



New Day in Medicine
Новый День в Медицине

NDM



TIBBIYOTDA YANGI KUN

Ilmiy referativ, marifiy-ma'naviy jurnal



AVICENNA-MED.UZ



ISSN 2181-712X.
EISSN 2181-2187

2 (88) 2026

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ТИББИЁТДА ЯНГИ КУН НОВЫЙ ДЕНЬ В МЕДИЦИНЕ NEW DAY IN MEDICINE

*Илмий-рефератив, маънавий-маърифий журнал
Научно-реферативный,
духовно-просветительский журнал*

УЧРЕДИТЕЛИ:

**БУХАРСКИЙ ГОСУДАРСТВЕННЫЙ
МЕДИЦИНСКИЙ ИНСТИТУТ
ООО «ТИББИЁТДА ЯНГИ КУН»**

Национальный медицинский
исследовательский центр хирургии имени
А.В. Вишневского является генеральным
научно-практическим
консультантом редакции

Журнал был включен в список журнальных
изданий, рецензируемых Высшей
Аттестационной Комиссией
Республики Узбекистан
(Протокол № 201/03 от 30.12.2013 г.)

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2 (88)

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2026 февраль

UDC 616.24-008.4-053.31:612.017.1

THE PROGNOSTIC SIGNIFICANCE OF CYTOKINE STATUS IN EARLY INFLAMMATORY RESPONSE IN THE DEVELOPMENT OF BRONCHOPULMONARY DYSPLASIA IN EXTREMELY PREMATURE INFANTS

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✓ Resume

Bronchopulmonary dysplasia (BPD) is one of the most common and severe chronic lung diseases in premature infants with extremely low birth weight (≤ 1000 g). The pathogenesis of the disease is associated with impaired normal lung tissue development combined with inflammatory processes.

In recent years, increasing attention has been paid to the study of cytokines as biomarkers of inflammation capable of predicting the development of BPD in the early stages of a child's life. This article systematises data on the role of key cytokines and their prognostic potential.

It has been established that in extremely premature infants, IL1PA levels > 712 pg/ml and IL6 > 30 pg/ml predict the development of BPD.

Keywords: IL1PA, IL6, IL10, BPD, extremely low birth weight, premature infants.

Relevance

One of the most important issues in modern perinatology is premature birth and the care of babies born before 32 weeks of gestation. Newborns with extremely low birth weight (ELBW) account for a significant proportion of all patients in resuscitation and intensive care units (ICUs). Thanks to the successful development of intensive care technologies and the optimisation of perinatal care, it has become possible to change the standards for registering infants born at 22 weeks of gestation or more and weighing 500 grams or more in accordance with the criteria of the World Health Organisation (WHO). The proportion of births at less than 32 weeks of gestation does not exceed 1.5-2%, but there is no downward trend, so the problem of prognosis and long-term outcomes of caring for premature babies remains relevant [4,7]. Profound morphological immaturity contributes to the development of bronchopulmonary dysplasia (BPD), retinopathy of prematurity, hydrocephalus, sensorineural deafness, psychomotor retardation (PMR), and cerebral palsy (CP) [2, 5, 9].

To date, the effectiveness of a number of therapeutic and preventive measures that increase the survival rate of extremely premature newborns has been convincingly proven. These include: antenatal use of corticosteroids, improvement of primary resuscitation and respiratory support (use of air or minimal concentrations of oxygen, non-invasive and high-frequency ventilation), early administration of surfactant preparations, development of basic neonatal care technologies, including early breastfeeding, thermal and sensory protection, and pain prevention [1, 5].

A topical issue is the choice of optimal obstetric tactics in premature labour. According to N.V. Bashmakova et al., the best survival rate for children with ENMT is observed at a gestational age of more than 26 weeks, with abdominal delivery being the most preferable method. At less than 26 weeks of gestation, abdominal delivery does not increase the chances of a favourable perinatal outcome [9]. An analysis of randomised studies from the Cochrane database also demonstrated no advantages of planned caesarean section compared to vaginal delivery.

BPD is diagnosed in premature infants who require oxygen support on the 28th day of life and/or at 36 weeks post-conceptual age. The risk of developing BPD is significantly higher in extremely low birth weight infants (≤ 1000 g), due to organ and tissue immaturity, mechanical ventilation, and inflammatory responses. The study of the immunopathogenesis of the 'new' or post-surfactant form of BPD, which develops predominantly in extremely premature newborns, is currently a particularly pressing issue. Its formation is associated with impaired lung development due to the action of a large number of prenatal and postnatal factors against the background of incomplete alveolar and angiogenesis processes [2].

It is believed that the conditions of intrauterine life and early childhood are of paramount importance for optimal growth and development of the respiratory system [3]. The literature contains data on the association of BPD with pre-eclampsia [5], chorioamnionitis [6], intrauterine inflammation [4, 7] and genetic predisposition [7]. Researchers are paying the most attention to the role of chronic inflammation of the lung tissue, since it is in deeply premature newborns that a pronounced reaction to high concentrations of oxygen in the inhaled mixture is observed, manifested by inflammation and, subsequently, cessation of alveolar growth and the development of BPD [3]. There is growing evidence that BPD is the result of an imbalance between pro- and anti-inflammatory mechanisms.

Many authors have studied the role of pro-inflammatory cytokines that predict the development of BPD in premature infants with ENMT: IL1RA, IL6, IL10, TNF- α . IL-6 is often elevated in premature infants who subsequently develop BPD. IL-6 levels on the first day of life correlate with the risk of developing the disease and the severity of the inflammatory response. IL-8 is a potent chemokine that attracts neutrophils, increases with more pronounced inflammatory responses, and may be associated with the future development of BPD. TNF- α is an inflammatory cytokine involved in tissue damage and modelling of inflammatory processes in the lungs, sometimes correlating with a more severe course of BPD. IL-10 has an anti-inflammatory effect and may weaken the development of the inflammatory response, which is potentially associated with a reduced risk of BPD [4,8].

Research objective: To evaluate immunological parameters in premature infants with extremely low birth weight for early prediction and prevention of bronchopulmonary dysplasia.

Materials and methods

The study was conducted at the Republican Specialised Scientific and Practical Medical Centre (RSSPMC) for Maternal and Child Health in the Bukhara Region between 2023 and 2025. Fifty premature babies born at 22–28 weeks of gestation and admitted to the neonatal intensive care unit were prospectively examined. In all cases, informed consent was obtained from the mothers for examination and treatment. On days 3.7–10, immunological studies of cytokines IL1, IL1PA, IL6 and IL10 in blood serum were performed using the solid-phase enzyme immunoassay ‘Sandwich’ method. Statistical data processing was performed using descriptive statistics and correlation analysis with the Statistica 6.1 software package and was expressed in the case of normal distribution of the trait as the arithmetic mean and its standard deviation ($M \pm SD$). Student's t-test was used to determine the statistical significance of differences. In cases of abnormal distribution, data were presented as median, 25–75% quartile; the non-parametric Mann–Whitney U test and Spearman's correlation coefficient (r) were used to determine the statistical significance of differences. Differences between qualitative characteristics were determined using criterion 2. For all statistical calculations, the critical error level p was taken to be 0.05.

Results and discussion

Gestational age ranged from 22.4 to 27.3 (24.9 ± 1.8 weeks), and birth weight ranged from 588.0 to 946.0 (767.0 ± 112.0). Body length was 33.2 ± 1.9 cm. Of the 50 children examined, 72% were boys. The premature infants examined were divided into two subgroups: 1) premature infants with BPD ($n = 28$) and 2) premature infants without BPD ($n = 22$). In group 1, the following diagnoses were made: ALV-associated pneumonia-20, surfactant therapy-21, connection to a ventilator-24, severe RDS syndrome-24; in the second group, 7; 22; 12; 8, respectively (Fig. 1).

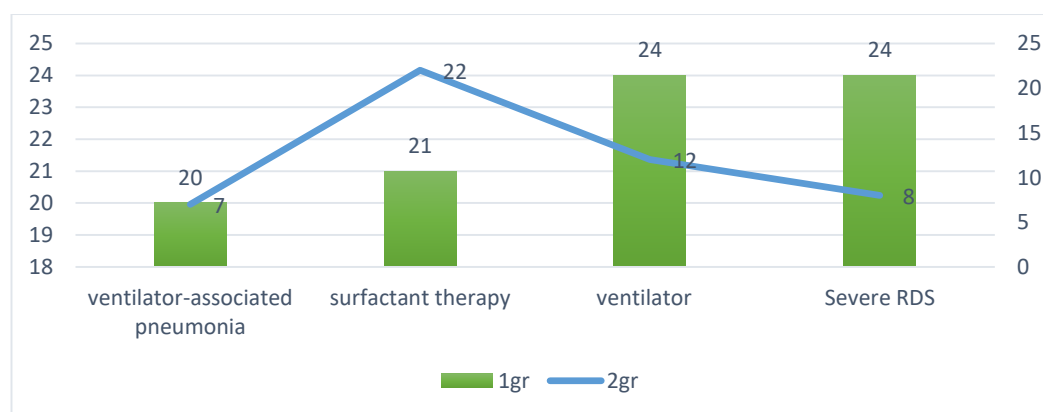


Fig. 1. Comparative general clinical characteristics of the children examined.

The study assessed the levels of pro- and anti-inflammatory cytokines (IL-6, IL-1PA, IL-10) were assessed to determine their contribution to the immunopathogenesis and prognosis of BPD in the dynamics on days 3-7-10 of life (Fig. 2). On the third day of life, children who subsequently developed BPD showed a significant increase in IL-1PA levels.

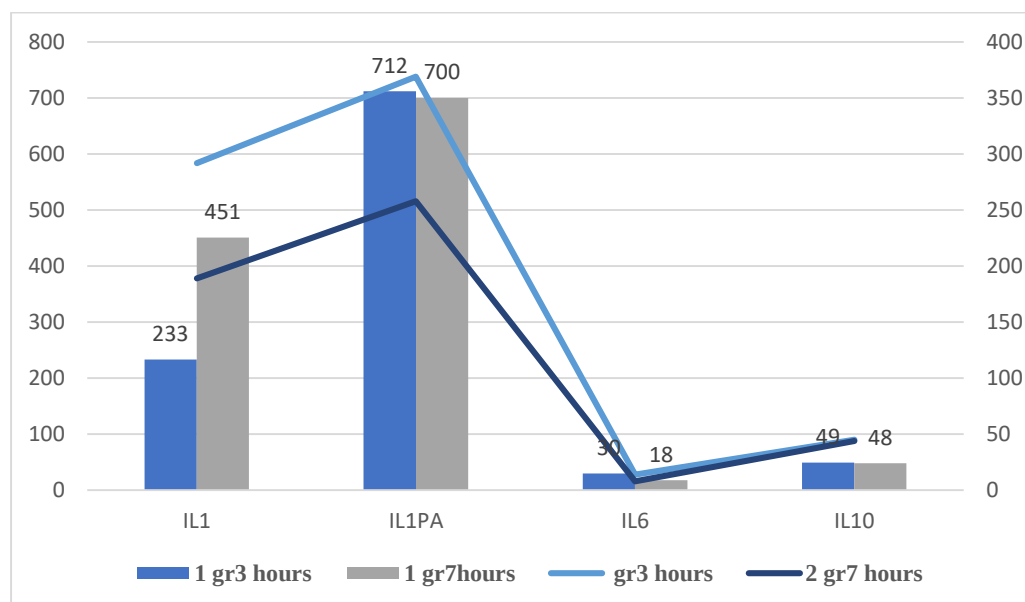


Fig. 2. Cytokine dynamics in blood serum in premature infants with ENMT.

Severe perinatal hypoxia and RDS combined with elevated serum IL-1RA levels on the third day of life may be predictors of BPD development. On the 7th day of life, serum levels of both pro- and anti-inflammatory cytokines were significantly elevated in children who subsequently developed BPD: cytokines of the IL-1 and IL-6 families are among the main mediators of acute inflammation. Compared to IL-1RA, the increase in IL-10 levels was less pronounced.

Threshold values of IL-1RA >712 pg/ml and IL-6 >30 pg/ml, determined in the first week of life, were associated with a 70–80% probability of developing BPD, whereas at values below these thresholds, 90% of the children examined did not develop BPD.

Conclusion

Cytokines are promising biomarkers for early prediction of BPD in extremely low birth weight infants. At the present stage, despite the introduction of exogenous surfactant preparations and continuous improvement of respiratory support methods, the development of bronchopulmonary dysplasia is predominantly observed in newborns with extremely low body weight born at less than 28 weeks of gestation. The incidence of BPD in this cohort of patients was 50.1%. A comparative analysis of the prognostic significance of pro- and anti-inflammatory cytokine levels in newborns who subsequently developed BPD demonstrated the greatest informative value of IL-1RA at a serum concentration >712 pg/ml and IL-6 >30 pg/ml.

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Entered 20.01.2026