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Neonatal Sepsis: Emerging Pathogens and Evolving Treatment Protocols

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Introduction

Neonatal sepsis remains a major global health concern, contributing significantly to neonatal morbidity and mortality, particularly in low- and middle-income countries. Defined as a clinical syndrome characterized by systemic signs of infection in the first 28 days of life, neonatal sepsis can be classified into Early-Onset Sepsis (EOS), occurring within the first 72 hours, and Late-Onset Sepsis (LOS), occurring after 72 hours of birth. While traditional pathogens like Group B Streptococcus (GBS) and Escherichia coli (E. coli) have been well-studied in the context of neonatal sepsis, there has been a disturbing rise in the prevalence of non-traditional and Multi-Drug Resistant (MDR) organisms. At the same time, the diagnostic challenges and changing patterns of antibiotic susceptibility have necessitated continual evolution in treatment protocols. This article explores the emerging pathogens in neonatal sepsis, discusses the shifting epidemiology, and examines the latest strategies in diagnosis, antimicrobial stewardship, and individualized therapeutic approaches [1].

Description

Neonatal sepsis can present subtly, with non-specific signs such as temperature instability, lethargy, poor feeding, respiratory distress, and apnea. These signs overlap with many other neonatal conditions, which complicates timely diagnosis. Traditional laboratory markers such as white blood cell count, C-Reactive Protein (CRP), and procalcitonin, though helpful, are limited by their lack of specificity and delayed kinetics. Recent interest has focused on novel biomarkers, including interleukins, presepsin, and molecular diagnostics such as Polymerase Chain Reaction (PCR)-based assays, which promise earlier and more accurate detection. The microbiological profile of neonatal sepsis has evolved in recent decades. In high-income countries, EOS is most commonly associated with GBS and E. coli, both typically acquired vertically from the maternal genital tract. The widespread implementation of Intrapartum Antibiotic Prophylaxis (IAP) has led to a reduction in GBS-related EOS, but it may also have contributed to the emergence of other gram-negative and resistant pathogens. Conversely, in low- and middle-income countries, Klebsiella pneumoniae, Acinetobacter baumannii, and other nosocomial pathogens dominate, reflecting differences in healthcare infrastructure, hygiene practices, and antibiotic stewardship [2].

Late-onset sepsis, particularly in preterm and low-birth-weight infants, is predominantly associated with organisms acquired postnatally, often through invasive procedures or environmental exposure in neonatal intensive care units (NICUs). Coagulase-Negative Staphylococci (CoNS), Staphylococcus aureus, Candida species, and gram-negative bacilli including Pseudomonas and Enterobacter are common. Alarmingly, many of these pathogens exhibit multidrug resistance, complicating therapeutic choices. Methicillin-Resistant Staphylococcus Aureus (MRSA), Extended-Spectrum β-Lactamase (ESBL) producing Enterobacteriaceae, and carbapenem-resistant Acinetobacter are increasingly reported, necessitating the use of second- and third-line antibiotics with higher toxicity profiles. One of the most pressing issues in the management of neonatal sepsis is the emergence of MDR organisms. In many settings, empirical antibiotic regimens that previously offered effective coverage are no longer sufficient. The empirical use of broad-spectrum antibiotics such as third-generation cephalosporins and carbapenems has driven resistance, creating a vicious cycle of treatment failure and increased mortality. The World Health Organization (WHO) and other bodies have emphasized the importance of antimicrobial stewardship to preserve the efficacy of existing antibiotics and reduce the selection pressure for resistant strains.

Treatment of neonatal sepsis typically begins with empirical antibiotic therapy, tailored to the likely pathogens and local resistance patterns. In EOS, a combination of ampicillin and gentamicin remains the standard initial regimen in many countries. For LOS, vancomycin plus an aminoglycoside or a broad-spectrum β-lactam such as cefotaxime or meropenem may be used, depending on institutional protocols and suspected organisms. De-escalation of therapy based on culture results and sensitivity patterns is critical to reducing unnecessary antibiotic exposure. Adjunctive therapies are also being explored to improve outcomes in neonatal sepsis. Intravenous immunoglobulins (IVIG), colony-stimulating factors, and lactoferrin have been studied for their potential to enhance neonatal immune responses, but current evidence does not support their routine use. The role of probiotics in preventing sepsis, particularly necrotizing enterocolitis-related infections in preterm infants, is promising, with some studies suggesting reduced sepsis rates with the use of specific probiotic strains.

Conclusion

Neonatal sepsis continues to be a formidable challenge in neonatology, made more complex by emerging pathogens and rising antimicrobial resistance. The evolving microbiological landscape necessitates constant vigilance and adaptation of treatment protocols. Empirical antibiotic regimens must be guided by local epidemiology and adjusted based on culture results to minimize resistance development. Advances in diagnostic tools, preventive strategies, and antimicrobial stewardship programs are critical for improving outcomes. In the face of limited new antibiotic options, a multi-pronged approach including infection prevention, maternal care, rapid diagnostics, and rational antibiotic use is essential to reduce the global burden of neonatal sepsis and safeguard neonatal survival in both high- and low-resource settings.

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Conflict of Interest

None.

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