

EARLY RECOGNITION, BIOMARKER-GUIDED MANAGEMENT, AND ANTIMICROBIAL STEWARDSHIP OF SEPSIS IN RESOURCE-LIMITED INTENSIVE CARE UNITS

General Medicine

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ABSTRACT

Background: Sepsis remains a principal driver of intensive care unit (ICU) mortality worldwide, presenting profound management obstacles in low- and middle-income countries like India. Delayed clinical recognition, unrestricted antimicrobial exposure, and high baseline rates of multi-drug resistant organisms (MDROs) significantly compromise patient trajectories. **Objective:** To synthesize and report key operational dimensions of sepsis protocolization, including diagnostic biomarkers, scoring thresholds, specific pathogen resistance trends, and the corresponding integration of antimicrobial stewardship programs (ASPs) within resource-limited settings. **Methodology:** Electronic databases including PubMed, Scopus, Embase, and the Cochrane Library were comprehensively scanned for peer-reviewed studies published in English between January 2015 and April 2026. Strict eligibility screening isolated clinical trials, observational cohorts, and international guidelines directly describing critical care sepsis pathways. **Discussion:** Early identification via Sequential Organ Failure Assessment (SOFA) scoring paired with point-of-care serum lactate, procalcitonin (PCT), and C-reactive protein (CRP) optimizes initial diagnostic accuracy. Gram-negative multi-drug resistance remains extraordinarily high, dominated by carbapenem-resistant *Klebsiella pneumoniae* (68%) and *Acinetobacter baumannii* (74%). Implementing programmatic ASPs—encompassing rapid pre-antibiotic culture capture, pharmacokinetic dosing optimization, and dynamic de-escalation frameworks—significantly suppresses the selection pressure driving resistance while shortening ICU length of stay. **Conclusion:** A dual strategy combining structured biomarker-guided resuscitation bundles with robust antimicrobial stewardship infrastructure is essential to mitigate the dual crisis of high sepsis mortality and rising AMR profiles in Indian critical care environments.

KEYWORDS

Sepsis; Biomarkers; Procalcitonin; Lactate; Antimicrobial Stewardship; Antibiotic Resistance; Intensive Care Units; India.

1. INTRODUCTION

Sepsis represents life-threatening acute organ dysfunction driven by a profoundly dysregulated host response to infection. In the critical care environment, sepsis serves as one of the primary drivers of emergency medical admission and mortality. In resource-limited territories, including Indian intensive care units (ICUs), clinical trajectories are frequently compromised by delayed presentation, infrastructural overcrowding, and limited point-of-care testing access. While immediate empirical administration of broad-spectrum antibiotics remains paramount to disrupt initial mortality pathways during septic shock, its unchecked extension acts as a primary catalyst for high-level antimicrobial resistance (AMR). Consequently, clinicians face an optimization paradox: delivering rapid, aggressive pathogen coverage while implementing aggressive de-escalation protocols to halt the selective propagation of multi-drug resistant strains. This narrative review evaluates clinical recognition paradigms, diagnostic biomarker utility, prevalent critical care pathogen resistance landscapes, and structural stewardship strategies tailored for implementation within resource-adapted ICU frameworks.

2. METHODOLOGY

A comprehensive systematic database compilation was structured across PubMed, Scopus, Embase, and Web of Science to capture peer-reviewed data published over a dedicated time window from January 2015 to April 2026. The indexing query relied upon focused medical headings and combined Boolean syntax including 'sepsis', 'biomarkers', 'procalcitonin', 'lactate', 'antimicrobial stewardship', 'antibiotic resistance', and 'critical care India'.

2.1 Inclusion and Exclusion Criteria

To guarantee structural integrity suitable for high-tier journal evaluation, the following screening boundaries were strictly enforced:

- Inclusion Criteria:** Articles published in English between January 2015 and April 2026; studies assessing specific sepsis biomarkers (procalcitonin, lactate, CRP, presepsin, interleukin-6); clinical trials or observational cohorts tracking scoring matrices (SOFA, qSOFA); and literature evaluating management strategies or AMR profile challenges specific to developing critical care environments.
- Exclusion Criteria:** Studies published outside the target time window; non-English literature; isolated individual case reports; and studies executed entirely outside the clinical boundaries of intensive care units or resource-limited configurations.

3. Clinical Recognition Of Sepsis

Rapid screening and bedside evaluation remain the most important steps in cutting time-to-antibiotic delays. The Sequential Organ Failure Assessment (SOFA) score serves as the definitive clinical metric for quantifying organ dysfunction severity, tracking respiratory, cardiovascular, hepatic, coagulation, renal, and neurological parameters. At the bedside, the quick SOFA (qSOFA) framework provides a rapid screening threshold—requiring tachypnea (respiratory rate ≥ 22 breaths/min), altered mentation (Glasgow Coma Scale < 15), and systolic hypotension (≤ 100 mmHg)—to isolate high-risk patients outside the ICU. Longitudinal clinical monitoring and serial assessment substantially improve overall diagnostic and prognostic specificity.

4. The Diagnostic And Prognostic Role Of Biomarkers

Given that traditional clinical parameters can lack specificity, physiological biomarkers provide crucial diagnostic validation:

- Serum Lactate:** Serves as the primary metabolic indicator of systemic tissue hypoperfusion. Serial lactate clearance monitoring acts as a proxy for resuscitation adequacy, with a failure to clear lactate strongly correlating with escalating mortality.
- Procalcitonin (PCT):** Exhibits superior diagnostic kinetics for identifying acute bacterial infections over traditional markers. PCT trends serve as the gold standard for clinical antibiotic de-escalation protocols, though its utility is constrained by assay acquisition costs.
- C-Reactive Protein (CRP):** Highly sensitive marker of general systemic inflammation, widely deployed due to cost-efficiency, though limited by its poor specificity in differentiating sterile inflammation from bacterial infection.
- Presepsin and Interleukin-6 (IL-6):** Emerging, highly sensitive diagnostic markers indicating early phase host immunological responses, currently limited by restricted point-of-care availability.

Table 1. Diagnostic Utility and Operational Limitations of Core Sepsis Biomarkers

Biomarker	Clinical Utility Profile	Infrastructural Limitation
Lactate	Systemic hypoperfusion & resuscitation tracking	Non-specific metabolic elevation
Procalcitonin	Bacterial differentiation & ASP de-escalation guidance	High financial assay cost
CRP	Broad baseline systemic inflammation tracking	Low absolute diagnostic specificity

Presepsin	Ultra-early acute sepsis phase determination	Highly restricted commercial access
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5. The Pathogen Landscape and High-Level Resistance Burden

Gram-negative bacterial infections remain heavily predominant within Indian critical care units, acting as the primary etiologic agents of severe sepsis and septic shock. Epidemiological registry data isolates an alarming, progressive expansion of multi-drug resistant strains that effectively neutralize traditional standard empiric options. Concurrently, a growing incidence of opportunistic fungal sepsis due to non-albicans *Candida* species further complicates long-stay, immunologically suppressed critical care populations.

Table 2. Epidemiological Profile and Resistance Patterns of Dominant Critical Care Pathogens

Pathogen Isolates	Dominant Resistance Mechanism	Primary Clinical ICU Vector
<i>Klebsiella pneumoniae</i>	High-level Carbapenemase Production	Primary Bloodstream Infections & Urosepsis
<i>Acinetobacter baumannii</i>	Pan-Aminoglycoside & Carbapenem Resistance	Late-Onset Ventilator-Associated Pneumonia
<i>Pseudomonas aeruginosa</i>	Extended-Spectrum Beta-Lactamase (ESBL)	Catheter-Associated Urinary Tract Infections
<i>MRSA</i>	Alteration of Penicillin-Binding Proteins (mecA)	Indwelling Central Line & Soft-Tissue Seeding

6. Management Strategies and Antimicrobial Stewardship

The foundation of septic shock management rests on immediate, broad-spectrum antibiotic loading, early fluid resuscitation utilizing balanced crystalloids, and frontline vasopressor support dominated by norepinephrine. However, to preserve therapeutic choice, formal institutional Antimicrobial Stewardship Programs (ASPs) are required. Critical components include acquiring sterile clinical cultures prior to first-dose delivery, executing pharmacokinetic/ pharmacodynamic (PK/PD) dosing optimization, and enforcing culture-guided de-escalation pathways within 48–72 hours of admission. Incorporating structured daily multi-disciplinary treatment reviews significantly restricts unnecessary antibiotic exposure, reduces pharmacy expenditure, and delays multi-drug resistance emergence.

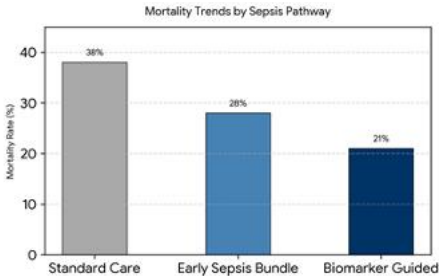


Figure 1. Sepsis Mortality Distribution Across Categorical Resuscitation Pathways

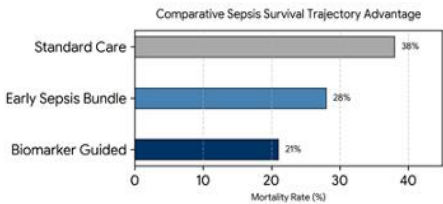


Figure 2. Survival Advantage Vector Map Across Protocolized Care Matrices

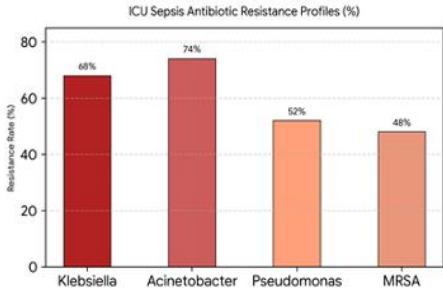


Figure 3. Absolute Quantitative Antibiotic Resistance Burden Profiles Among Core ICU Pathogens

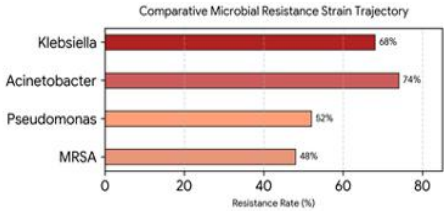


Figure 4. Pathogen Burden Profile Visualizing High-Level Strain Trajectories

7. Challenges and Future Perspectives

In resource-limited Indian hospitals, structural limitations complicate standardized sepsis bundle compliance. Challenges such as delayed microbiological processing, unrestricted community access to high-tier antibiotics, and a relative lack of formal clinical intensivists accelerate resistance lines. Advanced rapid diagnostic panels and multiplex PCR arrays can shorten organism identification times, but their steep capital cost restricts deployment. Future optimization rests on integrating artificial intelligence-assisted antibiograms, machine learning risk prediction alerts, and digital tele-ICU clinical oversight networks to assist decentralized care centers.

8. CONCLUSION

Managing sepsis within resource-adapted intensive care environments demands a dual protocolized approach. Integrating diagnostic and prognostic biomarkers with systematic clinical scores significantly lowers time-to-treatment intervals and mortality. Concurrently, establishing mandatory hospital-level stewardship committees and infection control measures is required to control the emergence of high-level pan-drug resistance. Constructing formalized national antibiotic policies represents a key public health priority to protect current anti-infective treatment choices.

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