "Infection specific to the perinatal period, unspecified" (P39,9, n=64), born to mothers (age 31,31 ± 2,08 years) with a complicated diagnosis and a control group (n=31) of infants.

Results: Clinical manifestations in newborns mainly included involvement of the central nervous system (57,8%), cardiovascular system (12,0%), congenital heart defects (2,8%), jaundice (11,0%), hepatosplenomegaly (5,2%), exanthema (9,0%), hypothermia (70,6%). Markers of inflammatory response confirmed an increase in the level of IL-1, a significant increase in IL-6 levels, the level of IL-8 in the studied contingent also significantly differs from the data of the control group, the level γ-IFN also exceeded the reference values by 2,4 times. Hypoxic-ischemic encephalopathy was detected in 63 infants (57,8%) and intracranial hemorrhage was diagnosed in 25 (22,9%) infants.

Conclusions: The values of cytokine profile parameters (IL-1, IL-6, IL-8, IL-10) on the first day of life varied within the reference values, but with significant differences from the values of the control group, which were 9,24; 20; 11 times, respectively. The levels of inflammatory mediators (γ-IFN, procalcitonin, neopterin, TNF-α, Pg E2) significantly differed from the data of the control group and exceeded the upper limit of reference values by 2,4; 40; 8,9; 25; 3,5 times, respectively.

KEY WORDS: newborns, infection specific to the perinatal period, early diagnosis

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INTRODUCTION

Given that the fetus develops in complex conditions of interaction with the mother's organism, if the mother has an infection, this is a risk factor for the development of severe pathological conditions of the fetus and newborn as well [1]. According to modern theories, infection of the fetus in the first trimester of pregnancy leads to the development of microcephaly, hydrocephalus, myocardial dysfunction, heart defects, defects of the gastrointestinal tract (GI), genitourinary system, skeleton, cataracts, deafness. Infection in the second and third trimesters causes hepatosplenomegaly, anemia, jaundice, hypotrophy, pneumonia, meningoencephalitis, sepsis in the fetus [2-4]. It has been established that the term of infection, the type of pathogen and the methods of its transmission can significantly affect the occurrence of clinical manifestations of intrauterine infections [5-7].

AIM

To improve early diagnosis by analyzing the pathological pattern of «mother-newborn» in newborns.

MATERIALS AND METHODS

The study group included infants with a diagnosis of "Infection specific to the perinatal period, unspecified" (P39,9, n=64), born to mothers (age 31,31 ± 2,08 years) with a complicated diagnosis and a control group (n=31) of infants. The average weight of preterm infants was 1477,69 ± 981,78 g (min – 600 g; max – 2450 g. Observation and treatment of newborns took place for 7 days (stay in the neonatology department and neonatal intensive care unit of the KNP "Uzhgorod City Maternity Hospital" of the Uzhgorod City Council).

RESULTS

Clinical manifestations in newborns mainly included involvement of the central nervous system (57,8%), cardiovascular system (12,0%), congenital heart defects (2,8%), jaundice (11,0%), hepatosplenomegaly (5,2%), exanthema (9,0%), hypothermia (70,6%) [8, 9, 10]. The most frequent components of the diagnosis were hypoxic-ischemic central nervous system damage and hypoxic-hemorrhagic central nervous sytem damage in the form of hypoxic-ischemic encephalopathy of the newborn (P91,6) in 57,8%, respiratory distress syndrome, severe respiratory distress, respiratory distress syndrome of the newborn (P22.0) – in 75,7%, intraventricular hemorrhage of various degree (P52) – 22,9%. Isolated cases of congenital pneumonia (P23) were detected less frequently – in 7,3% of newborns, neonatal meconium aspiration (P24.0) – in 2,8%. On the first day of life, jaundice (10%), gray skin color (80%), severe muscle hypotension (100%), hypothermia (95,6%), respiratory distress syndrome (75,7%), apnea (78,0%), hepatomegaly at birth (5.2%), CNS depression (47,8%), feeding problems (60%), inflammatory changes in the hemogram (100%), hypocalcemia (20,2%) and hypoglycemia (62%) were detected. Infants are often born with the background of intrauterine infection [4].

Hemogram data of the studied groups are considered in the following table (table 1).

According to the results of the hemogram, at the initial stage of the study, there are differences between the study group and the control group, except for insignificant differences between the levels of platelets (p2=0,19) and eosinophils (p2=0,34). An important point of the scientific study is the assessment of biochemical blood test parameters in infants with intrauterine infections (Table 2).

The study groups presented non-significant differences. Compared with the control group of infants, high levels of significance were observed for all studied parameters (p2<0.001). In particular, this is confirmed by a significant increase in the values of AST, ALT, Alkaline Phosphatase, Urea and Creatine Phosphokinase by 2-3 times compared with the data of the control group (p2<0,001), but within the reference values.

Indicators of electrolyte metabolism in children are considered in the following table (Table 3).

According to Table 4, no significant intergroup differences were observed compared to the control group. Also, insignificant differences were detected as for the parameter of Sodium level. Significant increases in potassium values were identified compared to the control group 5,50 ± 0,48 mmol/l, p2=0,0001). A significant decrease in Calcium levels was also found in infants compared to the control group (2,08 ± 0.20 versus 2,29 ± 0.21 mmol/l, p2<0.001).

Table IV presents the immunogram indicators of neonates.

IgM is a marker of the immune system, which provides the primary immune response. It does not pass through the placental barrier due to its large molecular structure and confirms the infection of the newborn, which is verified by our studies and presented by its increase in the group (3,68 ± 2,65 g/l versus the control group data of 0,71 ± 0,28 g/l, p = 0,96; p1 < 0,001; p2 < 0,001). On the contrary, IgG, by its structure, has the ability to overcome the placental barrier, that is, the newborn also receives maternal IgG. According to our data, there is a significant increase in the level of IgG by 2 times compared to the control group data (p2 = 0,0004).

The inflammatory response of the child's organism is a protective process that includes a multicomponent composition and diverse actions of components such as cytokines, chemokines, and other indicators of metabolic adaptation (Table 5).

According to Table 5, there is a significant increase in the level of IL-1 by 11 times (5,07 ± 1,44 pg/ml and compared to the data of the control group 0,63 ± 0,08 pg/ml, p2=<0,001), but within the reference values.

A significant increase in IL-6 levels by 24 times (22,31±14,43 pg/ml and compared with the control group of infants (0,78 ± 0,06 pg/ml, p<0,001) and by 2,2 times exceed the upper limit of reference values. The level of IL-8 in the studied contingent (8,97 ± 5,55 pg/ml) also significantly differs from the data of the control group (0,47 ± 0,09 pg/ml, p<0,001), almost 20 times, but the variation occurs within the reference range. There is also a significant difference in the values of IL-10 (17,58 ± 12,42 pg/ml from the values of the control group -1,42 ± 0,19 pg/ml, p<0,001), the ratio of which is about 11 times. The level γ-IFN (39,58 ± 39,04 pg/ml) also significantly differed (4 times) from the data of the control group (5,71 ± 0,23 pg/ml, p<0,001) and exceeded the reference values by 2,4 times. The value of procalcitonin (20,55 ± 18,51 ng/ml) significantly differed from the data of the control group (5,77 ± 0,49 ng/ml, p<0,001) and exceeded the upper reference limit by 40 times. The level of neopterin (85,71 ± 56,63 nmol/l) significantly differed (47 times) from the data of the control group (1,9 ± 0,04 nmol/l, p<0,001) and exceeded the upper reference limit by 8,9 times. The values of TNF-α levels (156,67 ± 20,45 pg/ml) significantly differed from the data of the control group (5,71 ± 0,13 pg/ml, p<0,001) and exceeded the upper reference limit by 25 times. The study of Pg E2, as one of the mediators of the inflammatory response in premature infants, also presented a significant difference in levels (1415,53 ± 172,2 pg/ml according to the groups and compared

Table 1. Hemogram results before the start of therapy (day 1)

Indicators	Studied group (n=64)	Control group (n=31)	Reliability of differences
Red blood cells, g/l	4,89 ± 0,77	5,58 ± 0,35	P<0,001
Hemoglobin, g/l	181,78 ± 33,15	196,89 ± 12,12	p=0,02
Platelets, g/l	207,56 ± 53,85	194,63 ± 20,04	p=0,19
White blood cells, g/l	20,06 ± 9,76	12,14 ± 1,15	p<0,001
Rod-nuclear neutrophils, %	7,64 ± 8,94	2,91 ± 0,93	p=0,004
Segmented neutrofils, %	55,56 ± 12,35	26,47 ± 4,41	p<0,001
Monocytes, %	12,31 ± 6,09	5,72 ± 1,69	p<0,001
Lymphocytes, %	25,88 ± 10,29	34,84 ± 3,75	p<0,001
Eosinophiles, %	3,11 ± 1,58	3,41 ± 1,15	p=0,34

Notes: p – probability of the difference between the parameters of the study and control groups.

Table 2. Assessment of biochemical parameters of the blood on the first day of life

Indicators	Studied group (n=64)	Control group (n=31)	Reliability of differences
Total protein, g/l	47,67 ± 8,44	60,99 ± 5,19	**p<0,001**
Urea, mmol/l	7,84 ± 3,44	3,59 ± 0,59	**p<0,001**
Glucose, mmol/l	4,19 ± 1,51	4,10 ± 1,02	**p=0,76**
AST, μmol/l	45,36 ± 18,75	10,22 ± 3,17	**p<0,001**
ALT, μmol/l	34,67 ± 29,17	10,49 ± 3,63	**p<0,001**
Alkaline phosphatase U/l	159,84 ± 55,74	88,99 ± 20,95	p<0,001
Creatine phosphokinase, U/l	151,74 ± 65,62	108,95 ± 9,51	**p=0,0005**
CRP, мг/л	10,40 ± 8,75	2,70 ± 1,19	**p<0,001**

Notes: p – probability of the difference between the parameters of the study and control groups.

Table 3. Parameters of electrolyte homeostasis in children (day 1)

Indicators	Studies group (n=64)	Control group (n=31)	Reliability of differences
K, mmol/l 3,5-5,5	6,53 ± 1,31	5,50 ± 0,48	p=0,0001
Na, mmol/l 135-145	139,35 ± 13,11	142,75 ± 6,8	p=0,18
Ca, mmol/l 2,2-2,6	2,08 ± 0,20	2,29 ± 0,21	p<0,001
Cl, mmol/l 101-111	106,47 ± 11,17	102,31 ± 4,20	p=0,05
Fe, mmol/l 17,9- 21,5	18,16 ± 2,70	21,36 ± 3,51	p<0,001

Notes: p – probability of difference between the parameters of the study and control groups.

to the data of the control group 379,79 ± 15,75 pg/ml, p<0,001), which was a significant difference in the data and exceeded the upper reference limit by 3,5 times.

Neurosonographic examination of brain structures was performed in all infants. Hypoxic-ischemic encephalopathy was detected in 63 infants (57,8%) and intracranial hemorrhage was diagnosed in 25 (22,9%) infants. We present the distribution of degrees of intraventricular hemorrhages in the brain in newborns according to the results of neurosonography (Fig. 1).

Intraventricular hemorrhages (IVH) are predictors of complications in prematurely born children, who, according to our data, constitute 22,9% of the studied group of infants. The number of cases of IVH of the II degree was the highest percentage: in the structure of the distribution I degree constituted 28%, II degree – 46%.

Let us consider the data of EchoCS and neurosonography in infants. This diagnostic study is performed in all infants. We present the most indicative figures of the study (Fig. 2, Fig.3, Fig.4)

Table 4. Immunogram results before treatment (day 1)

Indicators	Studied group (n=64)	Control group (n=31)	Reliability of differences
IgG, g/l 2,32-14,1	20,57 ± 16,55	9,58 ± 1,88	p=0,0004
IgM, g/l 0,03-1,45	3,68 ± 2,65	0,71 ± 0,28	p<0,001
IgE, IU/ml 0-87	1,79 ± 1,61	2,29 ± 1,66	p=0,16

Notes: p – probability of the difference between the parameters of the study and control groups.

Table 5. Markers of inflammatory response and metabolic adaptation of the child's organism on the first day of life

Indicators	Studied group (n=64)	Control group (n=31)	Reliability of differences
IL-1, pg/ml	5,07 ± 1,44	0,63 ± 0,08	p=<0,001
IL-6, pg/ml	22,31 ±14,43	0,78 ± 0,06	p<0,001
IL-8, pg/ml	8,97 ±5,55	0,47 ± 0,09	p<0,001
IL-10, pg/ml	17,58 ± 12,42	1,42 ± 0,19	p<0,001
γ-IFN, pg/ml	39,58 ± 39,04	5,71 ± 0,23	p<0,001
Procalcitonin, ng/ml	20,55 ± 18,51	5,77 ± 0,49	p_2<0,001
Neopterin, nmol/l	85,71 ± 56,63	1,9 ± 0,04	p<0,001
TNF-α, pg/ml	156,67 ± 20,45	5,71 ± 0,13	p<0,001
Pg E_2, pg/ml	1415,53 ± 172,2	379,79 ± 15,75	p<0,001

Notes: p – probability of the difference between the parameters of the study and control groups.

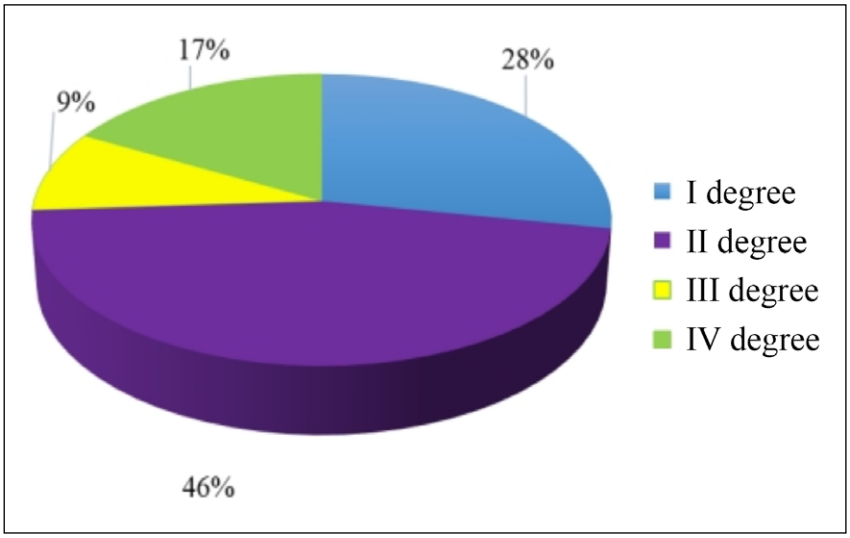

Fig. 1. Distribution of degrees of intraventricular hemorrhages in the brain in newborns, according to the results of neurosonography

It is also necessary to pay attention to the high level of hypoxic-ischemic encephalopathy in newborns (P91.6) diagnosed in our studied contingent (57,85%). Another statement, consistent with the conclusions of scientists, about the risks of mothers having a burdened history for infants [4,8].

DISCUSSION

It is known that the maternal immune system undergoes functional adaptation during pregnancy, which is considered physiological immunosuppression. This adaptation is crucial for creating a balance between the maternal and fetal immune systems, which is necessary for maintaining pregnancy itself and fetal development. When exposed to a viral infection, the balance is disrupted, the infection can spread and lead to negative consequences [9,10]. The reaction of the newborn to the influence of an infectious agent is determined by the physiological immaturity of all components that provide both nonspecific protection of the organism and its specific reactivity.

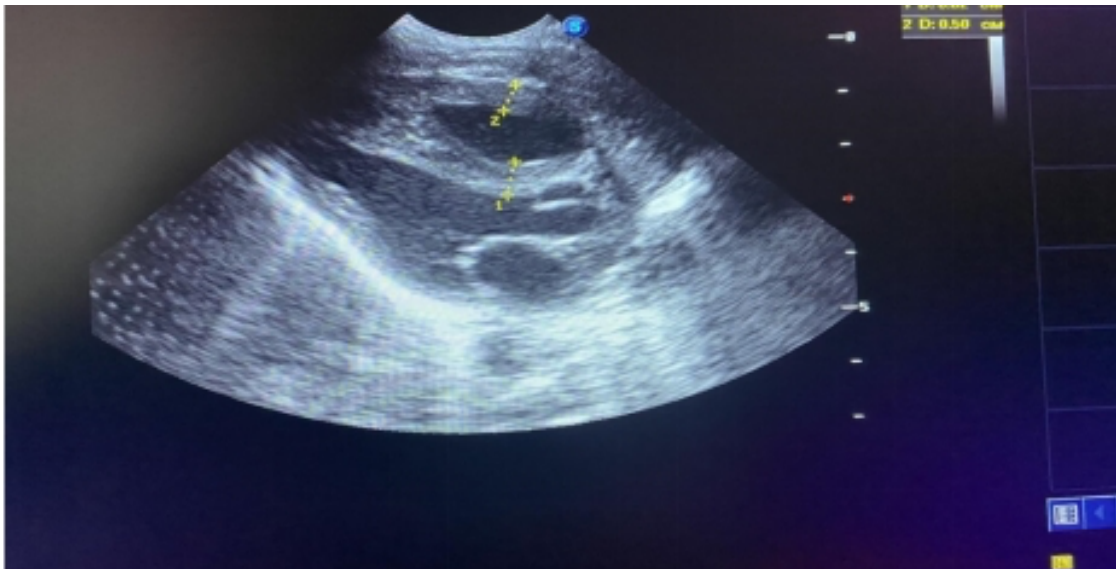

Fig. 2. ECHO of newborn M, 3 days old

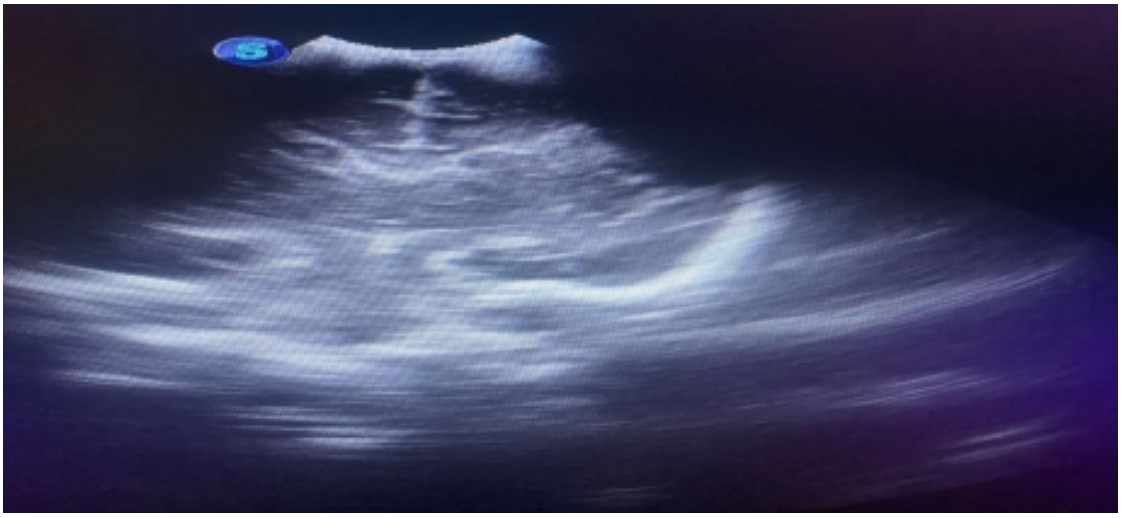

Fig. 3. Neurosonogram of newborn M, 3 days old

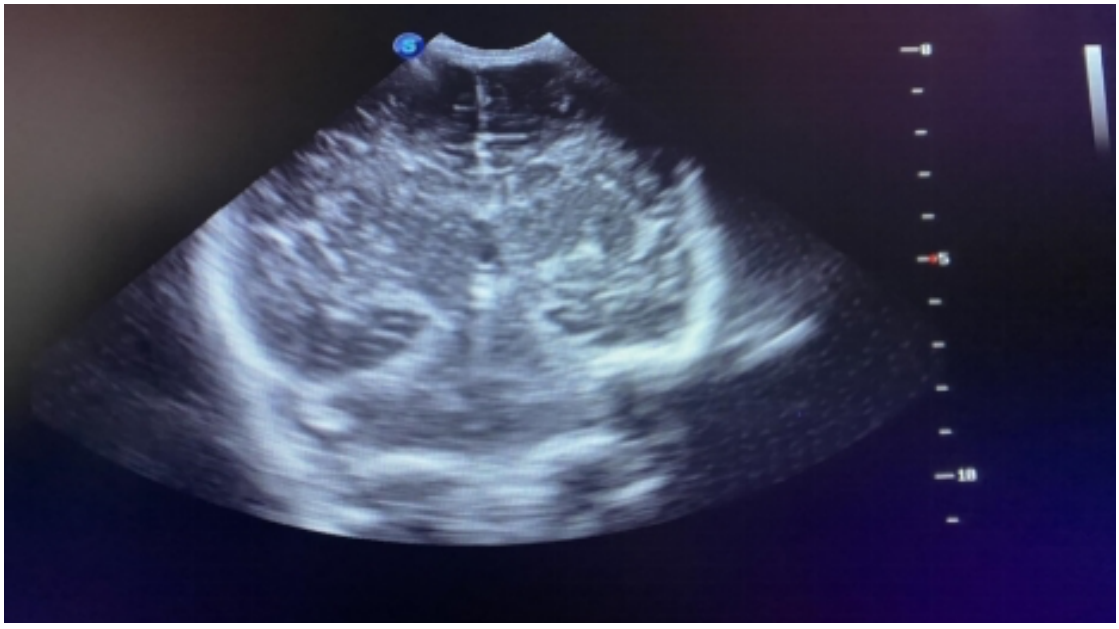

Fig. 4. Neurosonogram of newborn M, 3 days old

According to anatomical and physiological features, in infants, in particular, anatomical features of brain tissue, immaturity of autoregulatory mechanisms cause a high risk of developing central nervous system disorders in this population [11, 12].

It should be noted that ICH are not detected in all infants. Infectious and other inflammatory processes in the mother before childbirth or in the child after birth play a decisive influence on the development of the pathology. However, not all hemorrhages are associated with tissue trauma[13].

Cesarean section is one of the most common surgical measure in different countries. A WHO study showed that with a baseline cesarean section rate below 10%, maternal and neonatal mortality rates decrease if the frequency of this surgical intervention increases. If the cesarean section rate is 10–15%, then its further increase does not demonstrate a decrease in perinatal morbidity and mortality rates for infants born by cesarean section compared with infants born vaginally. Current data do not allow us to assess the association between maternal and neonatal mortality and cesarean section rates above 30%. Countries with a higher use of this intervention currently have higher neonatal morbidity and mortality rates [14]. Concerns have been raised about associations between cesarean section and a number of negative health outcomes for children [15,16].

Published studies have claimed that justified preterm delivery reduces the level of perinatal injuries. However, it should be noted that the improvement in neonatal outcomes occurs not only due to an increase in the frequency of cesarean sections, but also due to the use of modern technologies for managing the early neonatal period. [14,17].

CONCLUSIONS

1. The values of cytokine profile parameters (IL-1, IL-6, IL-8, IL-10) on the first day of life varied within the reference values, but with significant differences from the values of the control group, which were 9,24; 20; 11 times, respectively. A significant increase in IL-6 levels in both groups by 24 times (22,23 ± 14,79 and 22.31 ± 14.43 pg/ml) compared to the control group of infants (0.78 ± 0.06 pg/ml, p=0,98; p1<0,001; p2<0,001), and also by 2,2 times exceed the upper limit of reference values on the first day of life.
2. The levels of inflammatory mediators (γ-IFN, procalcitonin, neopterin, TNF-α, Pg E2) significantly differed from the data of the control group of infants and exceeded the upper limit of reference values by 2,4; 40; 8,9; 25; 3,5 times, respectively.
3. The presence of intrauterine infection of the mother and comorbid somatic pathology of an inflammatory nature cause functional changes in the cardiovascular system against the background of increased markers of inflammation in infants.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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