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COMMENTARY

Rethinking Pediatric Sepsis and Septic Shock: Beyond International Consensus Criteria

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Purpose/Objective: International pediatric sepsis consensus definitions play a critical role in evidence-based clinical practice, providing standardized tools for case identification. However, a common misconception is treating sepsis as a static diagnosis rather than recognizing it as a dynamic and evolving process. It is essential to integrate consensus criteria into a broader, more flexible clinical approach rather than applying them rigidly.

Materials/Methods – Literature Review: This expert commentary compares past and current pediatric sepsis definitions, analyzing their clinical implications, supporting evidence, and feasibility across diverse healthcare settings.

Findings/Results: The transition from a Systemic Inflammatory Response Syndrome-based model (2005 International Pediatric Sepsis Consensus Conference) to an organ dysfunction-based model (Phoenix Sepsis Score 2024) has improved specificity but may also delay early recognition by requiring established organ dysfunction.

Conclusion and Recommendations: Sepsis should be viewed as a continuum rather than a static state. This commentary does not oppose sepsis consensus criteria but advocates for clinicians to apply clinical judgment beyond them. Future definitions should balance specificity with early recognition while allowing for clinical adaptability in various healthcare contexts.

Keywords: sepsis, septic shock, pediatric, criteria, organ dysfunction

Background

Severe infection-related systemic syndromes have been recognized as leading causes of morbidity and mortality in children globally since the early 1900s. Over the last three decades, experts have worked to develop standardized definitions to individualize these complex conditions into well-defined clinical syndromes, such as sepsis, septic shock, and multiple organ dysfunction syndrome (MODS).[1–3] The primary goal of international consensus criteria is to facilitate the early identification of pediatric sepsis through scoring systems that are internationally validated and applicable across various settings. Developing such definition criteria is inherently challenging, requiring a balance between simplification and accuracy. Over the years, initial criteria have undergone revisions, and their definitions continue to evolve.[2–5] For a long time, the criteria for diagnosing sepsis and septic shock in children relied on the standards set by the first International Pediatric Sepsis Consensus Conference (IPSCC) in 2005, which were based on Systemic Inflammatory Response Syndrome (SIRS) criteria.[5] In 2016, the Third International Consensus Conference for Sepsis and Septic Shock (Sepsis-3) updated the definition of sepsis specifically for adult patients, characterizing it as a life-threatening organ dysfunction resulting from a dysregulated host response to infection. This definition relies on the Sequential Organ Failure Assessment (SOFA) score to evaluate the severity of organ dysfunction.[4] Similarly, the Pediatric SOFA (pSOFA) was developed and tested for validation in children. However, the sensitivity and positive predictive value of pediatric organ dysfunction scores remain unclear, as sepsis in children differs significantly from adult sepsis, including age-specific variability in vital signs, age-dependent immune function, and differences in pediatric-specific comorbidities, epidemiology, and outcomes.[6] Furthermore, both SOFA and pSOFA were primarily validated in emergency and intensive care settings, not across the full hospital continuum, and lack applicability in lower-resource settings.[2–4,6] In

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January 2024, the Society of Critical Care Medicine (SCCM) released the updated International Consensus Criteria for Pediatric Sepsis and Septic Shock, known as the Phoenix Sepsis criteria.[2,3] Developed by a multidisciplinary task force, these criteria aim to improve the diagnosis and treatment of pediatric sepsis with simplified definitions based on diverse global data, including from low-resource settings.[2,3] While recognizing the importance of international consensus criteria in case definition and early intervention, it is equally essential to avoid oversimplification or diagnostic shortcuts. This article highlights the imperative to consider sepsis and septic shock as progressive conditions during a serious infection, requiring a holistic and in-depth diagnostic approach beyond criteria and scores.

Current Definition of Pediatric Sepsis and Septic Shock

The Phoenix criteria for diagnosing sepsis and septic shock in children were developed and validated by the international SCCM Pediatric Sepsis Definition Task Force. This process employed a comprehensive approach, including analysis of a large international database, a survey, a systematic review with meta-analysis, and a modified Delphi consensus method. The findings were published online in The Journal of the American Medical Association (JAMA) on January 21, 2024: https://jamanetwork.com/journals/jama/fullarticle/2814297. The new International Consensus Criteria for Pediatric Sepsis consider four organ dysfunction criteria: respiratory, cardiovascular, coagulation, and neurological.[2,3] The Phoenix Sepsis Score comprehensively assesses various dysfunctions associated with pediatric sepsis. Sepsis in children is diagnosed when there is suspicion or confirmation of infection, along with a Phoenix Sepsis Score of at least 2 points.[3] Septic shock, on the other hand, is defined by the presence of at least one cardiovascular dysfunction criterion from the Phoenix Sepsis Score. The Phoenix criteria for diagnosing sepsis apply to individuals under 18 years of age, excluding neonates with a postconceptional age of less than 37 weeks.[3] Firstly, respiratory dysfunction is evaluated through the assessment of oxygenation parameters and the required respiratory support. Key measures of oxygenation, such as the Arterial oxygen tension to Fraction of inspired oxygen ratio (PaO2:FiO2 ratio) and/or the Peripheral oxygen saturation to Fraction of inspired oxygen ratio (SpO2:FiO2 ratio), are considered in the Phoenix score.[3] Secondly, the Phoenix score examines cardiovascular dysfunction by assessing the need for vasoactive medications, measuring Serum Lactate levels, and monitoring Mean Arterial Pressure (MAP).[3] Thirdly, hematological dysfunction evaluation focuses on coagulation impairment, involving assessments of platelet count, International Normalized Ratio (INR), D-dimer levels, and fibrinogen levels within the Phoenix criteria.[3] Lastly, neurological dysfunction assessment includes clinical evaluations of consciousness levels using the Glasgow Coma Scale and pupil examinations.[3]

Discussion: Challenges and Critical Insights on New Phoenix Sepsis Score

Complexities of Organ Dysfunction in Critically Ill Children

Organ dysfunction is a hallmark of critically ill patients, with the majority of children requiring intensive care exhibiting single or multiple organ dysfunctions. The pathophysiology of organ dysfunction in pediatric patients is very complex. It can involve a single organ or present as multiple organ dysfunction syndrome (MODS), stemming from infectious or non-infectious causes.[1,7] For instance, conditions such as acute poisoning, diabetic ketoacidosis, hypertensive emergencies, anaphylaxis, trauma, autoimmune diseases, or parasitic infections like malaria can cause acute single or multiple-organ dysfunction.[1] Clinical assessment tools for organ dysfunction are not solely exclusive to diagnosing sepsis or septic shock. Parameters of respiratory dysfunction, for instance, were utilized before the advent of the Phoenix score in assessing Pediatric Acute Respiratory Distress Syndrome (PARDS), as defined by the criteria established in the First and Second Pediatric Acute Lung Injury Consensus Conference (PALICC-1 and PALICC-2).[8,9] Similarly, cardiovascular, hematological (including coagulation), and neurological dysfunction have been evaluated in contemporary scoring tools for organ dysfunction prognosis or predicting mortality, such as the SOFA, pSOFA, or the Pediatric Organ Dysfunction Information Update Mandate (PODIUM).[1,4,6,7] Sepsis should be understood as a pathological evolution of severe infection that can culminate in septic shock, organ dysfunction, or death.[4] Severe infections can prompt various associated complications at the primary site of infection, in addition to systemic, remote sepsis-induced dysfunction in other organs. For example, a severe lung infection like bacterial pneumonia can lead to distant organ dysfunction, even septic shock, but can also result in local complications such as massive parapneumonic effusion, compromising

respiratory function and necessitating specific interventions. Identifying both these complications rapidly and accurately is pivotal for patient outcomes.A comprehensive diagnostic approach that extends beyond sepsis identification to include evaluation for potential complications and comorbidities is essential. In such instances, relying solely on infection-directed therapy may not suffice, and timely intervention for the specific complication (such as thoracic drainage of the parapneumonic effusion) is crucial for preserving the patient's life. Furthermore, the selection of only four organ dysfunction domains in the final version of the Phoenix Score (cardiovascular, respiratory, coagulation, and neurological) is based on their predictive value for mortality, not necessarily their causal role in sepsis progression.[3] This omission raises several challenges, such as the exclusion of renal and hepatic dysfunction in the score. While renal dysfunction is a well-documented consequence of sepsis and a strong independent predictor of mortality, acute kidney injury (AKI) is often underrecognized in early sepsis, yet its presence significantly alters fluid resuscitation strategies and drug dosing. Hepatic dysfunction in sepsis can alter drug metabolism, coagulopathy, and immune response, but it is also not included in the Phoenix model. A septic child with hepatic impairment may not meet the criteria for sepsis despite having a critically altered physiologic state. The exclusion of these organ systems is not based on a lack of clinical relevance but rather on model parsimony, raising concerns about the trade-off between statistical efficiency and real-world accuracy.

Shift From SIRS to Organ Dysfunction: A Double-Edged Sword

One of the major advancements of the Phoenix Sepsis Score is its higher specificity compared to the old SIRS-based IPSCC 2005 criteria.[3,5] The previous SIRS-based model often resulted in false positives, as many conditions (eg, viral infections, trauma, burns) triggered systemic inflammation without true sepsis. By requiring organ dysfunction for sepsis diagnosis, the new Sepsis Criteria (Phoenix Score) ensures that only truly severe cases are classified as sepsis, which aligns with the original intent of the term "life-threatening condition", reducing unnecessary treatments such as antibiotics and fluid overload from aggressive resuscitation.[3] While higher specificity reduces false positives, it also means that some children at high risk of deterioration, yet who may not meet the organ dysfunction thresholds defined by the Phoenix Score, may not be diagnosed until they have developed full-blown organ failure.[2,3] This delay in diagnosis can hinder early interventions and actually increase mortality or long-term morbidity in some patients. Sepsis should not be defined only at the point of organ failure; it is a progressive syndrome, and early recognition remains critical. Another important improvement in the Phoenix Sepsis Score is its effort to increase feasibility across different clinical settings, including low-resource environments. The Phoenix Score was designed with feasibility in mind and has alternative markers for certain dysfunctions that can be assessed even in low-resource hospitals.[2,3] This makes it more applicable than previous organ dysfunction scores (eg, SOFA), which heavily relied on advanced laboratory markers. For instance, the main respiratory dysfunction parameter, the PaO2/FiO2 ratio (arterial oxygen tension/fraction of inspired oxygen), recognizes that arterial blood gas (ABG) testing is not widely available in low-resource settings. The Phoenix Criteria allow for an alternative parameter: SpO2/FiO2 (peripheral oxygen saturation/fraction of inspired oxygen ratio). This adaptation improves accessibility and ensures that hospitals without ABG testing can still apply the criteria using pulse oximetry.[2,3] However, other key organ dysfunction criteria in the Phoenix Score still require laboratory-based parameters that many hospitals in low-resource settings may not have access to. For example, coagulation dysfunction requires D-dimer and INR measurements, which are not routinely available in many settings. Similarly, cardiovascular dysfunction criteria require lactate measurements, which may not be available in smaller hospitals.

Risks of Strict Reliance and Anchoring

While the Phoenix Sepsis Criteria represent an advancement in harmonizing the definition of pediatric sepsis and septic shock, their adoption raises critical questions about clinical applicability, specificity, and unintended consequences.[2,3] Sepsis is not a binary state (a simple "yes or no" condition) but rather a dynamic and complex syndrome with significant heterogeneity. Scoring systems, including the Phoenix Sepsis Criteria, define sepsis based on thresholds of organ dysfunction, but these thresholds may not fully capture early-stage sepsis or differentiate sepsis from other critical conditions. Rigid application of these criteria may lead to underdiagnosis (if the patient does not meet all the defined criteria) or overdiagnosis (if the criteria misclassify other critical illnesses as sepsis). A fundamental concern is the reliance on statistical modeling rather than pathophysiological insight. By focusing primarily on predefined organ

dysfunction scores, clinicians may become anchored to these criteria, leading to cognitive bias in decision-making. In a real-world example, a child with severe dengue, plasma leakage, and circulatory collapse could meet the Phoenix Sepsis Criteria for septic shock, yet the pathophysiology is distinct from bacterial sepsis. If misclassified, the child might receive broad-spectrum antibiotics and unnecessary septic shock management, diverting attention from specific dengue-targeted interventions. Similarly, a critically ill child with a metabolic crisis, trauma, or anaphylaxis may develop organ dysfunction that fulfills the Phoenix criteria but would not benefit from a sepsis-centered approach.[3] This highlights a critical paradox: while the Phoenix Criteria aim for better precision, they risk forcing heterogeneous syndromes into a single framework, potentially delaying appropriate intervention for non-sepsis critical illnesses. On the other hand, the Phoenix Score was developed to predict mortality, but sepsis recognition should prioritize early pathophysiological changes rather than just predicting death.[3] In its current form, the Phoenix Criteria may fail to detect early-stage sepsis in children who have emerging but not yet severe organ dysfunction.[3] The Phoenix Sepsis Score should be seen as a tool, not a definitive diagnostic endpoint. Clinicians must actively question whether strict adherence to criteria enhances or constrains clinical decision-making. Sepsis management requires an integration of pathophysiological insight rather than rigid mortality prediction models. Sepsis should always be recognized as a dynamic syndrome, where organ dysfunction evolves over time rather than presenting as a static threshold event. There is also an important need to consider flexible, setting-specific modifications, particularly in resource-limited environments. Ultimately, sepsis is not just a scoring problem; it is a clinical syndrome requiring contextualized, adaptive decision-making. While the Phoenix Criteria provide structure, they should not substitute for critical reasoning, pattern recognition, and individualized patient assessment.

Conclusion

Sepsis is not merely a condition to be identified at the point of organ dysfunction; it is a dynamic, evolving process that requires proactive recognition and intervention. A comprehensive approach ensures that underlying causes and broader clinical factors are not overlooked. Clinicians must integrate sepsis criteria with clinical judgment to improve patient outcomes. Sepsis identification should prompt an in-depth evaluation of the primary infection, organ dysfunctions, and comorbidities, rather than being treated as an endpoint. There is an urgent need to develop models beyond mortality prediction, incorporating a multi-stage sepsis recognition framework that integrates risk assessment and organ dysfunction scoring for earlier diagnosis and optimized interventions. Future pediatric sepsis definitions must balance specificity with early recognition and ensure flexibility across diverse healthcare settings. While achieving an adaptable international consensus remains challenging, it is essential for shifting sepsis care from late-stage diagnosis toward proactive, preventive strategies.

Perspectives and Recommendations

Sepsis research should shift toward early detection models based on pathophysiology, rather than focusing solely on refining organ dysfunction-based definitions. A Pre-Sepsis Risk Score should be developed to identify high-risk children before organ dysfunction occurs, integrating immune dysregulation, endothelial dysfunction, and metabolic markers, rather than relying solely on mortality-based models.

Abbreviations

FEU, fibrinogen equivalent units; FiO2, fraction of inspired oxygen; GCS, Glasgow Coma Scale; IMV, Invasive Mechanical Ventilation; INR, International Normalized Ratio; IPSCC, International Pediatric Sepsis Consensus Conference; MAP, Mean Arterial Pressure; PALICC-1, First Pediatric Acute Lung Injury Consensus Conference; PALICC-2, Second Pediatric Acute Lung Injury Consensus Conference; PaO2, Arterial oxygen tension; PaO2:FIO2, arterial partial pressure of oxygen to fraction of inspired oxygen ratio; PARDS, Pediatric Acute Respiratory Distress Syndrome; pSOFA, Pediatric Sequential Organ Failure Assessment; SCCM, Society of Critical Care Medicine; SIRS, Systemic Inflammatory Response Syndrome; SOFA, Sequential Organ Failure Assessment; SpO2, Peripheral oxygen saturation measured by pulse oximetry; SpO2:FiO2, Peripheral oxygen saturation to the fraction of inspired oxygen ratio.

Data Sharing Statement

All data generated and material supporting the conclusion of this review are included in the article.

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