Systems for Paediatric Sepsis: A Global Survey

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ABSTRACT

Objectives: *To evaluate the resources available for early diagnosis and treatment of paediatric sepsis at hospitals in developing and developed countries.*

Methods: *This was a voluntary online survey involving 101 hospitals from 41 countries solicited through the World Federation of Pediatric Intensive and Critical Care Societies contact list and website. The survey was designed to assess the spectrum of sepsis epidemiology, patterns of applied therapies, availability of resources and barriers to optimal sepsis treatment.*

Results: *Ninety per cent of respondents represented a tertiary or general hospital with paediatric intensive care facilities, including 63% from developed countries. Adequate triage services were absent in more than 20% of centres. Insufficiently trained personnel and lack of a sepsis protocol was reported in 40% of all sites. While there were specific guidelines for sepsis management in 78% of centres (n = 100), protocols for assessing sepsis patients were not applied in nearly 70% of centres. Lack of parental recognition of sepsis and failure of referring centres to diagnose sepsis were identified as major barriers by more than 50% of respondents.*

Conclusions: *Even among centres with no significant resource constraints and advanced medical systems, significant deficits in sepsis care exist. Early recognition and management remains a key issue and may be addressed through improved triage, augmented support for referring centres and public awareness. Focussed research is necessary at the institutional level to identify and address specific barriers.*

Keywords: Children, critical illness, developing world, infection, sepsis outcomes

Sistemas de Sepsis Pediátrica: Una Encuesta Global

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RESUMEN

Objetivos: *Evaluar los recursos disponibles para el diagnóstico precoz y el tratamiento de la sepsis pediátrica en hospitales de países desarrollados y en vías de desarrollo.*

Métodos: *Se realizó una encuesta voluntaria online que comprendió 101 hospitales de 41 países solicitados a través de la página web y la lista de contactos de la Federación Mundial de Sociedades del Cuidado Pediátrico Intensivo y Crítico. La encuesta fue diseñada para evaluar el espectro de epidemiología de la sepsis, los patrones de las terapias aplicadas, la disponibilidad de recursos, y las barreras al tratamiento óptimo de la sepsis.*

Resultados: *El noventa por ciento de los encuestados representó a un hospital terciario o general con instalaciones de cuidados intensivos pediátricos, incluyendo un 63% de países desarrollados. Los servicios adecuados de triaje estuvieron ausentes en más del 20% de los centros. Se reportó personal insuficientemente entrenado y falta de protocolo de sepsis en el 40% de todos los sitios. Aunque había normas específicas para el tratamiento de la sepsis en el 78% de los centros (n = 100), no se aplicaban los protocolos para la evaluación de pacientes de sepsis en casi el 70% de los centros. La ausencia de reconocimiento de la sepsis por parte de los padres, y el fracaso de los centros de referencia para diagnosticar sepsis, fueron identificados como los principales obstáculos por más del 50% de los encuestados.*

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Conclusiones: *Incluso entre los centros sin limitaciones significativas de recursos y sistemas médicos avanzados, existen déficits significativos en el cuidado de la sepsis. El reconocimiento y tratamiento temprano sigue siendo una cuestión clave, y puede resolverse mejorando el triaje, dando mayor apoyo a los centros de referencia, y aumentado la conciencia pública. Se necesita realizar investigaciones a nivel institucional, encaminadas a identificar y abordar las barreras específicas.*

Palabras claves: Niños, enfermedad crítica, mundo en desarrollo, infección, resultados de la sepsis

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INTRODUCTION

Severe sepsis and septic shock is the final common pathway and one of the leading causes of global childhood mortality (1, 2). Poor clinical outcomes are related to many factors including patient factors such as malnutrition, lack of readily available resources to appropriately triage, diagnose and treat sepsis, and suboptimal adherence to specific sepsis management guidelines (3–9). Even as evidence-based protocols directed at managing sepsis in resource dense and resource poor environments have emerged, the promise of reduced mortality has been difficult to realize (10–14). Efforts to improve outcomes such as nutrition, immunization and sanitation programmes have resulted in a decrease in the incidence of bacterial sepsis; however, in-hospital mortality has remained high with no significant reductions in more than a decade (12).

Specific programmes designed to improve triage processes and sepsis recognition and adherence to goal-directed care have improved outcomes at individual institutions in both resource rich and poor environments (14–17). At a global level, however, priority areas for research and intervention have not been systematically described. There is a need to identify common barriers as a basis for developing effective, scalable interventions that focus on the areas with the greatest potential impact.

This study is a global survey of paediatric institutions designed to evaluate the systems and barriers to optimal sepsis care. The objective of this survey is to assess the existing resources and procedures available for early diagnosis and treatment of paediatric sepsis at hospitals in developing and developed countries. This information is paramount for identification of key areas for future research and institutional support.

MATERIALS AND METHODS

This study was approved by the Institutional Review Board at British Columbia Children's Hospital and the University of British Columbia. An online survey was developed to assess the spectrum of sepsis diagnosis and care, including epidemiology, barriers to sepsis therapy, acute care and emergency management facilities, inpatient facilities including intensive care facilities, access to and use of intravenous fluids and medications, and laboratory resources. This survey was based on standards derived from the World Health Organization (WHO) Pocket Book of Hospital Care for Children (18), and other relevant WHO materials and is consistent with national standards and guidelines, such as guidelines developed by the international sepsis initiative of the World Federation of Pediatric Intensive and Critical Care Societies [WFPICCS] (11) and the Pocket Book. The survey was modified to specifically address the recognition and management of sepsis. It was not designed to represent findings specifically from developed or developing countries, or high-income or low-income countries.

Data collection

Information to access the online survey system was distributed *via* e-mail to all contacts on the WFPICCS sepsis ambassadors contact list. This is a list of individuals worldwide who are experts in the field of sepsis in children and those who have expressed an interest in issues related to sepsis (http://www.wfpiccs.org/projects/sepsis-initiative/). It is meant to be inclusive of anyone willing to participate and be listed as an ambassador on the web-based global sepsis initiative. The information to participate in this survey was also posted on the WFPICCS website. The survey invitation was open to all centres, regardless of WFPICCS membership. The survey was available in English language only.

A survey administrator was responsible for providing anonymous verification codes to interested centres, which were used to access the survey. Survey data were collected and managed using REDCap electronic data capture tools hosted at British Columbia Children's Hospital (19). When two or more people reported for the same centre, only the most complete survey was used and the others were discarded.

Statistical analysis

Only surveys with responses for at least 80% of items were considered complete and were included in the analysis. N values correspond to the total number of submitted responses for a particular item. Values are reported as the median or median (range). For categorical responses, frequencies are reported.

RESULTS

There were 101 surveys included in the analysis, originating from 41 countries on six continents, with 37% from developing countries. High-income and low-income countries represented 48% and 3%, respectively (Table 1).

Table 1: Countries by income status (based on gross national income per capita) and human development index score

Income status	Human development index score	Income status	Human development index score
High income ($12 616 or more)		**Upper middle income ($4086 to $12 615)**	
Australia	0.938	Algeria	0.713
Belgium	0.897	Argentina	0.811
Canada	0.911	Brazil	0.730
Chile	0.819	China	0.699
Czech Republic	0.873	Colombia	0.719
Estonia	0.846	Costa Rica	0.773
France	0.893	Cuba	0.780
Germany	0.920	Ecuador	0.724
Italy	0.881	Iran	0.742
Japan	0.912	Mexico	0.775
Lithuania	0.818	Peru	0.741
Saudi Arabia	0.782	Romania	0.786
Singapore	0.895	South Africa	0.629
Spain	0.885	Turkey	0.722
Switzerland	0.913		
United Kingdom	0.875		
United States	0.937		
Uruguay	0.792		
Lower middle income ($1036 to $4085)		**Low income ($1035 or less)**	
India	0.554	Malawi	0.418
Indonesia	0.629	Rwanda	0.434
Philippines	0.654	Uganda	0.456

Tertiary care children's or general hospital facilities accounted for 90%. Private hospitals accounted for 15%. There was a wide range in the number of patient visits in a year (range 6 to 1 600 000), inpatient admissions (range 20 to 290 000) and paediatric specialists per centre (range 1 to 400). Median values for the youngest and oldest patients at each centre were birth (range: birth to 1 year, n = 98) and 16 years (range: 4 to 25 years, n = 100). Median of patients evaluated for sepsis in emergency department was 245 (range 5 to 60 000) and inpatients admitted with sepsis as the primary diagnosis was 150 (range 0 to 8 400).

Table 2: Barriers to effective sepsis care

Barrier	Centres (%)
Deficits in parental education	50
Access to healthcare services	35
Lack of medical equipment resources	26
Lack of vascular access and crystalloid resuscitation	15
Lack of antibiotics	9
Failure to diagnose by referring facilities	50
Insufficient trained hospital personnel	42
No defined protocol for managing paediatric sepsis	38
Long triage waiting times	35

Barriers to sepsis therapy

Each centre reported perceived barriers to sepsis therapy. The most common barriers included deficits in parental ability to recognize the signs of sepsis and failure to diagnose sepsis by clinicians at referring facilities, which were each reported in 50% of all sites (Table 2). Insufficiently trained personnel and lack of a sepsis protocol was reported in 40% of all sites. Lack of access to medical equipment and interventions including vascular access, crystalloid resuscitation and/or antibiotics were the least prevalent.

Emergency department facilities and triage functions

An emergency area for assessment and management of acutely sick children was present in 92.1% (n = 101) of centres, with nearly all centres open at night (96%, n = 95) and on weekends (99%, n = 94). In terms of specific paediatric care, 90.4% (n = 94) had a paediatric area separate from the adult area that is open for a median 24 hours per day (n = 81).

While 81% (n = 101) of centres had a system for prioritizing sick children, medical personnel at 79% (n = 98) had specific triage training and only 79% (n = 97) indicated that children with suspected sepsis actually receive priority. Nurses were most commonly responsible for performing triage assessments (47%, n = 101). The median time to triage was 10 minutes (range: 0 to 120 minutes, n = 68). Guidelines used for prioritization include Integrated Management of Childhood Illness (22 centres), Emergency Triage Assess-

ment and Treatment (32 centres), Advanced Pediatric Life Support (48 centres), and American College of Critical Care Medicine/Pediatric Advanced Life Support (49 centres).

Initial resuscitation and management

When asked to describe the typical course of a paediatric patient with suspected sepsis, marked variation existed between centres (Table 3). There were specific guidelines for sepsis management in 78% of centres (n = 100). Patients with suspected sepsis were usually seen first by residents (46%) or paediatric specialists (26%, n = 101). The median time from triage to physician assessment was 18 minutes (range: 0 to 360 minutes, n = 64). Severity of illness was determined using physical examination alone in 61%, institutional protocol in 21%, and Integrated Management of Childhood Illness or Emergency Triage Assessment and Treatment algorithm in 10%.

Table 3: Self-reported priority actions for patients with suspected sepsis

Action	Typical time necessary to achieve action			
	< 1 hour (%)	> 1 hour (%)	Never (%)	Unreported (%)
Vascular access	88	3	7	2
Crystalloid bolus	95	2	3	0
Antibiotics	90	9	1	0
Central line	41	32	26	1
Arterial line	35	31	32	2
Blood cultures	87	10	2	1
Chest X-ray	78	16	3	3
Blood gas	84	6	10	0
Review by attending physician	87	11	2	0

Vascular access and crystalloid bolus administration was achieved within 15 minutes for 69% and 60% of centres, respectively (n = 101). However, across all centres, a median 50% (range: 0%–100%, n = 92) of patients with sepsis received intravenous fluid resuscitation according to the American College of Critical Care Medicine/Pediatric Advanced Life Support guidelines. Nurses were most commonly responsible for achieving vascular access and administering crystalloid boluses (41%, n = 100 and 47%, n = 101, respectively).

Antibiotics were administered within the first hour at 90% of centres (n = 101). Choice of antibiotic therapies was governed by paediatric specialists in 49% and residents in 46% (n = 100). Ceftriaxone was commonly used for treatment of sepsis in 84% of centres, followed by vancomycin in 43%, gentamicin in 30% and ampicillin in 28%. Other antibiotics were rarely used.

More than 80% of centres reported completing tasks such as blood cultures, blood gases and chest X-rays within the first hour of care. Although blood cultures were reportedly attained in 100% of patients (n = 98), only 37% of cultures yielded an isolate useful for patient management.

Central and arterial line placements were not typical for management of suspected sepsis in 30–40% of centres. In the remaining centres, these interventions typically occurred after initial resuscitation.

Inpatient care facilities and functions

A paediatric intensive care setting was available at 90% (n = 99) of all centres with 95% (n = 97) of centres having a physician on call for 24 hours. Paediatric residents (58%), specialists (30%) and to a lesser extent, nurses (10%), were responsible for receiving new patients on the ward. Similarly, paediatric residents (50%) and specialists (43%) are considered the frontline care-providers (n = 99). Equipment for monitoring such as cardiac monitors and pulse oximeters were available in all centres (n = 101).

Meeting the goals of sepsis therapy typically depended on improvements in blood pressure (95%, n = 97), peripheral perfusion (100%, n = 97), mental status (95%, n = 98), urine output (99%, n = 98) and serum markers such as lactate and mixed venous oxygen saturation (85%, n = 100). Patients who deteriorated in the emergency department were transferred to an alternate area in 75% of centres (n = 101). For those centres, 95% of transfers for these patients were to a paediatric intensive care unit. Only 32% of centres (n = 99) indicated that transfer notes are part of routine care for patients who change hospital areas.

Resource availability

Key resources for sepsis care in the acute care/emergency area and the paediatric ward, including equipment, medications and laboratory tests, were widely available among survey respondents (Table 4). Few items (*ie* central venous catheters, arterial catheters, and blood gas machines) had limited availability. Among antimicrobial medications, common empiric therapies for suspected bacterial sepsis, such as ceftriaxone, were almost universally present. The least commonly available medications were anti-malarial drugs such as coartemesin, which is expected given the prevalence of survey respondents from non-endemic areas.

Sepsis characteristics

All centres reported which infectious pathogens were most responsible for childhood deaths due to sepsis. Gram-nega-

Table 4: Availability of key medical equipment, medications and laboratory tests

General equipment	Emergency area (%)	Paediatric ward (%)
Guidelines for the management of paediatric sepsis	92	87
Weighing machines	94	95
Airway management and respiratory support		
Suction machines	100	98
Ambu bags and masks	100	98
Oxygen source	98	97
Facemask	98	97
Laryngoscope and endotracheal tubes	99	88
Mechanical ventilator	88	42
Intravenous access and fluid resuscitation		
Intravenous administration sets	100	100
Infusion pumps	91	97
Central line kits	78	57
Arterial line kits	75	45
Normal saline	100	100
Monitoring and laboratory testing		
Dextrose stix and glucometer	98	94
Blood gas machine	73	40
Pulse oximeter	100	97
Cardiac monitoring	97	82
Portable chest radiograph	94	77
Antimicrobials		
Ceftriaxone	92	92
Ampicillin	88	90
Vancomycin	80	82
Gentamicin	88	90
Coartemesin	19	26
Inotropes		
Epinephrine	99	94
Dopamine	91	67

tive bacilli were identified by the greatest number of centres as responsible for 75% (n = 101) of childhood deaths due to sepsis. Malnutrition represented a common comorbidity in 44% of centres (n = 98) and tuberculosis in 9% (n = 94). Overall, 50% of centres indicated a diverse list of other common co-morbidities, including immune deficiency secondary to HIV infection, immune suppression due to iatrogenic causes, congenital heart disease and underlying neurodevelopmental disorders.

Differences between developed and developing countries

In subgroup analyses, there was no difference between high and low income countries for any survey item.

DISCUSSION

This study provides baseline information from hospitals in more than 40 countries regarding the available systems for identifying and managing paediatric sepsis. Our data suggest that adequate human resources, knowledge of advanced training courses and appropriate laboratory facilities were available in nearly all centres, with no differences in subgroup analyses that compared survey parameters for high- and low-income countries.

These results were unexpected. Previous studies suggest that country income group and development status is strongly associated with disparities in health workforce, infrastructure and access to essential medicines (3−5, 18). Resource and capacity limitations in low-income countries are commonly identified as a challenge to improving health outcomes where sepsis is implicated as the most common cause of childhood mortality (12).

Our findings likely reflect selection bias: survey participation was voluntarily solicited online *via* the WFPICCS membership list, thereby focussing on a group of paediatric institutions that are motivated to participate in international research, have sufficient resources for Internet access, and subscribe to a global community of practice. Because this was an open survey, our results are not a representative sample of global paediatric centres. Indeed, participants comprised predominantly referral level facilities, even among respondents from the low-income group. Additionally, the survey was administered only in the English language and

may have precluded full participation. Taken together, our sample likely represents paediatric institutions with better resources and hence may give a more optimistic indication of available resources in the developing world.

Our sample shows that the availability of guidelines and resources alone does not guarantee optimal sepsis care. Even as standardized approaches to sepsis become more pervasive, many hospitals in high- and low-income countries struggle to integrate global learning on sepsis and comply with established protocols. Virtually all centres in our study indicated deficiencies in multiple areas. We found a low prevalence of appropriate triage, systematized severity assessments and specific protocols for sepsis treatment, even though each of these interventions is included in major published guidelines for sepsis recognition and management (10, 11). We expected that the prevalence of these foundational elements would be higher, especially among a sample that predominantly comprises centres with advanced medical systems. However, there are many barriers to guideline adoption beyond lack of resources, including the perception of restriction of autonomy, biases, lack of familiarity and awareness, lack of outcome expectancy and lack of motivation (20). Our findings are consistent with several studies from the United States of America (USA) showing that even in resource-rich centres, adherence to sepsis guidelines is not achieved for many patients despite a concerted effort by a dedicated team (16, 17, 21). Together, these data suggest that addressing cultural barriers such as knowledge, behaviour and attitude, in addition to ensuring adequate training and resources, should be key considerations for improving sepsis care.

Solutions for enhancing implementation are not universal; because cultural barriers are local impediments, what works in one setting will not necessarily work at another. Each institution, therefore, requires investigation of weaknesses specific to its environment. These institutions are worthy of further examination. There is increasing evidence to suggest that understanding epidemiologic and health systems data at the local level has a vital role in pushing toward improved health outcomes, including those set out in the Millennium Development Goals (22). Interventions should be developed and adapted to the local context in terms of physical and human infrastructure, hospital policy and culture, and other organizational barriers (23, 24). Whereas our study identifies some common deficiencies, we emphasize that our findings are hypothesis generating. Independent quality improvement research, including addressing culture and team dynamics, should be part of ongoing sepsis care at every centre. However, shared experiences from similar centres and regions can be beneficial if approached from the perspective of a community of practice whereby lessons learned may be beneficial to others (23, 24).

From an implementation standpoint, our study emphasizes the important finding that there are centres even in low-income settings with the basic systems necessary for good sepsis care. Learning more about how these "model" centres overcome specific structural and cultural barriers in a given national or local context is critical to planning for better services at scale. Similarly, our study emphasizes the need to develop methods to reach and learn more about institutions where systems for sepsis are weak and to explore the possible links between centres that have strong systems and those that do not.

One surprising result in our study was the absence of appropriate triage services in more than 20% of centres. Early recognition and management of sepsis is a key part of sepsis care and delays due to inadequate triage functions are consistently associated with poor outcomes (6−9). Similarly, effective triage is one of several areas where research and troubleshooting can result in striking improvements for patient outcomes with modest investment. At several centres in Malawi, for example, an improved triage system decreased sepsis mortality from 10–18% per week to 6–8% per week (14, 15). Other similar attempts in the USA have improved compliance with sepsis protocols and demonstrated a trend toward mortality benefit (25, 26). The prevalence of inadequate triage and possibility of significant clinical gains associated with triage systems suggest that this may be a useful focus area for additional research.

Another surprising result was the lack of difference in infectious pathogens between developed and developing (high- and low-income) countries. Limited epidemiological data from developing countries show higher rates of certain pathogens, such as nontyphoidal Salmonella (27). We hypothesize that the epidemiologic similarities suggested in our study may reflect limitations in laboratory resources, with the responsible infectious agent in many cases either assumed or unknown. For other diseases, such as HIV/AIDS, stigma associated with disease status may result in under-reporting.

Previous studies show that prompt recognition and treatment in the community confers a significant survival benefit (25, 26, 28). There is limited research regarding the profile of patients who present at peripheral compared to tertiary care sites. Peripheral centres are more likely to be located in under-developed or rural regions, where training resources may be limited and systems to enable rapid triage and treatment of children with sepsis may be suboptimal. Moreover, in many areas, transport systems are rudimentary or nonexistent and hence transport to higher levels of care may not confer any benefit if transport times are prolonged and deterioration during transport cannot be treated. There is a need for intensified efforts to understand sepsis epidemiology, practice dysfunctions and barriers to change at the community hospital level, as well as to support the development of specific training designed to improve peripheral systems for sepsis recognition, treatment, and referral.

The importance of public awareness is another common area for improvement, with 50% of centres indicating lack of parental recognition as a barrier to sepsis care. Parents can be taught to recognize the sensitive signs of sick

children and alert health-workers. In the United Kingdom, researchers from the Paediatric Intensive Care Society and the Meningitis Research Foundation conducted a successful campaign directed at parents to identify early signs of meningococcaemia, including petechiae and purpura (28). This was thought to be an important factor in improving outcomes for children with this condition (29, 30). Work in many developing countries to create distributed primary healthcare networks (using untrained adults as community health-workers) has helped expand the model of teaching laypeople to recognize basic signs of distress in children. In rural India, parents were taught to recognize poor feeding, diarrhoea and apnoea as warning signs. In these circumstances, rural healthcare workers administered intra-muscular and oral antibiotics, resulting in dramatic reductions in mortality (31). Although, there is currently no analogous programme to raise public awareness of sepsis in general, World Sepsis Day, coordinated by the Global Sepsis Alliance, is launching a broad public advocacy campaign to address this issue (32).

In summary, our global survey provides a broad assessment of health systems for paediatric sepsis and emphasizes some of the key barriers to improving outcomes. There are several limitations. The centres involved in this research were solicited from the WFPICCS, so all members had knowledge of the global standard-of-care for paediatric sepsis. This selection also resulted in survey respondents representing primarily tertiary paediatric or general hospitals. Furthermore, the survey was designed to provide an environmental scan, not to measure quality improvement indicators, and additional work is needed to evaluate systems for sepsis from a quality improvement perspective.

CONCLUSION

Paediatric sepsis contributes to a major portion of global childhood mortality. Although there are widely available guidelines for managing sepsis with strong evidence for improved outcomes, our study of 101 centres suggests that there are paediatric centres around the world, including in developing and low-income countries, with the basic resources and systems necessary to deliver good sepsis care. Nevertheless, there are often critical deficiencies. Key themes were the need for better early recognition and management, including a focus on understanding barriers to implementation of standard sepsis guidelines, support for sepsis systems at peripheral hospitals and development of a quality improvement framework at the institutional level.

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