Discussion paper

Challenges in the recognition and management of paediatric sepsis — The journey

Amanda Harley\textsuperscript{a,b,c,*}, Luregn J. Schlappbach\textsuperscript{b,d}, Amy N.B. Johnston\textsuperscript{a,e}, Debbie Massey\textsuperscript{f}

\textsuperscript{a} School of Nursing, Midwifery and Social Work, The University of Queensland, Brisbane, QLD, Australia
\textsuperscript{b} Child Health Research Centre, The University of Queensland, and Paediatric Intensive Care Unit, Queensland Children’s Hospital, Brisbane, QLD, Australia
\textsuperscript{c} Department of Emergency Medicine, Gold Coast University Hospital, Gold Coast, QLD, Australia
\textsuperscript{d} Department of Intensive Care Medicine and Neonatology, and Children’s Research Center, University Children's Hospital Zurich, Switzerland
\textsuperscript{e} Department of Emergency Medicine, Princess Alexandra Hospital, Brisbane, QLD, Australia
\textsuperscript{f} School of Nursing and Midwifery, Southern Cross University, Coolangatta, QLD, Australia

\textbf{A R T I C L E I N F O}

\textbf{Article history:}
Received 12 October 2020
Received in revised form 25 February 2021
Accepted 16 March 2021

Keywords:
Community
Emergency nurse
Guideline
Long-term outcome
Paediatric Sepsis

\textbf{A B S T R A C T}

Paediatric sepsis remains a leading cause of childhood death. Morbidity is high, with up to one third of children affected developing ongoing, sometimes lifelong sequelae. To address the major burden of sepsis on child health, there is need for a unified approach to care, as outlined in the Australian National Action Plan for sepsis. While the Surviving Sepsis Campaign 2020 guidelines provided evidence-based recommendations for sepsis management in hospital, additional emphasis on families, pre-hospital recognition and post-sepsis care incorporating the multidisciplinary team is paramount to achieve quality patient outcomes. The role of families, paramedics and nurses in recognising and managing paediatric sepsis remains an under-represented area in current literature. The aim of this paper is to critically discuss key challenges surrounding the journey of paediatric sepsis, drawing on contemporary literature to highlight key areas pertinent to recognition and management of sepsis in children. Application of a holistic, patient-centred focus will provide an overview of paediatric sepsis, aiming to inform future development for enhanced healthcare delivery and identify critical areas for further research.

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1. Introduction

Paediatric sepsis is a major cause of preventable mortality in children globally\cite{1}. Morbidity and mortality rates in some settings are comparable to those seen in critically unwell adult populations \cite{2}. Over half of the global reported incidence of sepsis relates to the neonatal and paediatric population \cite{3}. While the majority of the approximately three million paediatric infection-related deaths occur in low and middle income countries, the burden of disease is high even in well-resourced settings \cite{4}. In Australia, an estimated 55,000 patients across all age groups experience sepsis each year, and in 2017 an estimated 8700 deaths were recorded as being sepsis related \cite{3}. Approximately 25% of paediatric intensive care unit (PICU) deaths in Australia and New Zealand were related to severe infections \cite{5}. In addition, a rapidly growing body of evidence demonstrates the long-lasting impact of sepsis on patients and families \cite{6,7}. It is estimated that up to one third of children who survive sepsis are left with significant morbidity including amputations, cognitive impairment and other, sometimes life-long conditions which will affect their Quality of Life (QoL) \cite{2}.

In 2017, the World Health Organisation (WHO) launched a resolution highlighting the need for a coordinated international approach to improve prevention, recognition, and management of sepsis in both adult and paediatric populations \cite{8}. The George Institute for Global Health responded by producing a National Action Plan for sepsis, outlining key recommendations to reduce the impact of sepsis in Australia \cite{9}. To date, there is no reliable early diagnostic test to identify sepsis and no standardised assessment or management of sepsis across Australian or international health facilities \cite{10,11}.

Standardisation to improve recognition, escalation of care and management of sepsis has been the focus of a number of quality improvement campaigns on sepsis. The Surviving Sepsis Campaign

https://doi.org/10.1016/j.auec.2021.03.006
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Please cite this article as: Harley A, et al, Challenges in the recognition and management of paediatric sepsis — The journey, Australasian Emergency Care, https://doi.org/10.1016/j.auec.2021.03.006
What is already known about the topic?

• Paediatric sepsis is a leading cause of childhood death globally: deemed an international health priority by the World Health Organisation.
• Research findings over the past decade have enabled a better understanding of sepsis, prompting policy change.
• Early recognition and management are paramount to reducing morbidity and mortality, with focus primarily on the critical care phase.

What this paper adds

• This piece contributes a unique overview and critical discussion of literature around paediatric sepsis, extending beyond critical care to include community, pre-hospital, and post-sepsis care.
• It provides initiative for translation of the National and Global Action Plan for paediatric sepsis to guide the patient journey, aiming to enhance healthcare delivery.
• It highlights requirements for future nursing and pre-hospital role development and contribution to care to enable provision of a comprehensive, multifaceted approach.

(SSC) highlighted the importance of timely recognition of paediatric sepsis, using this as a trigger to launch a sepsis treatment bundle [12]. The role that parents, the community, and healthcare staff, including nurses, play in timely recognition of sepsis is increasingly recognised and acknowledged in care pathways [13,14].

A comprehensive approach to paediatric sepsis needs to integrate every phase of the patient’s journey inclusive of pre-hospital, Emergency Department (ED), PICU, and post-sepsis care. We aim to critically discuss key challenges around the recognition and management of paediatric sepsis, incorporating different factors, with complimentary perspectives that contribute to the paediatric patient journey. This critical discussion sheds light on current challenges and opportunities that healthcare workers and policy makers should consider when developing, implementing and evaluating interventions to improve the recognition and management of paediatric sepsis. The paper will follow the patient journey starting with the systematic recognition of sepsis, recognition by parents, pre-hospital and ED clinicians, followed by treatment and post sepsis care. Key contemporary literature is used to inform the discussion, including international studies to ensure the best available evidence has been included.

An overview of the complex journey for paediatric patients diagnosed with sepsis, including articulation of the key elements in this journey is provided schematically in Fig. 1.

2. Recognition

2.1. Systematic approaches to sepsis recognition

Febreile conditions account for up to one in five paediatric presentations to the ED [15] with viral illnesses ranking as the most common diagnosis, often presenting with similar signs and symptoms as children who subsequently develop fulminant sepsis [16]. Clinicians face unique challenges in discriminating between a child with a self-limiting viral illness or critical illness such as sepsis where symptoms can be hard to recognise in early stages [7,13,17,18]. A sentinel case review conducted in Queensland, Australia, from 2012 to 2014 identified 25% of events in paediatric cases were attributed to sepsis, with key contributory themes identified as delayed or missed diagnoses of sepsis and lack of a sepsis pathway [19]. Launey et al. explored 23 fatal cases of serious paediatric bacterial infection in France and reported suboptimal care in 76% of cases [20]. Of importance, the authors made reference to the SSC recommendations, suggesting implementation of a sepsis protocol to improve care [20]. Several observational studies from high income settings have identified earlier recognition and improved outcomes following implementation of tools such as sepsis pathways [21–25]. Accordingly, the latest iteration of the paediatric SSC guidelines acknowledges the difficulties with paediatric sepsis recognition, recommending institutions adopt a systematic screening approach to assist with early recognition [12]. The development of reliable screening tools for sepsis is hampered by insufficient specificity and sensitivity [26] attributed to the myriad of signs and symptoms that patients with sepsis develop and the complexity of the condition. In addition, implementation of systematic screening approaches must ensure adaptation and calibration to the respective epidemiology and setting of participating institutions [21,23,27].

Sepsis pathways are designed with the aim of guiding clinicians in recognising and managing sepsis, providing standardisation of approaches, cognitive aids, and assisting in data collection for benchmarking and evaluation. Pathways typically consist of screening and treatment components aimed at increasing the reliability of recognition and empowering clinicians to escalate care quickly [12]. Traditionally, recognition and treatment of sepsis has been in EDs or the hospital setting. However, with the increasing awareness that early recognition and prompt treatment modalities improve outcomes in paediatric sepsis, the importance of parental contribution to patient diagnosis has been established.

2.2. Recognition of sepsis by parents

Sepsis is predominantly acquired in the community, yet the role parents play as the expert of their child in recognising sepsis, remains poorly explored [13]. Sepsis is defined as infection with a dysregulated host response leading to life-threatening organ dysfunction, concepts which are challenging for the wider public to understand, which may be an obstacle to prompt presentations to a health service [28,29]. Indeed, a recent survey in Australia showed only 14% of Australians could identify a sign of sepsis [9] despite the increase in morbidity and mortality associated with delayed hospital presentation [29]. While parents may not be trained to recognise organ dysfunction, they often state “this illness was different” or “I sensed something was wrong” in relation to the deterioration of their child in the course of sepsis [13,30], concepts that have received little exploration in the literature. For example, parents may assist in clinician assessment of a child’s mental status based on their expertise on normal behaviour of their child. At present, “parental concern” is used as a trigger in several institutional sepsis recognition tools [31,32]. However, a recent systematic review on parental concern as a recognition tool for sepsis identified only one original study reporting on diagnostic accuracy [13]. In this study, covering 3981 children presenting to primary care centres with an acute infection, parental concern coupled with clinician’s gut feeling that something was wrong, provided superior identification compared to routine physiological-based criteria [33]. These data, while limited in generalisability, support the design of future sepsis awareness campaigns and triage clinician education. Future research should further ascertain the role parents can play in the early recognition of sepsis.

Parental education about the key features of sepsis has substantial potential to result in earlier recognition of sepsis. Not uncommonly, children with sepsis have been discharged home following clinical review in the ED with common diagnoses such as “flu-like symptoms”, “bronchiolitis”, or “gastroenteritis”, because the clinical features of sepsis were not yet evident. Re-presentation to health services represents a reoccurring pattern observed in
many root cause analyses on fatal paediatric sepsis [19]. In adults, up to 45% of patients hospitalised with sepsis presented to a health service within one week prior to hospitalisation [34], identifying an important gap in pre-sepsis encounters that could inform early recognition. Development of future models to improve community awareness including risk-stratification post discharge should expand to the paediatric population. Accordingly, efforts to improve community, including parental awareness of sepsis is a key recommendation from the National Action Plan on sepsis in Australia [9]. Despite such recommendations, previous literature has reported barriers for health professionals to embrace and empower parents to escalate concern [35,36], leaving an area warranting further investigation and evaluation. As many children with sepsis deteriorate in the community Emergency Medical Services (EMS) are often their first contact with health care. Thus, there is an urgent need to explore, assess and evaluate EMS ability to recognise sepsis in children.

2.3. Recognition of sepsis in the pre-hospital environment

The majority of sepsis studies focus on recognition and initiation of treatment at hospital presentation [34,37]. Importantly, over 50% of community-acquired paediatric sepsis fatalities occur within the first two days of hospital admission [38], highlighting the importance of early recognition and presentation to healthcare facilities to commence treatment. Recognition by EMS in the pre-hospital phase may contribute to improved outcomes [39–41]. Recognition of paediatric sepsis by EMS carries additional challenges as the physiological parameters indicating illness severity are different to those in adult populations. For example, unlike in adults with sepsis, hypotension is a late sign of sepsis in the paediatric population and initiation of treatment should not depend on presence of hypotension [38]. To date, there is no literature on EMS and paediatric sepsis recognition [39,41,42]. An EMS study focusing on adult patients indicated accurate recognition of sepsis in only 10.8% of cases highlighting a need for sepsis-specific training for EMS personnel. This important finding indicates that there is significant opportunity to improve recognition of sepsis and improve outcomes [41], which should extend to include the paediatric population. A recent randomised controlled study (RCT) was conducted on adults with sepsis to receive early, pre-hospital antibiotics. Although the trial did not report a mortality benefit, secondary analyses revealed that targeted education substantially improved recognition of sepsis by EMS personnel [43], recognition is key to improving outcomes [44], extending beyond mortality measures [12,45]. Further support for this finding stems from a study assessing the impact of a pre-hospital sepsis screening tool coupled with education that reported a recognition accuracy of 78.2% in a study of 629 adults [40]. Additional research and associated education is therefore needed to explore pre-hospital interventions in children with sepsis, targeting early recognition. The experience acquired with the implementation of sepsis recognition tools in the hospital setting should inform design of pre-hospital quality improvement initiatives in conjunction with targeted education.

2.4. Recognition of sepsis in Emergency Departments – the role of nurses

Acknowledgement of the fundamental role that nurses play in early recognition is evident through the development of
nursing-specific actions formulated from SSC guidelines [14,46,47], however their role in paediatric sepsis recognition has received limited exploration. Nurses in EDs are typically the first point of patient contact and responsible for initial patient assessment, including recognition and escalation of patient deterioration [37,48]. The integral function of nurses in initiating sepsis identification and management was highlighted in a 2019 qualitative study exploring nurses’ role in recognising and responding to sepsis [14]. Observed organisational and nurse’s knowledge deficits indicated a need for improved and contextually appropriate education. They also indicate the need for utilisation of a specific sepsis pathway to overcome perceived barriers such as roles and responsibilities in recognition and escalation of care [14]. Nurse-led pathways, or protocols for sepsis management advocate for nurse-led multidisciplinary teams to speed recognition, initiate treatment, and facilitate appropriate escalation [47,49]. The lack of standardisation of nursing education and variable empowerment of nurses across institutions may contribute to variability of care in sepsis recognition and management and negatively affect paediatric outcomes [14,37]. Structured education across health care services and disciplines is likely to improve reliability of sepsis recognition and treatment [48,50].

Studies exploring nurse’s knowledge of sepsis highlight limitations in current education curricula [14,37], although little is known about the translation of knowledge to practice in the field of sepsis. A Canadian study surveying 312 ED nurses identified knowledge of sepsis was in general low, despite receiving education on sepsis in multiple forums [51]. Further exploration on knowledge translation and contextual knowledge to understand these shortcomings is required [51]. Curriculum expansion to include specific education on topics such as recognising and responding to patient deterioration has been recommended for nursing education and should be extended to include paediatric sepsis [52,53], future efforts will require education and knowledge translation methodologies to operate in parallel.

Nurses play a central role promoting and enhancing patient safety by identifying critical status changes during patient deterioration [54] and activating protocols. Studies indicating low compliance with sepsis protocols and guidelines are of concern. For example, a 2009 audit revealed poor adherence with the American College of Critical Care Medicine-Paediatric Advanced Life Support guideline for children with sepsis [55]. The low compliance with the guideline is not an isolated result, variability in guideline application exists globally and nationally [56,57]. These findings highlight the need for comprehensive multidisciplinary approaches including nurses to enable improved implementation and maintenance of sepsis guidelines to ensure positive patient outcomes [58].

3. Treatment

3.1. Management of paediatric sepsis

Early treatment of paediatric sepsis can substantially decrease mortality rates based on observational data [56,59], however robust, high-quality evidence for current treatment regimes specifically for children, remains limited. Further complexity arises from the variable application of sepsis criteria in past studies, compounded by the lack of specificity in the 2005 criteria for ‘Systemic Inflammatory Response Syndrome’ (SIRS) criteria [60] and subsequent definition of sepsis. SIRS criteria is the nonspecific inflammatory process that occurs for many pathophysiological conditions, not isolated to sepsis. This current definition categorises children with an infection and SIRS criteria as sepsis [60]. Consequently, variable study results have been produced with varying illness severity amongst populations. The latest iteration of the Paediatric SSC uses the term “sepsis-associated organ dysfunction” [12]. A paediatric sepsis definition taskforce has been formed and revised criteria for an updated definition is eagerly awaited [51].

The concept that a combination of interventions, designated a care bundle, is more likely to result in improved outcomes has become widely adopted [24,25,56]. A ‘sepsis care bundle’ includes initial resuscitation and treatment actions such as blood culture collection, commencement of antibiotics and administration of fluid bolus(es) [12] within 180 min for children with sepsis-associated organ dysfunction and within 60 min for those with septic shock [12]. In a large cohort of children managed under the New York state mandate for sepsis care, lower mortality was observed in children with sepsis where treatment with a sepsis ‘bundle’ was administered within one hour of recognition [56]. In a single centre study in children, rapid delivery of antibiotics in children with septic shock correlated with lower mortality [62]. Additional paediatric studies are required to develop robust evidence focusing on other individual bundle elements to ascertain their impact on paediatric outcomes, and their relative contribution to the paediatric sepsis care bundle [56].

Based on evidence and biological rationale, blood culture collection and administration of antibiotics represent widely accepted bundle components [12,44]. The liberal use of fluids has however, recently come under scrutiny [63–67]. Historically, rapid high volume fluid administration in suspected sepsis has been a cornerstone of treatment [68]. More recently, observational studies indicate potential for harm associated with high volume fluid administration in sepsis in both adult and paediatric populations [63–65,67]. A large paediatric multicentre trial (FEAST) [64], performed in a low resource setting where intensive care was not available, demonstrated higher mortality in children receiving larger volumes of fluid. FEAST has served as the foundation for recent studies to assess fluid-restrictive strategies aimed at improving patient outcomes [63,69–73]. This indicates a need to test fluid-restrictive resuscitation algorithms [63,71,74,75] in paediatric populations, which can be achieved by earlier initiation of peripheral inotropes in lieu of additional fluid administration.

At present, various strategies exist to treat refractory septic shock, such as Hydrocortisone and immunomodulation, and extracorporeal therapies. A novel and highly controversial approach includes administration of Hydrocortisone, Thiamine and Vitamin C (HAT) [76], showing some promise for decreased mortality in a United States RCT (p < .001) [77]. A systematic review of metabolic resuscitation in septic shock revealed nine registered RCTs [78]. Recently, two such studies presented conflicting results based on a primary outcome reflecting resolution of septic shock [79,80]. Both studies were conducted in adult populations with small sample sizes, and similar metabolic studies on the management of paediatric septic shock are pending. Future studies for paediatrics should extend beyond shock resolution as a primary outcome to include focus on improvements (patient benefits) from reduction in measures of morbidity, such as long-term outcomes.

3.2. Management of care post-sepsis

The importance of long-term outcomes post-sepsis are increasingly recognised [6,81–84]. Research focus is shifting from predominately mortality outcomes [83], to include QoL and functional outcomes [5,84]. Such shifts are critical given the burden of sepsis sequelae on a child’s life can include physical, psychological and developmental compromise [45,81,85]. Recent guidelines highlight the need for research to identify and test predictors of long-term morbidity [86]. Given the high morbidity and life-long impacts of sepsis, it is important to look beyond the traditional acute phase of ‘avoid and treat organ dysfunction’ [45] and begin to recognise the role and value of patient-centred care for sepsis.
survivors and families [83,87], inclusive of those who have lost a child. Secondary to survival, clinicians and families of children admitted to PICU chose QoL as the preferred outcome measure for their child [88]. Families are at risk of isolation given the lack of formal support systems after sepsis. There is a lack of information on consumer perspectives and patient-focussed outcomes which may assist in reviewing the impact of sepsis on QoL. As we explore the ways to recognise and manage sepsis it is important to investigate the support structures and processes required by families and review the implications of sepsis recovery for survivors and the healthcare system on an ongoing basis, encompassing holistic patient care.

4. Concluding statement — the need for a national approach

This critical discussion of the key challenges around the recognition and management of paediatric sepsis highlights that, despite substantial progress in quality improvement initiatives and research, gaps in practice, research and education remain. In Australia, the National Action Plan for sepsis outlines how the WHO recommendations could be implemented locally [8,9]. Although currently, Australian states and territories do not have a standardised, nor mandated approach to sepsis care [12,44,89,90]. A streamlined, unified approach will enable standardised education, co-ordination, aligned care, and benchmarking, ensuring synergy between states and individual facilities. This is more likely to succeed by encompassing each of the different, yet complimentary perspectives and key components of sepsis recognition and management that contribute to the patient journey (Fig. 1). Specifically, Australia should leverage off the international experience in the field and adapt existing programs, such as the hospital training programs targeting sepsis recognition and management in the UK [91], alongside development of a national trust. New York State described improved outcomes stemming from implementation of mandated sepsis care [56]. Each of these programs has expanded to include community awareness initiatives. Interestingly, the state of New York has embedded sepsis education into the school curriculum to improve sepsis awareness [92,93]. In addition, sepsis education in undergraduate nursing and medical sectors is known to vary greatly across institutions [53]. Nursing education aims to prepare students for entry into the workforce [94], and thus should integrate contemporary updates and priorities for change such as sepsis care [8,9]. A national quality and safety standard of care on sepsis may provide further incentive for universities to develop a unified approach to curriculum development around sepsis [55]. In conclusion, integration of the community, healthcare and university sector targeting the recognition and management of children with sepsis is needed to enable a sustainable improvement in paediatric sepsis outcomes. This critical discussion can help direct healthcare workers and policy makers as they develop, implement and evaluate interventions to improve the recognition and management of paediatric sepsis.

Authorship contribution statement

AH and LJS were responsible for conceptualisation and design. AH drafted the manuscript and subsequent versions. All authors contributed to manuscript development, critical review, revision and approved the final manuscript.

Funding sources

No funding was provided.

Conflict of interest

There are no conflicts of interest to declare.

Acknowledgements

We would like to thank Queensland Children’s Hospital and Clinical Excellence Queensland for supporting the Paediatric Sepsis Project aiming to improve the care for children with sepsis. Katie East for assisting in graphic design. We also thank the families, clinicians and researchers for sharing insights into the journey of paediatric sepsis.

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