



## MULTIFACTORIAL ANALYSIS OF THE PARAMETERS FOR IMMUNITY IN PRETERM INFANTS

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### ABSTRACT

*The multifactorial analysis of the immunity for the preterm infants, born at 34–36 weeks gestation, has been performed. Three factors of the external load, which were 55.71% of the power load, have been determined with the method of principal components. As a result of the analysis, we can come to the conclusion about the feasibility of the advanced study, the parameters of the immune system for the preterm infants, are as follows: The complement fractions, The circulating immune complexes, T-lymphocytes, T-helper cells, B-lymphocytes, the immunoregulatory index, and IgE.*

**Keywords:** Immunity, Premature babies, Multifactorial analysis, T-lymphocytes, T-helper cells, B-lymphocytes, Immunoglobulin's.

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### Contribution/ Originality

This study is one of very few studies which have investigated parameter of immunity for preterm infants, study of the relationship of balance disorders and immune mechanisms in preterm infants will identify new approaches to the diagnosis of the pathology for neonatal period

## 1. INTRODUCTION

Premature birth (PB) is one of the most important aspects of the health problem of the mother and child. Despite the progress of modern medicine and the implementation of high-technology, the perinatal rate of premature birth and the birth of premature babies are growing steadily and from 4.0 to 15.0–20.0% [1]. In Ukraine the incidence of preterm birth varies in different years ranging from 3.0% to 12.0%, which corresponds to an average rate of the premature births in the world. There are about 13 million preterm infants in the world yearly. The share of the preterm infants is 60–70% of the neonatal mortality and 65–75% of the infant mortality [2, 3]. The perinatal mortality in preterm infants is recorded 33 times more often than full-term ones. The children born prematurely have higher morbidity rates of cerebral palsy, Attention deficit, Hyperactivity disorder and Respiratory pathologies. The most dangerous complication of the preterm pregnancy is the possibility of developing postpartum infectious and inflammatory processes for the mother, infection of the fetus and the newborn. Due to the imperfections of the protection mechanisms, the potential risk of infection for the fetal is significantly higher than for the mother [4]. The higher infection rate, the less gestational age the fetus has, which is determined by the relative imperfection of the mechanisms of antibacterial protection of the fetus and undeveloped bacteriostatic

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properties of the amniotic fluid under the preterm pregnancy. The infectious diseases, especially nosocomial infections, are an important cause of the morbidity for the preterm neonates and mortality due to the fact that many of them require intensive therapy and invasive procedures. For the infants born prematurely, the role of phylogenetic and ontogenetic earlier nonspecific protection factors is increasing as an anti-infectious protection [5, 6].

### 1.1. Objective

To determine the most significant laboratory markers and their associations based on the parameters of the multifactorial analysis of the immune system for a premature baby.

## 2. MATERIAL AND METHODS

The study has been conducted on the basis of the Odessa National Medical University - the Neonatology Department of the Maternity Hospital № 7, Odessa, Ukraine. The study of the immune system has been carried out in the first 3 days life of the child with the method of flow cytometry for 62 children who were born prematurely within 34-36 weeks of gestation without the perinatal pathological states. The relatives of the all examined patients received the oral information about all investigation procedures and they gave their informed consent to participate in the study. The statistical analysis of the obtained data has been performed using the STATISTICA 10.0 and IBM SPSS Statistics 22 packages. The average selected values of quantitative traits are given in the text as  $M \pm m$ , where  $M$  is the average selected,  $m$  is the average accuracy. The shares (percent) are presented with 95% confidence intervals (CI). The normality check of the distribution has been carrying out with two methods: graphic (with a "normal distribution charts" creating) and the Shapiro-Wilk test. The correlations are presented with the Pearson correlation coefficient. Under the all statistical analysis procedures while the null hypothesis checking, the critical significance level of  $p$  was assumed to be 0.05.

## 3. RESULTS AND DISCUSSION

The mothers' age of the studied children was  $26,41 \pm 0,95$  years, pregnancy  $2,54 \pm 0,15$ , childbirth  $1,55 \pm 0,11$  at an average gestational age of  $35,8 \pm 0,21$  weeks. The cervical incompetence - 75.58% (95% CI 70.26 - 81.73), dysfunction of the placenta - 63.38% (95% CI 56.51 - 69.48), uterine bleeding - 61.97% (95% CI 55.48 - 68.51) and infections of the different etiology and localization - 60.09% (95% CI 53.42 - 66.57) were often recorded as the risk factors of PB.

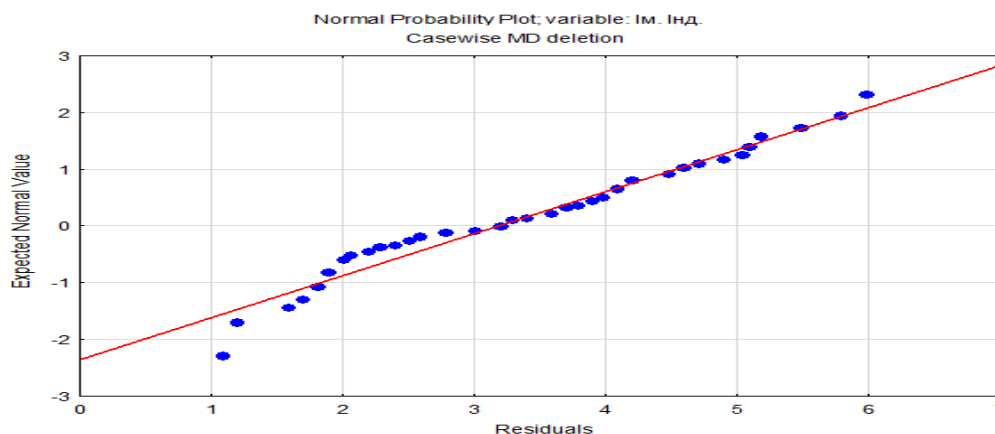


Figure-1. immunological index parameters distribution normality checking scattergram

Source: Self edition

To determine the possibility of multifactor correlation analysis, the definition of distribution studied parameters of the immune system has been carried out (figure 1). All the studied parameters of the immune system for the preterm infants introduced the relative homogeneity with the presence of the single "emissions".

The distribution of the total variance factors with the principal components method in the graphic terms (the method of "scree") is presented in Figure 2.

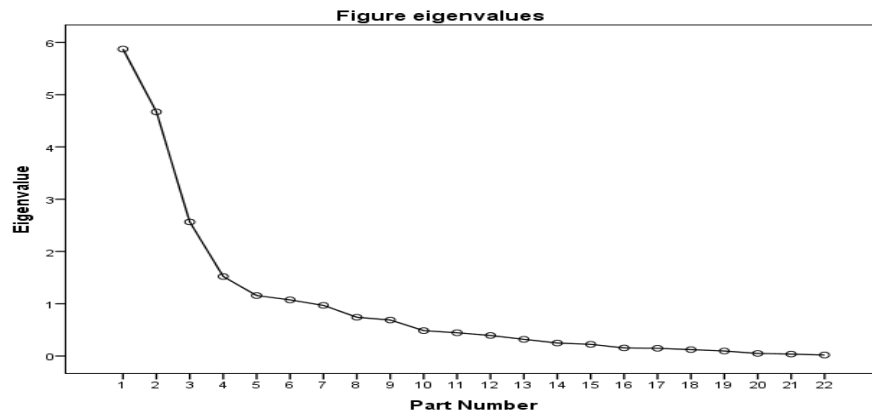


Figure-2. The total dispersion specific values graph

Source: Self edition

At the first stage of the multifactor correlation analysis with the method of the principal components the number of the external load factors have been determined (Table 1).

Table-1. The Number of Factors Determining for the Multifactor Correlation Analysis with the Principal Components Analysis

| Component | Initial available values |            |          | The sums of squares withdrawal downloads |             |            | The sums of squares rotation downloads |             |            |
|-----------|--------------------------|------------|----------|--|-------------|------------|--|-------------|------------|
|           | Total                    | Variance,% | Summary% | Total                                    | Variance, % | Summary, % | Total                                  | Variance, % | Summary, % |
| 1         | 7,031                    | 30,571     | 30,571   | 7,031                                    | 30,571      | 30,571     | 5,027                                  | 21,856      | 21,856     |
| 2         | 3,786                    | 16,463     | 47,034   | 3,786                                    | 16,463      | 47,034     | 3,680                                  | 16,001      | 37,857     |
| 3         | 1,996                    | 8,680      | 55,714   | 1,996                                    | 8,680       | 55,714     | 2,573                                  | 11,188      | 49,045     |
| 4         | 1,649                    | 7,170      | 62,885   |  |             |            |  |             |            |
| 5         | 1,407                    | 6,116      | 69,000   |  |             |            |  |             |            |
| 6         | 1,377                    | 5,987      | 74,988   |  |             |            |  |             |            |
| 7         | ,998                     | 4,338      | 79,325   |  |             |            |  |             |            |
| 8         | ,885                     | 3,849      | 83,174   |  |             |            |  |             |            |
| 9         | ,793                     | 3,449      | 86,623   |  |             |            |  |             |            |
| 10        | ,643                     | 2,797      | 89,420   |  |             |            |  |             |            |
| 11        | ,546                     | 2,376      | 91,795   |  |             |            |  |             |            |
| 12        | ,538                     | 2,337      | 94,132   |  |             |            |  |             |            |
| 13        | ,381                     | 1,655      | 95,787   |  |             |            |  |             |            |
| 14        | ,346                     | 1,505      | 97,292   |  |             |            |  |             |            |
| 15        | ,191                     | ,833       | 98,125   |  |             |            |  |             |            |
| 16        | ,157                     | ,681       | 98,806   |  |             |            |  |             |            |
| 17        | ,123                     | ,533       | 99,339   |  |             |            |  |             |            |
| 18        | ,088                     | ,383       | 99,722   |  |             |            |  |             |            |
| 19        | ,046                     | ,201       | 99,923   |  |             |            |  |             |            |
| 20        | ,010                     | ,042       | 99,965   |  |             |            |  |             |            |
| 21        | ,004                     | ,017       | 99,982   |  |             |            |  |             |            |
| 22        | ,003                     | ,013       | 99,995   |  |             |            |  |             |            |
| 23        | ,001                     | ,005       | 100,000  |  |             |            |  |             |            |

Selection factors Method: principal components method.

Source: Self edition

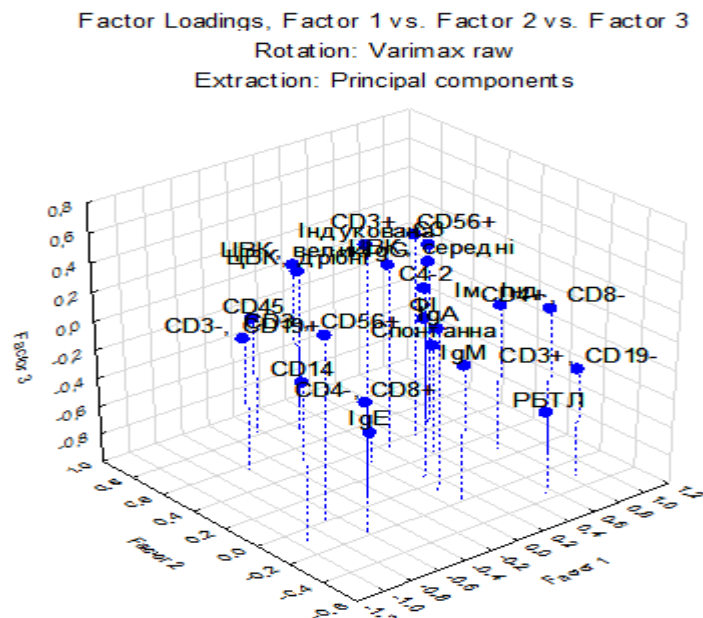
As a result of principal component analysis, we can conclude that three factors, in which 55.71% of the power load is selected, are the most expedient is to apply for the external load.

The commencement of the multifactor correlation analysis as the three-factor loading matrix using Varimax raw turn is presented in Table 2 and in Figure 3.

**Table-2.** The matrix of factor loadings after the turn with the Varimax raw immunity parameters method for the preterm infants

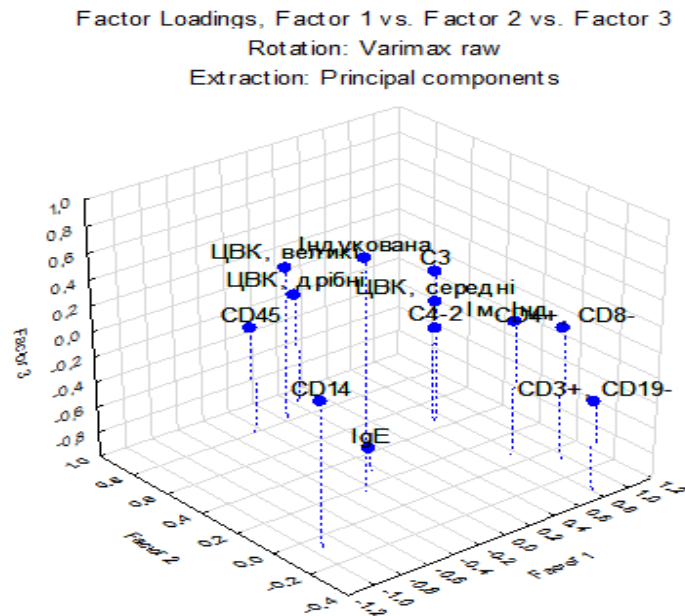
| Parameter                                 | Factor 1  | Factor 2  | Factor 3  |
|---|-----------|-----------|-----------|
| IgA                                       | 0,078627  | -0,062845 | 0,141282  |
| IgM                                       | 0,115232  | -0,187935 | -0,066000 |
| IgG                                       | 0,249378  | 0,366204  | 0,293460  |
| IgE                                       | 0,020254  | 0,303570  | -0,789396 |
| C3  | 0,667556  | 0,459308  | 0,273658  |
| C4-2                                      | 0,730142  | 0,526955  | -0,094817 |
| Spontaneous                               | 0,401144  | 0,216800  | -0,223586 |
| Induced                                   | -0,277011 | 0,077442  | 0,730358  |
| Phagocytic index (LPA)                    | 0,129964  | 0,063260  | 0,117354  |
| Circulating immune complexes (CIC), large | -0,006652 | 0,740223  | 0,171785  |
| CIC, medium                               | 0,700751  | 0,467878  | 0,134818  |
| CIC, small                                | 0,227067  | 0,923930  | -0,041454 |
| CD3+, CD19-                               | 0,836874  | -0,315052 | -0,243473 |
| CD4+, CD8-                                | 0,948399  | -0,072921 | 0,018628  |
| CD4-, CD8+                                | -0,596620 | -0,174189 | -0,102692 |
| Immunological Index                       | 0,738967  | 0,069401  | 0,028164  |
| CD3+, CD56+                               | 0,467841  | 0,383417  | 0,422880  |
| CD3-, CD56+                               | -0,685192 | 0,004277  | 0,282151  |
| CD3-, CD19+                               | -0,599498 | 0,566093  | -0,080915 |
| CD14                                      | -0,943901 | -0,088609 | 0,101181  |
| CD45                                      | -0,232900 | 0,820137  | -0,191466 |

Source: Self edition



**Figure-3.** The commencement of the three-factor analysis of immune parameters for preterm infants graphical reflection (Varimax raw rotation method)

Source: Self edition



**Figure-4.** The outcome of the three-factor analysis of immune parameters for preterm infants Graphical reflection (Varimax raw rotation method)  
Source: Self edition

The outcome parameters of the multifactor correlation analysis with the three external factors are presented in Table 3 and Figure 4.

**Table-3.** The matrix of factor loadings after the turn with the Varimax raw immunity parameters method for the preterm infants (final version)

| Parameter           | Factor 1  | Factor 2  | Factor 3  |
|---------------------|-----------|-----------|-----------|
| Ig.E                | -0,050233 | 0,278750  | -0,830824 |
| C3                  | 0,720882  | 0,462717  | 0,195765  |
| C4-2                | 0,739066  | 0,473317  | -0,271642 |
| Induced             | -0,256254 | 0,168622  | 0,800421  |
| CEC, big            | 0,044084  | 0,828457  | 0,207941  |
| CIC, medium         | 0,729570  | 0,471943  | -0,051634 |
| CIC, small          | 0,244951  | 0,916341  | -0,127582 |
| CD3+, CD19-         | 0,807142  | -0,333385 | -0,305575 |
| CD4+, CD8-          | 0,947495  | -0,079625 | 0,037272  |
| Immunological Index | 0,749679  | 0,064421  | 0,051962  |
| CD14                | -0,925940 | -0,073693 | 0,120254  |
| CD45                | -0,256264 | 0,803958  | -0,169667 |

Source: Self edition

According to multifactor analysis with Varimax raw rotation it can be noted that the most significant immune parameters for the premature infants were distributed into three main factor components. The fractions of the complement C3 and C4-2, CIC medium density, T-lymphocytes, T-helper cells, B-lymphocytes and immunoregulatory index compounded the first sector (factor1). The cells C3 and C4-2 with correlation coefficients 0.72 and 0.73, CIC medium density 0.72, CD3+, CD19- 0.80, CD4+, CD8- 0.94, immunological index with coefficient correlation 0, 74 are presented with the direct dependence. The power connection index for the CD14 parameter was equal to minus 0.92.

Factor 2 is presented with the circulating immune complexes and leukocyte common antigen: CIC big and CIC small Virage are displayed with the direct correlation 0.82 and 0.91 respectively, the power connection coefficient CD45 is equal to 0.80.

The factor 3 includes parameters of the induced activity of the immune cells and the IgE level. The functional activity of immune cells induced with the correlation parameter 0.80 is submitted with the direct connection. The parameter of IgE with a correlation coefficient 0.83 is presented with negative correlation. All the parameters of the power connection are significant at  $p < 0.05$ .

#### 4. CONCLUSION

As a result result of the analysis, we can come to the conclusion as to the advisability of the advanced investigation of the following parameters of the immune system for the preterm infants: complement fractions, circulating immune complexes, T-lymphocytes, T-helper cells, B-lymphocytes, the immunoregulatory index. The fractions of circulating immune complexes and the leukocyte common antigen are recommended as well for the further study in premature babies immunogram. The continuous study of the induced activity of immune cells in conjunction with the definition of IgE levels are of independent interest.

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Contributors/Acknowledgement: All authors contributed equally to the conception and design of the study.

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