

Editorial

Sepsis - Definition and Classification in Indian Setting: An Update

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INTRODUCTION

Sepsis is a critical global health concern, claiming millions of lives annually and placing a significant burden on healthcare systems worldwide. Despite advancements in medical science, diagnosing and managing sepsis remains challenging, particularly in resource-limited settings. Recognized as a global health priority by the World Health Organization (WHO) in 2017, sepsis demands urgent attention and innovative approaches to improve patient outcomes.¹

The origin of the term sepsis dates to more than 2700 years ago when the Greek word “sepo” was used by the physician Hippocrates, meaning “I rot”, for description of a process of internal decay, believed to happen to unlucky individuals.² Over time, its understanding and definition has changed to its latest definition, as “life-threatening organ dysfunction caused by a dysregulated host response to infection”, as per the latest surviving sepsis campaign: International guidelines for management of sepsis and septic shock, 2021 (Sepsis-3).³

In 1992, convention of experts formalized the universal definition of sepsis, and it was identified as “an inflammatory process triggered by infection”, and was clinically diagnosed based on the presence of two or more signs of SIRS together with evidence or suspicion of an infection.^{4,5} This was widely utilized for more than two decades despite facing criticism, the major one being that the SIRS criteria frequently reflected an appropriate physiological response to infection rather

than indicating a pathological condition. The SIRS criteria—including fever, tachycardia, hypotension, and leukocytosis—highlight the inflammatory response, a hallmark of various critical conditions such as trauma, pancreatitis, and postsurgical inflammation⁶

Because inflammation is a natural and often beneficial response to infection, defining sepsis presents the challenge of differentiating between a normal immune reaction and the severe, dysregulated inflammatory response seen in life-threatening sepsis⁷

The 2016 Sepsis Task Force defined sepsis as a life-threatening state of organ dysfunction triggered by a dysregulated response of the host to infection³ Clinically, sepsis is identified by an acute rise of two or more points in the SOFA score in the context of suspected infection^{3,8} There are various available scoring systems such as SOFA, NEWS, APACHE, LODS, etc., which predict the prognosis in terms of morbidity and mortality related to sepsis, however, they can't diagnose sepsis with accuracy. More than 250 biomarkers have been identified and studied in the context of sepsis, but only procalcitonin (PCT) and c-reactive protein (CRP) have some use. None of the biomarkers lack the sensitivity and specificity for the diagnosis of sepsis.

As part of broader antimicrobial stewardship efforts, sepsis definition and/or its classification for the right diagnosis enables the rational use of antimicrobials, thus playing a significant role in combating antimicrobial resistance (AMR), especially by reducing

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the misuse of antimicrobials. However, the whole world is looking for it, especially in terms of classification, including India.

SEPSIS UPDATE FROM INDIAN SETTING

Due to these shortcomings in the latest definition/classification of sepsis and the absence of any gold standard test to diagnose sepsis, a recent longitudinal observational study was conducted at All India Institute of Medical Sciences (AIIMS) Rishikesh, a tertiary care and teaching centre in the North of India, spanning over 12 months.⁹ This study formulated and utilized a new three-step method developed for classifying sepsis, whose flowchart and other details are depicted in Figure 1 and Table 1. NEWS-2 score, being relatively much easier to use with parameters not requiring laboratory investigations, was used to find evidence of dysregulated host response, however, no specific modifications or adaptations were done, used in its original form, for this study.

Figure 1: 3-Step Model for sepsis classification.

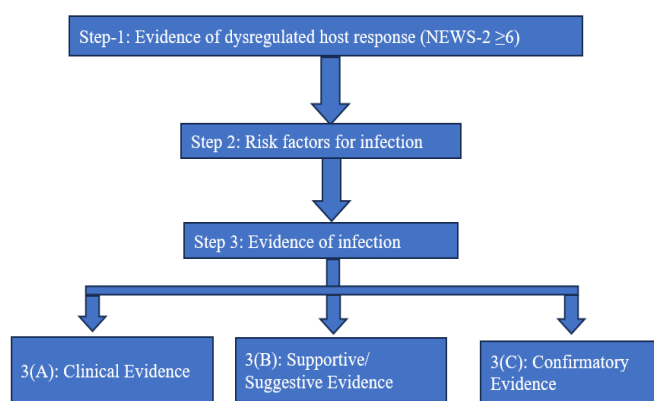


Table 1: Proposed criteria for Sepsis Classification.

Steps	Description
Step 1: Evidence of Dysregulated Host Response	Assessed using the National Early Warning Score-2 (NEWS-2) ≥ 6
Step 2: Risk Factors for Infection	Evaluated based on the presence of risk factors such as chronic illnesses, malnutrition, unhygienic living conditions, immunosuppressive states, age, trauma, structural diseases, recent surgery, travel history, animal bites, and previous hospitalizations
Step 3: Evidence of Infection	Determined through:
3(A) Clinical Evidence	Syndromic diagnosis including pyelonephritis, infective endocarditis, intra-abdominal infections, skin and soft tissue infections, meningitis, cerebrospinal fluid shunt infections, catheter-related infections, osteomyelitis, abscesses, and pneumonia

3(B) Supportive/Suggestive Evidence	Imaging (X-ray, ultrasound, computed tomography, magnetic resonance imaging, positron emission tomography) and biomarkers (blood, urine, other fluids)
3(C) Confirmatory Evidence	Direct visualization, endoscopic evidence, microscopy and culture growth, polymerase chain reaction/gene detection, and immunological methods

Proposed criteria to classify sepsis:	
Interpretation	Sepsis Class
(i) Step-1 = negative (ii) Step-1 &/or 2 = positive with step-3 = negative	Asepsis
Step-1, 2 & 3(a) = positive	Possible sepsis
Step-1, 2 & 3(b) = positive	Probable sepsis
Step-1, 2 & 3(c) = positive	Confirmed sepsis

This study included 230 patients as per inclusion criteria from screened 1867 patients who were on antimicrobials and were categorized into various sepsis categories (asepsis, possible, probable, and confirmed sepsis as per model) on various days during hospital stay (Day-1, 7, 14 and outcome) demonstrating the dynamic nature of sepsis. The study showed a significant finding that throughout the hospital stay, the sepsis category was changed from the initial majority of the probable sepsis group to the final majority of the asepsis group; similar trends were also observed in other groups.

One of the most significant findings from this study is that one can classify sepsis into asepsis, possible, probable, and confirmed sepsis from day zero of admission into the hospital based on available evidence, and with time, it can reclassify the same as evidence emerges. Many scoring and classification systems, simple and complex, are available for sepsis globally; however, they do not incorporate any aspects of sepsis for diagnosis, such as risk factors, clinical scenarios, and the dynamic nature of sepsis, making their use limited for sepsis diagnosis, therefore, used for majorly for prognostication and mortality assessment.¹⁰ Hence, they are not true sepsis classification systems. The various available scores for sepsis are majorly of prognostic significance rather than providing primary diagnostic importance, and this lacuna can be fulfilled with the utilization of this 3-step novel approach, which primarily focuses on the diagnostic part of sepsis followed by its management strategies. Deaths due to AMR is rising and will rise further to devastating levels if not controlled, as recently predicted in a global database.¹¹ This is the right time to classify sepsis first; then, only data on AMR mortality in sepsis can be predicted correctly.

CONCLUSIONS

This study explores challenges in sepsis diagnosis and ways to overcome them, emphasizing a structured approach, particularly in the resource-limiting settings. The three-step approach, when integrated with the NEWS-2 score, provides a useful and pragmatic framework for early and accurate identification. It highlights sepsis classification as a dynamic process, calling for further research to refine diagnostic criteria and develop tools to distinguish sepsis from similar conditions. Enhancing the early detection of sepsis can greatly decrease morbidity and mortality, supporting the WHO's global health objectives. The 3-step model effectively classifies sepsis into asepsis, possible, probable, and confirmed cases. Multi-centric validation studies can confirm its accuracy, with organisations like SASPI potentially leading India in this effort. With careful implementation, this approach could transform sepsis management in resource-limited settings, reducing antimicrobial misuse and combating AMR.

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CONFLICTS OF INTEREST STATEMENT

The authors declare no conflict of interest

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ETHICS STATEMENT INCLUDING PATIENT CONSENT

Not applicable

AUTHOR'S CONTRIBUTIONS

Both authors qualified for authorship as per ICMJ criteria. They approved the manuscript.

AI DECLARATION

No AI tool was used to generate research data, perform data analysis, interpret findings, formulate scientific conclusions, or make editorial decisions. All AI-assisted content was critically reviewed, verified, and revised by the authors. The authors take full responsibility for the accuracy, originality, integrity, and final content of the manuscript.

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