

Comparative Assessment of Cytokine Pattern in Early and Late Onset of Neonatal Sepsis

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Abstract

© 2017 Kh. S. Khaertynov et al. Neonatal sepsis is a significant health issue associated with high mortality. Immune responses associated with neonatal sepsis, such as proinflammatory cytokine production, are believed to play a central role in the pathogenesis of this disease. In the present study, serum levels of the proinflammatory cytokines TNF- α , IL1- β , and IL-6 and the anti-inflammatory cytokines IL-4 and IL-10 were evaluated for 25 subjects with neonatal sepsis. We observed that subjects with late onset of sepsis (LOS), as well as those with early onset of sepsis (EOS), had a substantial increase in serum TNF- α . In contrast to EOS, subjects with LOS demonstrated a significant increase in serum levels IL-6 and IL-10. Additionally, we observed a significant difference in cytokine profiles between acute and postacute cases of neonatal sepsis. For instance, the level of proinflammatory cytokines, such as TNF- α and IL-6, was elevated in the acute phase, whereas the production of anti-inflammatory cytokines, such as IL-10, became substantially upregulated during the postacute phase. Additionally, no correlation was observed between cytokine levels and CRP levels or lymphocyte counts. Thus, in contrast to CRP levels and lymphocyte counts, examination of the cytokine profile can provide valuable information when determining the most effective therapy for treating neonatal sepsis. This information may be useful to physicians when determining if anti-inflammatory or immune stimulatory therapy is warranted.

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References

- [1] A. Camacho-Gonzalez, P. W. Spearman, and B. J. Stoll, "Neonatal infectious diseases: evaluation of neonatal sepsis," *Pediatric Clinics of North America*, vol. 60, no. 2, pp. 367-389, 2013.
- [2] J. L. Wynn and O. Levy, "Role of innate host defenses in susceptibility to early-onset neonatal sepsis," *Clinics in Perinatology*, vol. 37, no. 2, pp. 307-337, 2010.
- [3] R. Frost, H. Newsham, S. Parmar, and A. Gonzalez-Ruiz, "Impact of delayed antimicrobial therapy in septic ITU patients," *Critical Care*, vol. 14, supplement 2, p. P20, 2010.
- [4] K. Reinhart, M. Bauer, N. C. Riedemann, and C. S. Hartog, "New approaches to sepsis: molecular diagnostics and biomarkers," *Clinical Microbiology Reviews*, vol. 25, no. 4, pp. 609-634, 2012.
- [5] E. Torres-Martos, M. Pérez-Ruiz, I. Pedrosa-Corral et al., "Evaluation of the LightCycler SeptiFast test in newborns and infants with clinical suspicion of sepsis," *Enfermedades Infecciosas y Microbiología Clínica*, vol. 31, no. 6, pp. 375-379, 2013.
- [6] D. G. Remick, "Pathophysiology of sepsis," *American Journal of Pathology*, vol. 170, no. 5, pp. 1435-1444, 2007.
- [7] R. S. Hotchkiss and I. E. Karl, "The pathophysiology and treatment of sepsis," *New England Journal of Medicine*, vol. 348, no. 2, pp. 138-150, 2003.

- [8] B. G. Sood, S. Shankaran, R. L. Schelonka et al., "Cytokine profiles of preterm neonates with fungal and bacterial sepsis," *Pediatric Research*, vol. 72, no. 2, pp. 212-220, 2012.
- [9] R. A. Polin, L.-A. Papile, J. E. Baley et al., "Management of neonates with suspected or proven early-onset bacterial sepsis," *Pediatrics*, vol. 129, no. 5, pp. 1006-1015, 2012.
- [10] E. Kocabaş, A. Sarikçioğlu, N. Aksaray, G. Seydaoğlu, Y. Seyhun, and A. Yaman, "Role of procalcitonin, C-reactive protein, interleukin-6, interleukin-8 and tumor necrosis factor-alpha in the diagnosis of neonatal sepsis," *Turkish Journal of Pediatrics*, vol. 49, no. 1, pp. 7-20, 2007.
- [11] A. Leviton, T. M. O'Shea, F. J. Bednarek, E. N. Allred, R. N. Fichorova, and O. Dammann, "Systemic responses of preterm newborns with presumed or documented bacteraemia," *Acta Paediatrica, International Journal of Paediatrics*, vol. 101, no. 4, pp. 355-359, 2012.
- [12] A. Prashant, P. Vishwanath, P. Kulkarni et al., "Comparative assessment of cytokines and other inflammatory markers for the early diagnosis of neonatal sepsis-a case control study," *PLoS ONE*, vol. 8, no. 7, Article ID e68426, 2013.
- [13] European Medicines Agency, Report on the Expert Meeting on Neonatal and Paediatric Sepsis, EMA, London, UK, 2010, http://www.ema.europa.eu/docs/en_GB/document_library/Report/2010/12/WC500100199.pdf.
- [14] G. Klinger, I. Levy, L. Sirota, V. Boyko, B. Reichman, and L. Lerner-Geva, "Epidemiology and risk factors for early onset sepsis among very-low-birthweight infants," *American Journal of Obstetrics and Gynecology*, vol. 201, no. 1, pp. 38.e1-38.e6, 2009.
- [15] M. Cohen-Wolkowicz, C. Moran, D. K. Benjamin et al., "Early and late onset sepsis in late preterm infants," *Pediatric Infectious Disease Journal*, vol. 28, no. 12, pp. 1052-1056, 2009.
- [16] B. Clyne and J. S. Olshaker, "The C-reactive protein," *Journal of Emergency Medicine*, vol. 17, no. 6, pp. 1019-1025, 1999.
- [17] R. S. Hotchkiss, G. Monneret, and D. Payen, "Immunosuppression in sepsis: a novel understanding of the disorder and a new therapeutic approach," *The Lancet Infectious Diseases*, vol. 13, no. 3, pp. 260-268, 2013.
- [18] J. Reis Machado, D. F. Soave, M. V. Da Silva et al., "Neonatal sepsis and inflammatory mediators," *Mediators of Inflammation*, vol. 2014, Article ID 269681, 10 pages, 2014.
- [19] V. Bhandari, "Effective biomarkers for diagnosis of neonatal sepsis," *Journal of the Pediatric Infectious Diseases Society*, vol. 3, no. 3, pp. 234-245, 2014.
- [20] B. Shouman and R. Badr, "Regulated on activation, normal T cell expressed and secreted and tumor necrosis factor- in septic neonates," *Journal of Perinatology*, vol. 30, no. 3, pp. 192-196, 2010.
- [21] J. Bender, J. Thaarup, K. Varming, H. Krarup, S. Ellermann-Eriksen, and F. Ebbesen, "Early and late markers for the detection of early-onset neonatal sepsis," *Danish Medical Bulletin*, vol. 55, no. 4, pp. 219-223, 2008.
- [22] S. S. Oguz, E. Sipahi, and U. Dilmen, "C-reactive protein and interleukin-6 responses for differentiating fungal and bacterial aetiology in late-onset neonatal sepsis," *Mycoses*, vol. 54, no. 3, pp. 212-216, 2011.
- [23] J. M. Melville and T. J. M. Moss, "The immune consequences of preterm birth," *Frontiers in Neuroscience*, vol. 7, article no. 79, 2013.
- [24] P. Tissières, A. Ochoda, I. Dunn-Siegrist et al., "Innate immune deficiency of extremely premature neonates can be reversed by interferon-," *PLoS ONE*, vol. 7, no. 3, Article ID e32863, 2012.
- [25] A. G. Cuenca, J. L. Wynn, L. L. Moldawer, and O. Levy, "Role of innate immunity in neonatal infection," *American Journal of Perinatology*, vol. 30, no. 2, pp. 105-112, 2013.
- [26] P. Jabandziev, M. Smerek, J. Michalek Sr. et al., "Multiple gene-gene interactions in children with sepsis: a combination of five gene variants predicts outcome of life-threatening sepsis," *Critical Care*, vol. 18, no. 1, article no. R1, 2014.
- [27] A.-Q. Zhang, W. Pan, J.-W. Gao et al., "Associations between interleukin-1 gene polymorphisms and sepsis risk: a meta-analysis," *BMC Medical Genetics*, vol. 15, no. 1, article 8, 2014.
- [28] A. A. H. Zeitoun, S. S. Gad, F. M. Attia, A. S. Abu Maziad, and E. F. Bell, "Evaluation of neutrophilic CD64, interleukin 10 and procalcitonin as diagnostic markers of early- and late-onset neonatal sepsis," *Scandinavian Journal of Infectious Diseases*, vol. 42, no. 4, pp. 299-305, 2010.
- [29] J. Perloth, B. Choi, and B. Spellberg, "Nosocomial fungal infections: epidemiology, diagnosis, and treatment," *Medical Mycology*, vol. 45, no. 4, pp. 321-346, 2007.
- [30] Z.-Q. Wang, A. S. Bapat, R. J. Rayanade, A. S. Dagtas, and M. K. Hoffmann, "Interleukin-10 induces macrophage apoptosis and expression of CD16 (FcγRIII) whose engagement blocks the cell death programme and facilitates differentiation," *Immunology*, vol. 102, no. 3, pp. 331-337, 2001.
- [31] L. A. Bouton, C. D. Ramirez, D. P. Bailey et al., "Costimulation with interleukin-4 and interleukin-10 induces mast cell apoptosis and cell-cycle arrest: the role of p53 and the mitochondrion," *Experimental Hematology*, vol. 32, no. 12, pp. 1137-1145, 2004.
- [32] D. C. Angus and T. van der Poll, "Severe sepsis and septic shock," *The New England Journal of Medicine*, vol. 369, no. 21, pp. 840-851, 2013.