10. Raz N, Feinmesser L, Moore O, Haimovich S. Endometrial polyps: diagnosis and treatment options—a review of the literature. Minim Invasive Ther Allied Technol. 2021;30(5):278–287. doi:10.1080/13645706.2021.1948867.
11. Reinikka S, Mehine M, von Nandelstadh P, Ahvenainen T, Khamaiseh S, Nousiainen S, et al. Genomic landscape of endometrial polyps. Genome Med. 2025;17:132. doi:10.1186/s13073-025-01556-z.
12. Ren H, Duan H, Wang S, Chang Y. Hysteroscopy combined with laser vaporesection for endometrial polyps. J Invest Surg. 2022;35(10):1772-1778. doi:10.1080/08941939.2022.2116134.
13. Rotenberg O, Doulaveris G, Fridman D, Renz M, Kaplan J, Xie X, Goldberg GL, Dar P. Risk of endometrial polyp and surgical intervention in postmenopausal women with proliferative endometrium. Maturitas. 2023;178:107847. doi:10.1016/j.maturitas.2023.107847.
14. Tekin S, Ocal A, Sisman E, Bilginer C, Cetin A. Histological assessment of endometrial polyps resected by hysteroscopy. Eur Rev Med Pharmacol Sci. 2024 Apr;28(8):3241-3250. doi: 10.26355/eurrev_202404_36052
15. Sharon A, Zidane M, Aiob A, Apel-Sarid L, Bornstein J. Nonelectric shaving of endometrial polyp by hysteroscopy: a new technique to eliminate thermal damage. Eur J Obstet Gynecol Reprod Biol. 2023;285:170-174. doi:10.1016/j.ejogrb.2023.04.018.

**Conflict of interest.** The authors have no conflicts of interest to declare.

**ORCID:** Parvana A.J. https://orcid.org/0009-0000-2707-7452.

Article received: 27.06.2025

**DOI 10.26724/2079-8334-2026-2-96-107-110**
**UDC 616.94-053.31:577.112.6:612.017.1**

**Polukhova A.E., Kerimova N.T.**
**Scientific Research Institute of Pediatrics named after K.Y. Farajova, Baku, Azerbaijan**

# CHANGES IN ALPHA-DEFENSIN AS AN INFLAMMATORY MARKER DURING NEONATAL SEPSIS IN TERM AND PRETERM INFANTS

e-mail: etplaboratoriya@mail.ru

Neonatal sepsis remains one of the most important causes of infectious morbidity in newborns, especially among infants born prematurely. The study evaluated alpha-defensin as an inflammatory marker in 130 newborns, including term and preterm infants with sepsis and healthy newborns in the control group. The concentration of alpha-defensin was markedly higher in septic newborns than in healthy infants and decreased during repeated assessment, reflecting attenuation of the inflammatory process. In term infants with sepsis, alpha-defensin exceeded control values by more than fifteenfold, and a similar increase was observed in preterm infants with both early and late disease onset. Positive associations with interleukin-6 and interleukin-8 indicate that alpha-defensin reflects activation of innate immune mechanisms. The findings support the use of alpha-defensin as an additional laboratory marker for assessing the severity of inflammation and immune status in neonatal sepsis.

**Key words:** neonatal sepsis, alpha-defensin, innate immunity, inflammatory markers, preterm infants, term infants.

**Полухова А.Є., Керімова Н.Т.**

# ЗМІНИ РІВНЯ АЛЬФА-ДЕФЕНЗИНУ ЯК МАРКЕРА ЗАПАЛЕННЯ ПРИ НЕОНАТАЛЬНОМУ СЕПСИСІ У ДОНОШЕНИХ ТА НЕДОНОШЕНИХ ДІТЕЙ

Неонатальний сепсис залишається однією з найважливіших причин інфекційної захворюваності новонароджених, особливо серед дітей, що народилися передчасно. У дослідженні оцінювали альфа-дефензин як маркер запалення у 130 новонароджених, включаючи доношених і недоношених дітей із сепсисом та здорових новонароджених контрольної групи. Концентрація альфа-дефензину у дітей із сепсисом була значно вищою, ніж у здорових новонароджених, і знижувалася під час повторного обстеження, що свідчило про зменшення активності запального процесу. У доношених дітей із сепсисом рівень альфа-дефензину перевищував контрольні значення більш ніж у п’ятнадцять разів; подібне підвищення виявлено у недоношених дітей при ранньому та пізньому початку захворювання. Позитивні зв’язки з інтерлейкіном-6 та інтерлейкіном-8 вказують на те, що альфа-дефензин відображає активацію вродженого імунітету. Отримані дані підтверджують можливість його використання як додаткового лабораторного маркера тяжкості запалення та імунного статусу при неонатальному сепсисі.

**Ключові слова:** неонатальний сепсис, альфа-дефензин, вроджений імунітет, запальні маркери, недоношені діти, доношені діти.

Current understanding of the pathophysiology of sepsis is based mainly on studies conducted in mature adult populations. However, both experimental and clinical studies demonstrate that newborns have immune responses to infection that differ substantially from those of adults and older children [17]. These differences are especially important in preterm infants, whose survival and long-term outcomes depend on timely recognition of generalized inflammatory disease.

The immature immune system is a major factor contributing to increased susceptibility to sepsis in the neonatal period. Polymorphonuclear neutrophils, macrophages, T lymphocytes, and B lymphocytes in newborns have functional features that limit the ability to mount a quantitatively and qualitatively adequate inflammatory response. In addition, transplacental transfer of immunoglobulins is reduced in preterm infants, further increasing the risk of severe infection [1, 2].

Cytokines and antimicrobial peptides synthesized by immune and other immunocompetent cells play important roles in immune regulation. Pro-inflammatory cytokines and anti-inflammatory cytokines participate in antibacterial and antiviral defense, while antimicrobial peptides provide broad protection against bacteria, viruses, and fungi and also modulate inflammation through effects on chemokines, immune-cell migration, and cytokine production [1, 3, 7].

Defensins are among the most extensively studied antimicrobial peptides. Alpha-defensins are stored predominantly in neutrophil granules and are released during inflammatory activation. Their biological activity includes direct antimicrobial effects, support of chemotaxis, interaction with cytokine networks, and participation in the regulation of innate immunity [2, 8].

In neonatal sepsis, clinical signs are often nonspecific, while traditional laboratory parameters may not be sufficiently sensitive during the earliest phase of infection. Therefore, the search for additional biomarkers that reflect innate immune activation and disease severity remains clinically relevant [4, 6, 13]. In accordance with this need, the present study assessed dynamic changes in alpha-defensin levels in term and preterm infants with neonatal sepsis.

**The purpose** of the study was to investigate the diagnostic and pathogenetic significance of alpha-defensin as an inflammatory marker in term and preterm infants with neonatal sepsis, including the dynamics of this marker during the course of the disease and its relationship with selected cytokines.

**Materials and methods.** This observational comparative study included 130 newborns examined at the Scientific Research Institute of Pediatrics named after K.Y. Farajova. The study population comprised 100 newborns receiving inpatient treatment for neonatal sepsis and 30 healthy newborns included in the control group. The infants with sepsis were divided according to gestational age and the period of disease onset.

Group I included 35 term newborns diagnosed with sepsis and born at a gestational age of 38–41 weeks. Group II included 65 preterm newborns diagnosed with sepsis and born at a gestational age of 27–37 weeks. The control group included 30 healthy newborns, of whom 23 were term infants and 7 were preterm infants. Among the preterm infants with sepsis, early neonatal sepsis was registered in 15 cases and late neonatal sepsis in 50 cases.

Laboratory examinations were performed in the immunological laboratory of the Scientific Research Institute of Pediatrics. Alpha-defensin was determined by a standard solid-phase sandwich enzyme-linked immunosorbent assay using the Elisys UNO-Human fully automated analyzer (Germany). Interleukin-6 and interleukin-8 were assessed as inflammatory cytokines to evaluate the relationship between antimicrobial peptide activity and cytokine response.

The data are presented as mean values with standard errors and ranges. Intergroup comparisons were performed using non-parametric criteria for independent and paired samples, and correlation analysis was used to assess relationships between alpha-defensin and cytokine concentrations. Differences were considered statistically significant at p values below 0.05.

The study was conducted in accordance with the principles of the Declaration of Helsinki and the Convention on Human Rights and Biomedicine. The work used anonymized clinical and laboratory data obtained during routine diagnostic assessment and did not involve additional invasive interventions or changes in treatment tactics. For this reason, a separate meeting of the institutional bioethics committee was not convened before the start of the study. Confidentiality of patient data was preserved throughout all stages of analysis.

**Results of the study.** In term infants with neonatal sepsis, alpha-defensin levels were sharply elevated during the initial examination. The mean value reached 771.8±37.6 ng/mL, while the corresponding value in the control group was 48.4±1.3 ng/mL. During repeated examination, the concentration decreased to 380.0±21.1 ng/mL, but remained significantly higher than in healthy newborns (Table 1).

Table 1

**Alpha-defensin indicators in term infants with sepsis**

| Indicators | Control group (n=23) | Neonatal sepsis (n=35) | | P1 | P2 |
|---|---|---|---|---|---|
| | | Initial examination | Repeated examination | | |
| α-defensin (ng/mL) | 48.4±1.3 (31.2-58.4) | 771.8±37.6 (323.9-1098.0) | 380.0±21.1 (113.4-625.7) | <0.001 | <0.001 |

Note: P1 – comparison with the control group; P2 – comparison between initial and repeated examinations in patients with neonatal sepsis.

In preterm infants, both early and late forms of neonatal sepsis were characterized by similarly high alpha-defensin concentrations at the initial examination. In early neonatal sepsis, the initial value was 716.7±53.3 ng/mL; in late neonatal sepsis, it was 731.3±31.8 ng/mL. During dynamic observation, the marker decreased in both subgroups, reaching 336.7±31.6 ng/mL in early sepsis and 371.2±16.2 ng/mL in late sepsis (Table 2).

Table 2

**Alpha-defensin indicators in preterm infants with sepsis**

| Indicators | Control group (n=7) | Neonatal sepsis | | | |
|---|---|---|---|---|---|
| | | Early sepsis (n=15) | | Late sepsis (n=50) | |
| | | Initial examination | Repeated examination | Initial examination | Repeated examination |
| α-defensin (ng/mL) | 41.9±4.2 (25.8-58.4) | 716.7±53.3 (448.7-1033) | 336.7±31.6 (155.5-521.5) | 731.3±31.8 (397.2-1076) | 371.2±16.2 (189.4-655.8) |

Note: early sepsis was defined as disease onset during the first days of life; late sepsis was defined as later disease onset. Values are presented as mean±standard error and range.

Correlation analysis demonstrated that alpha-defensin had positive relationships with interleukin six at both examinations. At the first examination, the relationship was strong and statistically significant ($r=0.715$; $p<0.001$). During repeated examination, the correlation remained significant ($r=0.625$; $p<0.001$).

Alpha-defensin was also positively associated with interleukin eight. The correlation was statistically significant at the initial examination ($r=0.427$; $p<0.001$) and at repeated assessment ($r=0.395$; $p=0.001$). These findings show that alpha-defensin changes occur in parallel with cytokine activation and reflect the intensity of the inflammatory response.

In healthy newborns, the relationships between antimicrobial peptides and cytokines were weaker and reflected physiological immune interactions rather than generalized inflammation. A weak correlation was found between interleukin eight and the antimicrobial peptides analyzed. Endotoxin showed a significant positive association with interleukin six in healthy children ($r=0.499$; $p=0.015$), which may reflect coordinated low-level changes in innate immune parameters.

**Discussion.** The results of the study confirm that alpha-defensin increases markedly from the first days of neonatal sepsis and decreases during dynamic observation as the inflammatory process weakens. The degree of elevation was high both in term and preterm infants, which indicates that alpha-defensin is involved in the innate immune response regardless of gestational maturity.

The absence of a pronounced difference between early and late neonatal sepsis at the first examination suggests that alpha-defensin reflects the intensity of systemic inflammation rather than only the timing of disease onset. In preterm infants, high initial concentrations may be associated with pre-activation of fetal and neonatal innate immune cells under the influence of infectious and inflammatory factors during pregnancy and the perinatal period.

The positive correlations between alpha-defensin and interleukin six and interleukin eight are consistent with the known role of antimicrobial peptides as active participants in the inflammatory network. These correlations have practical importance because interleukin six and interleukin eight are considered early cytokine markers of infection, while alpha-defensin may additionally characterize neutrophil activation and the antimicrobial component of innate immunity [3, 5, 11].

The findings are also consistent with current data showing that no single biomarker can fully confirm or exclude neonatal sepsis. A combined approach that includes clinical assessment, microbiological testing, routine biochemical parameters, cytokines, and innate immune markers is more informative for early diagnosis and prognosis [4, 6, 13]. Therefore, alpha-defensin should be considered an additional marker rather than a replacement for established diagnostic approaches.

The study has limitations. The sample size was moderate, and the work was performed in a single specialized center. The timing of repeated examination was determined by clinical observation, which may introduce variability. Further multicenter studies with standardized sampling points and analysis of diagnostic thresholds are required before alpha-defensin can be recommended as a routine independent diagnostic test.

## Conclusions

1. Alpha-defensin levels were significantly higher in newborns with sepsis than in healthy newborns, both among term and preterm infants.

2. During repeated examination, alpha-defensin concentrations decreased, indicating a relationship between this marker and the dynamics of the inflammatory process.

3. Early and late neonatal sepsis in preterm infants were characterized by comparable initial elevations of alpha-defensin, which reflects the intensity of systemic inflammation.

4. Significant positive correlations between alpha-defensin and interleukin six and interleukin eight support the pathogenetic connection between antimicrobial peptide activation and cytokine response.

5. Alpha-defensin may be used as an additional laboratory criterion for assessing immune status, inflammatory activity, and the severity of neonatal sepsis when interpreted together with clinical and laboratory data.

*Prospects for further research. Further studies should include larger cohorts of term and preterm newborns, standardized sampling time points, analysis of diagnostic cut-off values, and assessment of alpha-defensin alongside cytokines, traditional inflammatory markers, blood culture results, and clinical outcomes. Such research may help determine the prognostic value of alpha-defensin and its potential role in neonatal sepsis diagnostic algorithms.*

## References

1. Agakidou E, Agakidis C, Kontou A, Chotas W, Sarafidis K. Antimicrobial peptides in early-life host defense, perinatal infections, and necrotizing enterocolitis. J Clin Med. 2022;11(17):5074. doi: 10.3390/jcm11175074.
2. Battersby AJ, Khara J, Wright VJ, Levy O, Kampmann B. Antimicrobial proteins and peptides in early life: ontogeny and translational opportunities. Front Immunol. 2016;7:309. doi: 10.3389/fimmu.2016.00309.
3. Boscarino G, Migliorino R, Carbone G, Davino G, Dell'Orto VG, Perrone S, et al. Biomarkers of neonatal sepsis: where we are and where we are going. Antibiotics (Basel). 2023;12(8):1233. doi: 10.3390/antibiotics12081233.
4. Gilfillan M, Bhandari V. Neonatal sepsis biomarkers: where are we now? Res Rep Neonatol. 2019;9:9-20. doi: 10.2147/RRN.S163082.
5. Gude SS, Peddi NC, Vuppalapati S, Gopal SV, Ramesh HM, Suryadevara N. Biomarkers of neonatal sepsis: from being mere numbers to becoming guiding diagnostics. Cureus. 2022;14(3):e23215. doi: 10.7759/cureus.23215.
6. Humberg A, Neuenburg L, Boeckel H, Fortmann MI, Härtel C, Herting E, et al. Antimicrobial skin peptides in premature infants: comparison with term infants and impact of perinatal factors. Front Immunol. 2023;14:1093340. doi: 10.3389/fimmu.2023.1093340.
7. Kerimova NT. Comparative characterization of alpha-defensins, endotoxins, and several biochemical parameters in early and late neonatal sepsis. Azerbaijan Journal of Physiology. 2024;39(1):51-58. doi: 10.59883/ajp.96.
8. Li X, Wei Y, Xu Z, Li T, Dong G, Liu X, et al. Lymphocyte-to-C-reactive protein ratio as an early sepsis biomarker for neonates with suspected sepsis. Mediators Inflamm. 2023;2023:9077787. doi: 10.1155/2023/9077787.
9. Ma J, Chen X, Wang X, Liang J, Guo L, Su Y, et al. The accuracy of soluble urokinase-type plasminogen activator receptor for the diagnosis of neonatal sepsis: a meta-analysis. Front Med (Lausanne). 2023;10:1169114. doi: 10.3389/fmed.2023.1169114.
10. Morad EA, Rabie RA, Almalky MA, Gebriel MG. Evaluation of procalcitonin, C-reactive protein, and interleukin-6 as early markers for diagnosis of neonatal sepsis. Int J Microbiol. 2020;2020:8889086. doi: 10.1155/2020/8889086.
11. Mubaraki MA, Faqihi A, AlQhtani F, Hafiz TA, Alalhareth A, Thagfan FA, et al. Blood biomarkers of neonatal sepsis with special emphasis on the monocyte distribution width value as an early sepsis index. Medicina (Kaunas). 2023;59(8):1425. doi: 10.3390/medicina59081425.
12. Mwesigye P, Rizwan F, Alassaf N, Khan R. The role and validity of diagnostic biomarkers in late-onset neonatal sepsis. Cureus. 2021;13(8):e17065. doi: 10.7759/cureus.17065.
13. Oncul U, Dalgıç N, Demir M, Karadeniz P, Karadağ ÇA. Use of procalcitonin as a biomarker for sepsis in pediatric burns. Eur J Pediatr. 2023;182(4):1561-1567. doi: 10.1007/s00431-023-04831-6.
14. Pariente N, on behalf of the PLOS Biology Staff Editors. The antimicrobial resistance crisis needs action now. PLoS Biol. 2022;20(11):e3001918. doi: 10.1371/journal.pbio.3001918.
15. Rallis D, Giapros V, Serbis A, Kosmeri C, Baltogianni M. Fighting Antimicrobial Resistance in Neonatal Intensive Care Units: Rational Use of Antibiotics in Neonatal Sepsis. Antibiotics (Basel). 2023 Mar 3;12(3):508. doi: 10.3390/antibiotics12030508.
16. Raymond SL, Stortz JA, Mira JC, Larson SD, Wynn JL, Moldawer LL. Immunological defects in neonatal sepsis and potential therapeutic approaches. Front Pediatr. 2017;5:14. doi: 10.3389/fped.2017.00014.

**Conflict of interest.** The authors have no conflicts of interest to declare.

**ORCID:** Polukhova A.E. https://orcid.org/0009-0005-5647-4840, Kerimova N.T. https://orcid.org/0000-0003-4549-4465.

Article received: 9.06.2025