Early Sepsis Recognition in Pediatrics: A Literature Review

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Abstract

Despite advances in prevention and treatment, sepsis remains to be one of the leading causes of child mortality worldwide. Inability to notice the transition from a local infectious inflammatory condition to a generalized one delays the initiation of diagnosis and treatment. The sooner therapy is initiated, the greater the patient's chances of survival. The purpose of this study is to go over current diagnostic and treatment guidelines for sepsis and septic shock in children and to discusses the current definitions, epidemiology, and strategies for detecting pediatric sepsis early.

Keywords: Sepsis; Pediatric; Recognition

1. Introduction

Sepsis and its classification are life-threatening conditions with high morbidity and mortality rates, so that in 2020, the World Health Organization officially stated that sepsis cases are included in the main causes of maternal and infant morbidity and mortality [1,2]. Sepsis is an organ dysfunction that can threaten a human's life and is typically brought on by a severe infection. Septic shock is defined as sepsis accompanied by cardio-vascular dysfunction that continues to manifest despite the administration of fluid resuscitation [3,4]. It is a subtype of sepsis characterized by significant circulatory, cellular, and metabolic abnormalities with a higher mortality risk [2]. Respiratory, urinary tract, and skin infections are the most common causes of sepsis. Sepsis is caused by a variety of etiological agents, which might include bacterial, viral, mycoplasma, and fungal infections, either alone or in combination [5].

The concept of pediatric sepsis is continually evolving, and there is a significant disparity between the research and clinical definitions of sepsis, which affects the implementation of research findings to clinical practice. It often results in differences in understanding among doctors which results in the frequent occurrence of underdiagnosed/over diagnosed sepsis in patients treated. In fact, sepsis has a tendency to cause conditions to quickly change to life-threatening conditions [6]. In spite of this, early diagnosis and implementation of current treatment guidelines have been found to enhance patient outcomes [7–9]. On the other hand, there is a relatively low level of compliance with treatment guidelines at the moment, and it has been shown that enhanced care and outcomes can be achieved only through the implementation of protocols [8].

2. Epidemiology

Globally, sepsis is the leading cause of child morbidity, mortality, and healthcare utilization [3]. There are an estimated 22 cases of children sepsis per 100,000 person-years and 2,202 cases of neonatal sepsis per 100,000 live births worldwide, resulting in an annual incidence of 1.2 million cases of childhood sepsis [10]. Sepsis

affects more than 4% of all hospitalized children under the age of 18 and 8% of patients treated to PICUs in high-income nations [3,11]. Children with sepsis have a mortality rate ranging from 4% to 50%, depending on the severity of the illness, risk factors, and demographic [12–14]. The majority of children who die from sepsis have refractory shock and/or multiple organ dysfunction syndrome, and many die within 48 to 72 hours of undergoing treatment [15]. Early recognition, resuscitation, and care are thus important to improving outcomes for children with sepsis.

3. Pathophysiology

The progression of sepsis is a complex interaction between bacteria that cause infections and immunological responses from the host. The innate immune cells activate, which are constituted mostly of macrophages, monocytes, neutrophils, and natural killer (NK) cells, is the initial stage in the start of a host immunological response to a pathogen. This activates intracellular signal transduction pathways, resulting in the transcription and release of proinflammatory cytokines, including various proinflammatory interleukins (ILs), such as IL-1, IL-12, IL-18, tumor necrosis factor alpha (TNF-), and interferon (IFN), as well as clinical symptoms [16]. This further activates cytokines complement and coagulation pathways and, via negative feedback, downregulates adaptive immune system components [17]. The progression of clinical symptoms in sepsis is frequently linked to the detection of elevated levels of these cells, which is in turn correlated with increased spontaneous production and release of neutrophil extracellular traps (NETs) [18]. NETs are loose structures outside of cells that are made of decondensed chromatin, granular proteins, and nuclei that can stop pathogens from moving. The increased number of NETs, which can be caused by too much production or insufficient degradation, has been referred to hypercoagulability and endothelial damage, both of which are closely linked to organ dysfunction [19].

4. Diagnostic Approach

In all health-care settings, early diagnosis of sepsis is crucial. Because the vast majority of sepsis patients occur in the community, the first point of contact with health workers in primary care, ambulance services, or the emergency department (ED) is crucial for detecting sepsis early [20,21]. Early detection in non-acute and prehospital situations has been linked to faster treatment and better outcomes [20]. The clinician must undertake a comprehensive anamnesis and physical examination to decide if the patient has sepsis risk factors [22]. Table 1 lists signs and symptoms that require clinical concern for sepsis [23]:

Table 1. Warning signs and symptoms for sepsis

Warning signs and symptoms for sepsis	
Fever > 38°C	Hypothermia
Tachypnea	Apnea
Difficulty in breathing / respiratory distress	Cyanotic / mottled skin / ashen appearance
Tachycardia	Bradycardia
Abnormal capillary refill time (> 3 seconds)	Reduced urine output
Weak pulses	Non-blanching rash
Altered mental status (irritability, inappropriate crying, confused)	Abnormal drowsiness (difficult to arouse, lethargic or obtunded)

White Blood Cell (WBC) count and differential, C-reactive protein (CRP), and procalcitonin (PCT) are non-specific indicators of an ongoing inflammatory response that are used to diagnose sepsis. No test is sensitive or specific enough to diagnose sepsis, and there is no evidence that they can reliably identify sepsis [21,24].

Despite the lack of prospective pediatric sepsis research and ongoing issues with diagnostic criteria, it has been shown that early recognition and provision of medication (within one hour) are the most crucial aspects of sepsis management [6–9,25]. While timely diagnosis is essential, it can be challenging. To minimize delays in recognizing severe sepsis and septic shock, each pediatric institution should develop multidisciplinary protocols/guidelines to promote early identification and treatment. The main components of the introductory bundle recommended by the Pediatric Surviving Sepsis Campaign International Guidelines 2020 include [3]:

4.1. Systematic Screening for Identification

A septic shock identification or trigger tool should be implemented in health facilities/institutions that should consist of clinical diagnoses and findings (eg, high-risk conditions, vital signs, and/or physical findings) that prompt further evaluation. The tool's algorithms are trained to conduct difficult tasks on vast amounts of data to anticipate unfavorable outcomes, rather than using rule-based criteria like SIRS, the pediatric sequential organ failure assessment, or the pediatric early warning score. Those allow incorporation of vital sign changes, which are more sensitive in identifying changes in a patient's clinical status than absolute readings, especially in patients with abnormal baseline vital signs or laboratory data [2,26]. An example of a sepsis trigger tool designed incorporating vital sign thresholds used in the Pediatric Advanced Life Support is provided [27–29]. Each institution should base their vital sign triggers on their best interpretation of the evidence and what will be most functional in their system [3,26].

4.2. Rapid Clinical Assessment

Once the sepsis trigger tool suggests that a patient may have severe condition of sepsis/septic shock, all clinicians involved should evaluate the patient within 15 minutes to confirm septic shock, integrate further monitoring, and decide the most appropriate resuscitation plan [29].

4.3. Rapid initiation of resuscitation

Resuscitation should be initiated within 15 minutes of confirming of septic shock. Within the first few hours of care, goal-targeted therapy for septic shock refers to an intensive, methodical strategy to resuscitation aimed at increasing physiologic indications of perfusion and vital organ function [3,29]. Essential actions included:

- Identification of septic shock
- Vascular access and rapid fluid resuscitation
- Empiric antimicrobial therapy
- Initiation of vasoactive agents to patients not responding sufficiently to fluid resuscitation

5. Conclusion

Sepsis in pediatrics continues to have a significant global impact. The definition of sepsis that evolving will ease the implementation of new research findings into clinical practice. The treatment of sepsis begins with an accurate and early recognition; best practice alerts and the application of guidelines have frequently showed a reduction in the time to the first intervention. Integration of a trigger tool into the real-world clinical setting is just as crucial. Combining technological learning with human factors principles leading to a better diagnostic of sepsis with early recognition to improves patient outcomes.

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