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Review Article

Strategies for early identification and management of sepsis in children

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ABSTRACT

Pediatric sepsis continues to be a major public health concern, leading to considerable morbidity and mortality despite progress in medical treatments. This review explores methods for the prompt detection and management of sepsis in children, highlighting the importance of early recognition and intervention. Diagnosing sepsis in children is difficult because of its non-specific symptoms and the diverse ways it presents in different age groups. Key strategies include enhancing parental education, improving pre-hospital recognition by emergency medical services (EMS), and leveraging the pivotal role of nurses in emergency settings. Effective management involves prompt administration of antimicrobials, appropriate use of vasoactive agents, and comprehensive post-sepsis care to improve long-term outcomes. Advanced diagnostic tools and rapid, reliable biomarkers are crucial for early detection. Additionally, antimicrobial stewardship programs and public health campaigns play a vital role in reducing sepsis incidence. By focusing on these strategies, healthcare providers can significantly improve the early identification and management of sepsis in children, enhancing survival rates and long-term quality of life for pediatric sepsis survivors.

Keywords: Pediatric sepsis, Early identification, Management, Antimicrobial therapy, Vasoactive agents

INTRODUCTION

Sepsis is a clinical condition arising from an abnormal host response to severe infection. Pediatric sepsis remains a major public health challenge and a leading cause of morbidity and mortality despite the adoption of standardized treatment protocols, widespread immunization efforts, and advanced intensive care support technologies.[1] Severe sepsis represents over 8% of all admissions to pediatric intensive care units (PICUs) and results in more than 4.5 million childhood deaths worldwide each year.[2-4] The incidence of sepsis throughout life is significantly age-dependent, with the highest rates found in preterm neonates, followed by neonates, infants, and children.[5] Although the epidemiology is often divided into neonatal and pediatric age groups, the justification for the traditional 1-month-of-age cut-off is weak. Sepsis in very preterm neonates exposed to various iatrogenic risks differs significantly from vertically transmitted early-onset sepsis in a term newborn, pneumococcal sepsis in a young

infant, hospital-acquired sepsis in a neutropenic child, or staphylococcal toxic shock in an adolescent. Accurate disease characterization remains challenging, even though the sepsis-3 concept of suspected or confirmed infection with organ dysfunction is theoretically applicable to both pediatric and neonatal populations.[6]

While inflammation is a crucial component of the host's response to infection, dysregulation of this process can initiate a cascade of events leading to significant tissue damage, disturbances in the immune system and microcirculation, and symptoms of systemic inflammatory response syndrome (SIRS).This unchecked and self-perpetuating intravascular inflammation can lead to end-organ dysfunction in areas far from the initial infection, quickly advancing to septic shock and multiple organ failure.[1] If not treated promptly, death may result from refractory shock, which accounts for one-third of fatalities within the first 72 hours, or from multiple organ dysfunction syndrome (MODS), with respiratory and neurological failures being the primary causes of death.[7] Identifying sepsis in children is difficult due to the widespread occurrence of common febrile infections, the lack of specific distinguishing features, and the capacity of children's physiology to compensate until the shock has progressed to an advanced stage.[2]

The outcomes of sepsis in children are influenced by the speed of recognition and treatment. Global initiatives and guidelines stress the importance of early detection and diagnosis, coupled with prompt and effective management. This includes the immediate administration of empiric antimicrobials and the early escalation of care.[2,8] While these measures have been demonstrated to decrease mortality, the rates of death in high-income settings have not improved.[3]

METHODS

This study is based on a comprehensive literature search conducted on 23 July 2024, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed strategies for early identification and management of sepsis in children. There were no restrictions on date, language, participant age, or type of publication.

DISCUSSION

Sepsis in children arises from a range of causative organisms and factors, including age, underlying health conditions, and infection sources. Neonates commonly suffer from pathogens like group B *Streptococci* and *Herpes simplex virus*, while young children frequently experience sepsis from *Haemophilus influenzae* type b and *Streptococcus pneumoniae*. Vaccinations have reduced mortality from these bacteria. Risk factors such as immunocompromised states, indwelling devices, and chronic illnesses heighten susceptibility to sepsis from less typical organisms and fungi. Viral causes, including influenza, and COVID-19, are significant, alongside endemic infections like malaria and dengue. Accurate diagnosis requires considering these diverse factors.[9]

Neonatal sepsis presents with nonspecific symptoms like irritability and poor feeding (Table 1).[10]

Table 1: Summarizing the clinical manifestations of sepsis in neonates and children.[10]

Aspect	Description
Early symptoms in neonates	Irritability, lethargy, poor feeding
Alternative presentation	Hypothermia (instead of fever), normal physical examination possible
High-risk factors	Prematurity, maternal history of positive group B *Streptococcus* status, chorioamnioniti, prolonged rupture of membranes
Hemodynamic response in children	Lower cardiac reserve, profound hypovolemia, low cardiac output, elevated systemic vascular resistance (cold shock)
Late signs	Hypotension (may appear late in the progression of sepsis)

Early diagnosis

Traditionally, sepsis diagnosis and treatment have been limited to emergency departments (EDs) or hospital settings. However, increasing awareness of the benefits of early recognition and prompt treatment for pediatric sepsis has highlighted the importance of parental involvement in patient diagnosis.[11]

Recognition of sepsis by parents

Sepsis is commonly acquired in the community, but the role of parents—who are the primary observers of their child's condition in recognizing it remains insufficiently studied.[12] A recent Australian survey revealed that only 14% of the population could identify a sign of sepsis, despite the increased morbidity and mortality associated with delayed hospital presentations. Parents' observations, such as changes in their child's mental status or behavior, can provide valuable insights for clinicians. Currently, parental concern is included as a trigger in several institutional sepsis recognition tools.[11]

Recognition of sepsis in the pre-hospital environment

Most sepsis research focuses on recognition and treatment initiation upon hospital presentation.[11] However, over 50%

of deaths from community-acquired pediatric sepsis occur within the first two days of hospital admission, underscoring the need for early recognition and prompt presentation to healthcare facilities.[13] Recognition by emergency medical services (EMS) in the pre-hospital phase is crucial for improving outcomes.[11]

The recognition of pediatric sepsis by EMS presents unique challenges due to differing physiological parameters compared to adults. For instance, hypotension, a late sign of sepsis in adults, may not be present in pediatric cases, making it an unreliable indicator for initiating treatment.[13]

Role of nurses

The role of nurses in early sepsis recognition, particularly in EDs, is crucial and based on surviving sepsis campaign (SSC) guidelines.[14] Nurses are often the first to assess patients with sepsis.[11] A 2019 qualitative study highlighted the importance of nurses in sepsis identification, revealing organizational and knowledge gaps and suggesting the need for context-specific education.[15] Implementing nurse-led sepsis pathways can address these gaps by expediting recognition and treatment. Consistent education and empowerment across institutions are essential for reliable sepsis management.[11]

Management

Antimicrobial therapy

Early and prompt administration of antibiotics is crucial for improving outcomes in patients with sepsis and septic shock.[16] It is widely recommended that broad-spectrum antibiotics be administered within one hour of diagnosis.[2] The selection of empiric broad-spectrum antimicrobials should be based on local epidemiology and resistance patterns. Considerations include the infection source, presence of indwelling devices or catheters, immunocompromised status, recent hospital admissions, and known colonization with specific pathogens.[9] Adhering to local antimicrobial policies and established protocols, such as those from the National Institute for Health and Care Excellence (NICE) guidelines and the surviving sepsis campaign (SSC), is crucial for effective management (Table 2).[2,9]

Microbiological samples, including blood, urine, sputum, and cerebrospinal fluid (CSF), should be collected before initiating antibiotics. However, diagnostic testing should not delay the start of antibiotic therapy. A lumbar puncture should be avoided if there are concerns about hemodynamic instability, elevated intracranial pressure, abnormal coagulation, or infection at the puncture site. Once clinically appropriate, interventions to achieve source control must be promptly carried out.[2] This includes removing infected indwelling devices, draining abscesses, debriding necrotizing soft tissue, and draining septic joints or empyemas. Antimicrobial stewardship is vital in sepsis management, involving the de-escalation of antibiotics when appropriate to minimize toxicity and prevent prolonged use. The discontinuation of antimicrobials should be considered if a non-infectious etiology is identified, and therapy should be narrowed based on microbiological data.[17] Clinical decisions should be guided by improvements in the patient's condition, the infection site, source control, and pathogen identification with sensitivity results. Consulting with infectious disease specialists for complex cases is recommended to ensure optimal management.

Table 2: Antimicrobial therapy guidance based on NICE and SSC recommendations.[9]

Variables	Therapy
Neonates presenting within the first 72 hours	Benzylpenicillin and gentamicin
Children <3 months	Ampicillin/amoxicillin (against listeria) and third generation cephalosporin
Community acquired sepsis	Ceftriaxone
Meningococcal disease suspected	Ceftriaxone
MRSA or ceftriaxone resistant pneumococci	Vancomycin and third generation cephalosporin
Toxic shock syndrome/ necrotising fasciitis	Third generation cephalosporin and clindamycin and consider IVIG
Elevated risk resistant gram-negative infection	Piperacillin-tazobactam and gentamicin
Immunocompromised patient	Meropenem OR IV piperacillin-tazobactam
Abdominal source suspected	Metronidazole to be added along with a third generation cephalosporin
Febrile neutropenia	Piperacillin-tazobactam

IVIG: Intravenous immunoglobulin; MRSA: methicillin-resistant *Staphylococcus aureus.*

Vasoactive agents

For children who remain in shock despite receiving 40–60 ml/kg of fluid resuscitation within the first hour, initiating vasoactive medications is essential.[2] They may continue to receive fluid boluses along with vasoactive agents. If shock persists, intubation and ventilation may be required, with non-invasive positive pressure ventilation as an option depending on the clinical situation and available resources.

Dopamine, once a first-line drug, is now largely replaced by epinephrine and norepinephrine due to their better safety profiles and efficacy.[9] Both agents offer vasopressor and inotropic effects, making them preferred for septic shock management. Vasoactive agents can be administered peripherally if central access is delayed. Epinephrine is officially approved for peripheral administration, while

norepinephrine may be used peripherally in certain situations. Central venous access should be established as soon as possible.[2,18] The choice between epinephrine and norepinephrine depends on clinical judgment, local protocols, and specific physiological considerations. Epinephrine is used for low cardiac output shock, while norepinephrine is preferred for vasodilatory shock with decreased systemic vascular resistance. Vasoactive agents should be carefully adjusted to achieve a mean arterial pressure (MAP) within the 5th to 50th percentile for the child's age, while also maintaining adequate urine output and peripheral perfusion. In cases of catecholamine-resistant shock, vasopressin-receptor agonists such as vasopressin or terlipressin may be considered. For low cardiac output, inodilators like milrinone can be used. These advanced treatments are typically administered in an intensive care unit with sophisticated hemodynamic monitoring.[9]

Corticosteroids

Children at increased risk for adrenal insufficiency, such as those with a history of chronic or recent steroid treatment or congenital adrenal insufficiency, should receive stress-dose hydrocortisone early.[19,20]

Vascular access and fluid therapy

Hypovolemia in sepsis is caused by capillary leak, vasodilation, and fluid loss, making fluid resuscitation crucial. Immediate vascular access is essential, preferably with two wide-bore peripheral venous cannulas. If venous access is not achieved within 5 minutes, intraosseous access should be obtained. Essential tests include blood gas analysis, a full blood count, a clotting screen, and renal and liver function tests. For children without cardiovascular compromise, maintenance fluid therapy should be started.[21] In cases of shock, administer fluid boluses of 10–20 ml/kg while closely monitoring heart rate, capillary refill, blood pressure, urine output, and lactate levels. In advanced care settings, fluid boluses can be increased up to 60 ml/kg within the first hour.[21,22] Lower-resource settings should limit to 40 ml/kg. Balanced crystalloid solutions are preferred over high-chloride crystalloids due to lower risks of complications.[23,24] Colloid solutions are not recommended for routine use due to cost and increased risks.[9]

Respiratory support

Children with sepsis should receive supplemental oxygen unless their oxygen saturation is >95% on room air. Non-invasive positive pressure ventilation may be used to reduce breathing effort and improve oxygenation.[25] Mechanical ventilation is necessary for acute respiratory failure, persistent shock, or hypoxemia. Rapid sequence induction and intubation by an experienced clinician are recommended, avoiding agents like propofol that may exacerbate shock. Use lung-protective ventilation with minimal tidal volumes, high positive end-expiratory pressure (PEEP), and minimal inspired oxygen. Nitric oxide may be considered for severe pulmonary hypertension or right ventricular dysfunction.[9]

Metabolites and electrolytes

Children with sepsis frequently display electrolyte imbalances such as hypoglycemia, hypocalcemia, hypokalemia, and hypomagnesemia. Regular monitoring and correction of plasma electrolytes are crucial. Hypoglycemia should be addressed with rapid intravenous dextrose infusion, and routine insulin use for tight glucose control is not advised unless hyperglycemia is linked to clinical compromise.[2,26] Hypocalcemia should be corrected to maintain ionized calcium levels above 1 mmol/l, while hypomagnesemia should be managed cautiously to prevent exacerbating hypotension.[9]

Blood transfusion

Children in shock who do not respond to fluid resuscitation and vasoactive agents may benefit from a packed red blood cell transfusion if their hemoglobin level is below 7 g/dl.[27] Disseminated intravascular coagulopathy may require transfusion of platelets, fresh frozen plasma, or cryoprecipitate to manage significant bleeding. Prophylactic transfusions are not recommended, but platelet transfusion is advised for exceptionally low platelet counts (<20,000/mm^3) due to a heightened risk of bleeding.[2]

Post-sepsis care

The importance of long-term outcomes post-sepsis is increasingly recognized. Research is shifting focus from mortality to quality of life (QoL) and functional outcomes, acknowledging the substantial impact of sepsis on a child's physical, psychological, and developmental well-being. Recent guidelines emphasize the need for research on predictors of long-term morbidity, highlighting the necessity of patient-centered care for sepsis survivors and their families. Families often face isolation due to a lack of formal support systems, and there is limited information on consumer perspectives and patient-focused outcomes.[11]

Understanding the impact of sepsis recovery on QoL and the healthcare system is crucial. Clinicians and families prioritize QoL as a key outcome measure, indicating the need for comprehensive support structures and processes. Holistic care approaches should address the long-term implications of sepsis recovery, ensuring support for survivors and their families throughout their journey.[28]

Future directions

Future research should focus on developing and validating rapid diagnostic tools and biomarkers to facilitate early sepsis detection in children. Additionally, there is a need for large-scale studies to evaluate the effectiveness of educational programs for parents and training for EMS

personnel in recognizing sepsis symptoms. Further investigation into the role of advanced technologies, such as artificial intelligence and machine learning, in predicting and diagnosing paediatric sepsis is essential. Expanding antimicrobial stewardship programs and exploring novel therapeutic agents could also enhance treatment efficacy. Lastly, comprehensive long-term studies on the quality of life and functional outcomes of sepsis survivors are necessary to inform holistic post-sepsis care strategies and support systems for children and their families.

CONCLUSION

Early identification and management of sepsis in children are crucial to reducing morbidity and mortality. Implementing advanced diagnostic tools, improving education for parents and EMS personnel, and optimizing antimicrobial therapy and post-sepsis care can significantly enhance outcomes. Continued research and innovative approaches are essential to further improve the survival and quality of life for pediatric sepsis survivors.

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