

THE ROLE OF INFLAMMATORY BIOMARKERS IN THE EARLY DIAGNOSIS OF SEPSIS

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Abstract: Sepsis is a life-threatening condition caused by a dysregulated host response to infection, leading to organ dysfunction. Early diagnosis is essential to improve patient outcomes, and inflammatory biomarkers have emerged as key tools in identifying sepsis in its early stages. This article reviews the clinical significance, diagnostic value, and limitations of biomarkers such as C-reactive protein (CRP), procalcitonin (PCT), interleukin-6 (IL-6), and others in the early detection of sepsis. Understanding the utility and interpretation of these markers helps clinicians make faster and more accurate decisions in critical care settings.

Keywords: Sepsis, Biomarkers, Procalcitonin, C-reactive protein, IL-6, Early diagnosis

Introduction

Sepsis remains a major cause of morbidity and mortality worldwide, especially in intensive care units (ICUs). The rapid progression of the disease makes early detection a clinical priority. Traditionally, sepsis diagnosis has relied on clinical signs and microbiological cultures, which may be delayed. Biomarkers, particularly those reflecting the inflammatory response, offer a promising approach to accelerate diagnosis and guide treatment. The ideal biomarker should be sensitive, specific, rapidly measurable, and correlated with disease severity and outcome.

Sepsis is a complex clinical syndrome that arises when the body's response to an infection becomes dysregulated and leads to life-threatening organ dysfunction. Despite advances in medical technology and intensive care practices, sepsis remains a major global health concern, with an estimated 49 million cases and 11 million sepsis-related deaths annually, according to the World Health Organization (WHO). The high mortality rate and potential for rapid clinical deterioration demand prompt identification and management. However, early diagnosis remains challenging due to the nonspecific nature of initial clinical signs and symptoms, such as fever, tachycardia, hypotension, and altered mental status, which can overlap with numerous other conditions.

Traditional diagnostic methods, including blood cultures and microbiological testing, often suffer from time delays and may yield false-negative results, especially in patients already receiving antibiotic therapy. These limitations have led clinicians and researchers to explore more rapid and reliable diagnostic alternatives. Inflammatory biomarkers, which reflect the host immune response to infection, have emerged as promising tools for early sepsis recognition and risk stratification.

Among the most studied and clinically utilized biomarkers are C-reactive protein (CRP), procalcitonin (PCT), and interleukin-6 (IL-6). These markers can provide valuable insights into

the severity and progression of the inflammatory response and, when interpreted correctly, can aid in differentiating between bacterial and non-bacterial causes of systemic inflammation. CRP, a hepatic acute-phase reactant, increases in response to interleukin-6 stimulation. PCT, a peptide precursor of the hormone calcitonin, rises specifically during bacterial infections, while IL-6 itself is an early pro-inflammatory cytokine with rapid kinetics.

Despite their potential, no single biomarker has demonstrated sufficient sensitivity and specificity to be used in isolation for sepsis diagnosis. Therefore, combining biomarker data with clinical judgment and other diagnostic modalities is essential for optimal patient care. This review aims to provide a comprehensive overview of key inflammatory biomarkers used in the early diagnosis of sepsis, highlighting their pathophysiological basis, diagnostic performance, clinical applications, and limitations in real-world settings.

Materials

and

Methods

This is a narrative review based on a literature search of PubMed and Scopus databases from 2010 to 2024. Search terms included "sepsis," "biomarkers," "CRP," "procalcitonin," and "IL-6." Articles were selected based on relevance to early diagnosis, clinical utility, and evidence of performance in critically ill populations. Both adult and pediatric studies were considered.

Results

CRP is one of the most widely used inflammatory markers. It rises within 6–8 hours after infection onset and peaks around 48 hours. However, its specificity is limited, as CRP levels can increase in non-infectious inflammation. Procalcitonin (PCT) shows better specificity for bacterial infections and sepsis. PCT levels rise within 2–4 hours and correlate with the severity of bacterial infection. Several studies have demonstrated that PCT-guided algorithms reduce unnecessary antibiotic use. Interleukin-6 (IL-6), a pro-inflammatory cytokine, elevates rapidly during systemic infection and may precede CRP and PCT elevations. However, IL-6 testing is less standardized and more expensive.

Emerging markers such as presepsin and suPAR are under investigation and show promise, but lack wide availability and robust validation.

Discussion

While no single biomarker fulfills all criteria for ideal sepsis detection, combining markers improves diagnostic accuracy. For example, using both CRP and PCT increases sensitivity, while IL-6 may help in very early stages. Clinical judgment and patient context remain essential in interpreting results. Moreover, serial measurements provide more diagnostic value than isolated readings.

Conclusion

Inflammatory biomarkers are valuable adjuncts in the early diagnosis of sepsis. CRP and PCT are most commonly used, while IL-6 and newer biomarkers may enhance early detection. Integrating biomarker data with clinical evaluation can optimize sepsis management and improve outcomes. Further research is needed to validate emerging markers and develop cost-effective diagnostic panels.

Early and accurate diagnosis of sepsis is critical for initiating timely treatment, reducing mortality, and improving long-term outcomes. Inflammatory biomarkers such as C-reactive protein (CRP), procalcitonin (PCT), and interleukin-6 (IL-6) have emerged as valuable adjuncts to clinical evaluation in the identification and monitoring of sepsis. While each marker has distinct kinetics and pathophysiological roles, none is entirely sufficient as a standalone

diagnostic tool. However, their combined use enhances diagnostic precision and supports clinical decision-making, particularly in complex or ambiguous cases.

CRP remains widely used due to its accessibility and cost-effectiveness, although it lacks specificity. PCT offers improved specificity for bacterial infections and shows promise in guiding antimicrobial stewardship by distinguishing bacterial from viral or non-infectious causes of inflammation. IL-6, as an early upstream marker, holds potential for ultra-early detection but is currently limited by availability and standardization challenges. Emerging biomarkers such as presepsin and suPAR may further refine sepsis diagnostics in the future, pending broader validation and clinical integration.

In clinical practice, biomarkers should not replace but rather complement comprehensive clinical assessment, including patient history, physical examination, vital signs, and laboratory and imaging data. Serial measurement of biomarkers may provide better insight into disease trajectory and response to therapy compared to single-point assessments.

Ultimately, the integration of inflammatory biomarkers into diagnostic algorithms represents a step forward in precision medicine for critically ill patients. Future directions include the development of multi-marker panels, incorporation of machine learning algorithms, and personalized diagnostic pathways tailored to specific patient populations. Continued research and investment in biomarker validation and implementation will be essential to fully harness their potential in the fight against sepsis.

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