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FEATURES OF PREMATURE INFANTS IMMUNE SYSTEM

N. L. Aryaev[1], V. G. Marichereda[1], I. M. Shevchenko[1], T. Ya. Moskalenko[2], J. M. El Mezevgi[1], N. V. Shevchenko[2]

[1] Odessa National Medical University, Odessa, Ukraine.

[2] Maternity hospital № 7, Odessa, Ukraine

e-mail: valmar@i.ua

Abstract

Premature birth (PB) is the most important aspects in maternal and child health care. The frequency of PB and birth of immature infants is increasing and ranges from 4.0 to 15.0-20.0%. In Ukraine its frequency varies from 3.0% to 12.0%. Preterm infants account for 60-70% of early neonatal and 65-75% of infant mortality. **The aim**: to examine the main premature baby's immune system indexes as it is the immune system state that determines survival of a newborn child, the peculiarity of its life in neonatal period, effectiveness of therapeutic and rehabilitation measures, as well as the degree of disability. There were two groups of premature children under study: the I group, n = 62 premature infants, the age of gestation 34-36 weeks without perinatal pathology. The IId group (control) was represented by 15 healthy newborns, aged 38-40 weeks of gestation. The study was carried out in the first 3 days of the child's life by flow cytofluorometry. In premature infants, the immaturity of the immune system was noted in the form of decrease in all indices of nonspecific immunity: the level of the complement component of C3, the level of immunoglobulins class A, G and M and the values of T-killers and B-lymphocytes.

Key words: **premature birth, premature child immune system, indexes of immune system.**

Introduction. Premature birth (PB) is one of the most important aspects of the problem of maternal and child health care. Despite the progress of modern medicine and introduction of highly effective perinatal technologies, the frequency of PB and birth of immature infants is steadily increasing and ranges from 4.0 to 15.0-20.0%. In Ukraine, the frequency of PB varies from 3.0% to 12.0% in different years, which corresponds to the average frequency of PB in the world [1, 2], where every year about 13 million premature infants are born. Preterm infants account for 60-70% of early neonatal and 65-75% of infant mortality. Perinatal mortality in preterm infants is 33 times more frequent than in term infants [3, 4, 5]. The prematurely born children have higher cerebral palsy, attention deficit disorder, respiratory pathology morbidity rates; they are more likely to have learning problems compared to children born on time. The most dangerous complication in preterm pregnancy is the possibility of postpartum development of infectious-inflammatory processes in the mother, fetal and new-born infection [6]. Because of immature defense mechanisms, the potential risk of fetal infection is much higher than in mother. The incidence of infectious disease is the higher, the less is fetus' gestational age, which is determined by relative immaturity of the mechanisms of antibacterial protection of the fetus and the undeveloped bacteriostatic properties of the amniotic fluid in preterm pregnancy. [7] Many of immature infants need intensive care and use of invasive technologies. Infectious diseases, especially nosocomial infections, are an important cause of morbidity and mortality in premature infants. Congenital immune system provides the first line of defense against invading pathogens. The main cells that provide an adaptive immune response are neutrophils, monocytes, macrophages and dendritic cells. These cells develop and mature during the period of intrauterine life at different times. The function of all components of innate immunity is weak in newborns compared with later stages of life [8]. The immune system state determines survival of a newborn child, the peculiarity of its life neonatal period, effectiveness of therapeutic and rehabilitation measures, as well as the degree of disability, as it is one of the most sensitive to any pathogenic factors and regulating the functioning of homeostasis systems in the development of pathological processes [9,10]. Most researches are based on the study of separate links of immunity, which does not allow to accurately assess the complex interconnection of immune processes and their responses in premature infants.

The aim of the research: to examine the main premature baby's immune system indexes.

Material and methods. The study was conducted on the basis of the Odessa National Medical University (Ukraine), in the neonatal department of the municipal maternity hospital

N 7. The first group consisted of 62 premature infants, the age of gestation 34-36 weeks without perinatal pathology. The second group (control) was represented by 15 healthy newborns, aged 38-40 weeks of gestation. The study was carried out in the first 3 days of the child's life by flow cytofluorometry. Relatives of all patients got oral information about all the procedures of the study and gave informed consent for participation in the study.

Statistical analysis of the data was carried out using STATISTICA 10.0 and MicrosoftExcel 2010 packages with the AtteStat 12.5 add-on, the SISA Internet calculator (Simple Interactive Statistical Analysis). The average sample values of the quantitative characteristics are given in the text in the form M ± m, where M is the mean sample, m is the error of the mean. Proportion (percent) are presented with 95% confidence intervals (CI). In all statistical analysis procedures, when checking null hypotheses, the critical significance level p was taken to be 0.05. One-way ANOVA was used to compare the main quantitative parameters of the groups.

The results obtained and their discussion. The mothers of the first group children aged 26.41 ± 0.95 y. o., the pregnancy was 2.54 ± 0.15, the labours were 1.55 ± 0.11, with an average gestation period of 35.8 ± 0.21 weeks. In the control group, the age of women was 24.95 ± 0.46 y. o., the pregnancy was 2.12 ± 0.22, the birth was 1.69 ± 0.21 at the term 39 ± 0.42 weeks.

There were no statistically significant differences between the groups according to the age parameters, the number of pregnancies and childbirths. The risk factors for PB in the first group were more often fixed by cervical incompetence - 75.58% (95% CI 70.26 - 81.73), placental dysfunction – 63.38% (95% CI 56.51 - 69.48), uterine bleeding 61.97% (95% CI 55.48 - 68.51) and infections of different etiology and localization - 60.09% (95% CI 53 , 42-66.57). In the control group, these factors were presented as follows: infections of different etiology and localization - 13.33% (95% CI -4.02 - 30.02), cervical incompetence 6.66% (95% CI - 5.91 – 19.91), placenta dysfunction - 6.66% (95% CI-5.91 - 19.91), uterine bleedings were not observed. In the terms of gender there were no statistically significant differences among the children in the groups under study.

While investigating the amount of the complement system central component (complement component C3), statistically significant differences were found in the groups under study - 0.76 ± 0.02 in prematurity group, 1.33 ± 0.06 in the full-term group, Fisher’s coefficient (F) was equal to 94,73 at a significance level of $p<0.001$.

The C4-2 component of the complement system in the main group was 0.13 ± 0.01, in the control group it was 0.30 ± 0.01 ($F = 82.53$, $p <0.001$), (Table 1).

Table 1

The result of the one-factor dispersed analysis of ANOVA of the indices under study of nonspecific immunity in the compared groups of children

Indicator	Preterm, M±m; n=62	Term, M ± m; n = 15	Fisher's Criterion, F	Significance of differences, p
C3 component (g / l)	0.76 ± 0.02	1.33 ± 0.06	94.73	p <0.001
C4-2 component (g / l)	0.13 ± 0.01	0.30 ± 0.01	82.53	p <0.001
Phagocytic index	2.09 ± 0.03	2.46 ± 0.06	29.38	p <0.001
NK cells (%)	3.17 ± 0.2	4.98 ± 0.20	16.21	p <0.001
Macrophages (%)	4.22 ± 0.16	7.22 ± 0.42	60.35	p <0.001

Also statistically significant differences in the activity of phagocytic cells were revealed - the phagocytic index in the compared groups of children was, respectively, 2.09 ± 0.03 and 2.46 ± 0.06 in the control group (F = 29.38, p <0.001). To a greater extent, preterm infants showed a decrease in the level of macrophages - 4.22 ± 0.16 and 7.22 ± 0.42 - the statistical significance of the differences was F = 60.35, p <0.001.

When comparing blood serum immunoglobulins, the greatest differences were noted in the content of IgA-Fisher's variability test was determined at the level of 88.13 for p <0.001 and IgG-51.06 for p <0.001. IgE indices in prematurity did not statistically significantly differ from the level in the term infants, (Table 2).

Table 2

The result of a single-factor analysis of ANOVA of serum immunoglobulins in the compared groups of children

Indicator	Preterm M ± m (n = 62)	Term, M ± m (n = 15)	Fisher's criterion (F)	The significance of the differences (p)
IgA (g / l)	0.16 ± 0.01	0.36 ± 0.01	88.13	p <0.001
IgM (g / l)	0.24 ± 0.01	0.27 ± 0.01	17.01	p <0.001
IgG (g / l)	7.59 ± 1.43	11.96 ± 1.76	51.06	p <0.001
IgE (IU / ml)	0.18 ± 0.01	0.12 ± 0.01	3.53	p = 0.064

When comparing the parameters of the reaction of blast transformation of lymphocytes (RBTL), it can be noted that the proliferative activity of lymphocytes in the compared groups is not statistically significantly different from each other: F = 0.86, p = 0.35 (Figure 1).

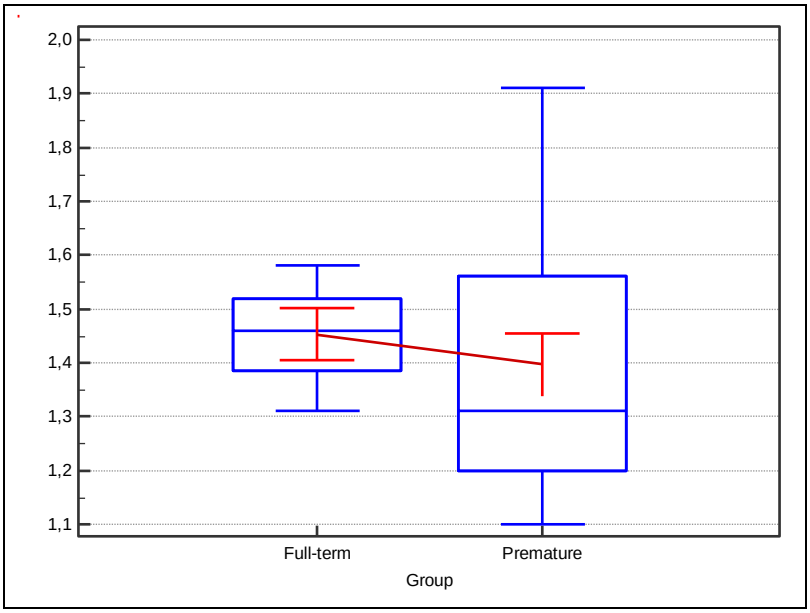

Fig.1. The result of the one-way ANOVA variance analysis of RBTL indicators in the compared groups of children in graphical expression.

In assessing the functional activity of immune cells, the greatest differences were observed in spontaneous cell activity (F = 41.28, p <0.001). Induced activity (F = 0.03, p = 0.85), like RBTL, did not change statistically significantly (Table 3). Evaluation of fractions of circulating immune complexes (CIC) is of interest: if larger (F = 6.87, p = 0.011) and middle CIC fractions (F = 3.04, p = 0.08) were more often found in the term infants, then in the group of premature infants small CIC (F = 5.16, p = 0.02) were more often noted, (Table 3).

Table 3

The result of single-factor despersed analysis of ANOVA functional activity of immune cells of circulating immune complexes in the compared groups of children

Index (optical units)	Preterm, M ± m (n = 62)	Term, M ± m (n = 15)	Fisher's criterion, F	The significance of the differences, p
RBTL	1.39 ± 0.02	1.45 ± 0.02	0.86	p = 0.35
Spontaneous activity	100.48 ± 1.51	121.8 ± 2.46	41.28	p <0.001
Induced activity	264.74 ± 3.55	266.33 ± 9.47	0.03	p = 0.85
CIC, large	6.83 ± 0.76	11.00 ± 0.51	6.87	p = 0.011
CIC, middle	62.3 ± 2.46	71.33 ± 2.41	3.04	p = 0.08
CIC, small	155.93 ± 2.02	146.33 ± 1.79	5.16	p = 0.02

The indices of cellular immunity are presented in Table 4. In the group of premature infants, a higher level of the relative number of T-lymphocytes compared with the group of full-term children is noted (F = 23.04, p <0.001). At the same time, there were no statistically significant differences in the composition of T-helper and T-suppressors (F = 2.82, p = 0.09 and F = 0.04, p = 0.84).

Table 4

The result of a single-factor analysis of ANOVA cellular immunity in the compared groups of children

Index, %	**Preterm, M±m, n=62**	**Term, M±m, n=15**	**Fisher's criterion**	**The significance of the differences**
CD3 +, CD19 - (%)	83.45 ± 0.85	76.13 ± 1.58	23.04	p <0.001
CD4 +, CD8 - (%)	59.74 ± 1.44	**54.71** ±1.18	**2.82**	**p=0.09**
CD4-, CD8+(%)	**20.49** ±0.80	**20.13** ±1.34	**0.04**	**p=0.84**
CD3+, CD56+(%)	**0.97** ±0.04	**1.87** ±0.13	**69.17**	p <0.001
CD3-, CD19+(%)	**6.01** ±0.53	**12.07** ±0.64	**21.41**	p <0.001
CD45(%)	**96.59** ±0.22	**97.02** ±0.29	**0.74**	**p=0.39**

The immaturity of cellular immunity in preterm infants manifested itself as a decrease in the level of T-killers and B-lymphocytes (F = 69.17, p <0.001 and F = 21.41, p <0.001). The relative indices of the total leukocyte antigen content in the groups under study did not differ statistically significantly (F = 0.74, p = 0.39).

Conclusions

In premature infants, the immaturity of the immune system is noted in the form of decrease in all indices of nonspecific immunity. The most pronounced decrease in the level of the complement component of C3 takes place. Compared to full-term babies, a statistically significant decrease in the level of immunoglobulins class A, G and M. was observed in premature babies. When comparing the parameters of cellular immunity, the lowest values of T-killers and B-lymphocytes are most pronounced.

Conflict of interest statement. The authors declare that the research was carried out in the absence of any commercial or financial relations that could be construed as a potential

conflict of interest.

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