Advances and Challenges in Sepsis Care in Low-Resource Settings

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KEYWORDS

• Sepsis • Global health • Low resource settings • Epidemiology

KEY POINTS

- The diagnosis of sepsis in low-resource settings (LRS) often relies on clinical criteria but may be enhanced by point-of-care testing, including lactate and ultrasonography.
- Empiric antimicrobial therapy should reflect local epidemiology, but a lack of regional antibiogram data can make this difficult.
- Fluid resuscitation should be cautious; early peripheral vasopressors can be safe and effective.
- Noninvasive forms of oxygen support can be effective in the absence of invasive mechanical ventilation.
- To improve sepsis care in LRS, we need to improve training, resources, and region-specific data and protocols.

INTRODUCTION

Sepsis is a form of life-threatening organ dysfunction caused by a dysregulated host response to infection. Globally, nearly 50 million cases of sepsis occur per year, with approximately 11 million deaths.[1] Of these cases, nearly 80% occur in low-resource settings (LRS), including low-income and middle-income countries, as well as remote and underserved regions within wealthier countries. Health care infrastructure is often inadequate to meet the needs of these patients in LRS due to limitations in consumables, the local workforce, and diagnostic testing.[2,3] Recommendations for the care of patients with sepsis, such as the international Surviving Sepsis Campaign guidelines, are primarily derived from studies conducted in high-income countries (HICs).[4] Nonetheless, recent pivotal trials have called into question the direct applicability of those studies to LRS.

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Abbreviations	
AMR	antimicrobial resistance
CT	computed tomography
ECMO	extracorporeal membrane oxygenation
HIC	high-income countries
HRS	high-resource Settings
ICU	intensive care unit
LRS	low-resource settings
NEWS	National Early Warning Score
NIV	noninvasive ventilation
POCUS	point-of-care ultrasound
SSC	surviving sepsis campaign

Multiple factors drive the disproportionate burden of sepsis in LRS. The prevalence of infectious diseases is generally higher in LRS, driven by decreased availability of preventive care such as vaccines, as well as by limitations in nutrition, water quality, and food safety.[5,6] Endemic diseases, such as malaria, dengue, and meningococcal infection, occur with increased frequency in many LRS, with mortality affecting children most acutely.[7–9] Trained staff may be scarce; countries defined as low-income by the World Bank have 0.3 physicians per 1000 population, compared with 3.7 per 1000 in high-income countries.[10] Intensive care unit (ICU) availability is similarly reduced, with 0.1 and 6.0 ICU beds per 100,000 population in Uganda and South Africa, respectively, compared with 10 to 30 beds per 100,000 population in high-resource regions.[10,11] Outcomes of patients with sepsis are harmed not only by limited bed capabilities but by overcrowding in existing facilities, with a 10% increase in bed occupancy associated with a 7% increase in mortality in South African ICUs.[12] This lack of capacity shifts the burden of sepsis care to non-ICU settings, such as general medical-surgical wards and emergency departments (EDs), with decreased capacity for monitoring and an increased risk of mortality.[13]

Sepsis care in LRS is therefore an area of great importance, and improved sepsis care in LRS has the potential to reduce the global risk of death markedly. It is important to remember that critical care is a concept, not a location; efforts to improve sepsis care cannot be confined to the ED or to the ICU. Similarly, the 2019 coronavirus disease (COVID-19) pandemic showed that any city in any nation can become a low-resource setting when faced with overwhelming patient numbers that exceed our capabilities. Improving care in LRS may have lessons for the entire world.

PRINCIPLES OF SEPSIS MANAGEMENT

Sepsis is not a single disease but many, united by the common feature of an underlying infection complicated by organ dysfunction.[4] Despite this heterogeneity, there are common aspects to sepsis management that hold true regardless of pathogen, syndrome, or setting. We will review these aspects here, highlighting features that are unique to LRS.

Early Recognition of Sepsis

Prompt care for patients with sepsis is often hampered in LRS by the heterogeneity of sepsis, a limited understanding of its relevant symptoms, and the relative lack of advanced diagnostics, all leading to an increased risk of death.[14,15] Continuous monitoring systems and biomarker testing, for example, venous lactate, are typically limited

in availability.[7] Clinical prognostic tools, such as the National Early Warning Score (NEWS) and its derivatives, may serve as valuable adjuncts in the absence of advanced diagnostics. However, their performance in LRS appears to be less sensitive and specific compared with studies in high-resource settings (HRS).[16,17] Locally-validated tools, such as the Universal Vital Assessment score, appear to outperform NEWS in predictive accuracy in studies conducted in sub-Saharan Africa, presumably resulting from their validation using local cohorts rather than patients in North America and Europe.[18,19] Lastly, purely clinical signs, such as somnolence, decreasing urine output, and poor capillary refill time, are reasonable surrogates for tissue perfusion and may identify patients with suspected sepsis sufficiently well to trigger intervention (**Table 1**).[20]

Antimicrobial Therapy

Rapid, active empiric antimicrobial therapy is one of the cornerstones of effective sepsis care. Mortality in HRS increases by 7% to 10% with each hour of delay in antibiotic therapy in patients with septic shock.[21] Although less marked, delayed antibiotics due to delays in sepsis recognition over 6 hours are still linked to increased mortality in hemodynamically-stable patients.[22] Data from LRS are limited, but it is reasonable to assume that similar delays will have comparable, if not greater, impacts on outcomes.[14]

Severe malaria can present as sepsis in endemic regions, with a high rate of bacterial coinfection (10%). and often coexists (10%) with bacterial infections. Malaria diagnosis requires either microscopy by an experienced expert or newer methods such as rapid antigen testing and polymerase chain reaction, may be limited by lower sensitivity or increased cost, respectively. In patients with suspected sepsis in a malaria-endemic region, empiric antimalarial treatment is recommended when malaria cannot be rapidly excluded. Intravenous artesunate is the preferred therapy; alternatives include intramuscular artemether or IV quinine. Oral regimens, such as artemether-lumefantrine, may serve as temporizing options.

Antimicrobial resistance (AMR) is highly prevalent in many LRS, with an estimated 1.27 million deaths attributed to bacterial AMR alone in 2019.[23] In some regions, greater than 75% of *Escherichia coli* and *Klebsiella pneumoniae* clinical isolates are resistant to third-generation cephalosporins, and from 7% to 36% of hospitalized patients in a multinational cohort in Bangladesh, Botswana, Chile, Guatemala, India, and Kenya were found to be colonized with carbapenem-resistant Enterobacterales.[24] This high rate of resistance leads to inadequate empiric therapy or, alternatively, overuse of highly broad-spectrum agents. However, routine diagnostics are often limited in these settings, and many hospitals lack regular, updated cumulative antibiograms to guide empiric therapy.[25,26]

Source Control

Rapid, effective source control is as critical to sepsis care as antibiotics, but its availability depends on resources such as surgical capacity, anesthesia, blood banks, and postoperative care. Observational studies from HRS describe that early source control within 6 hours of presentation is associated with reduced mortality.[27,28] Unfortunately, the Lancet Commission on Global Surgery reported in 2015 that an estimated 5 billion people worldwide lacked timely access to safe, affordable surgical and anesthetic care. In practice, this leads to delays in source control, higher rates of uncontrolled intra-abdominal infection, and ultimately worse sepsis outcomes.[29] Progress has been limited in achieving the goals of the Lancet Commission, in part due to health system disruptions during the COVID-19 pandemic.[30] Improving

Table 1
Key distinctions in sepsis care between high-resource and low-resource settings

Domain	High-Resource Settings	Low-Resource Settings
Epidemiology & burden	Lower incidence and mortality; older populations; sepsis often healthcare-associated	Disproportionately high global burden (~ 80% of cases); younger patients; endemic infections (malaria, dengue, and tuberculosis) common
Diagnostics	Broad access to laboratories (lactate, blood gas, and cultures) and imaging (CT and formal ultrasound)	Limited laboratories and imaging; point-of-care lactate and POCUS emphasized; diagnostic delays common
Microbiology & AMR	Routine blood cultures and updated antibiograms guide empiric therapy	Limited culture capacity; sparse or absent antibiograms; very high AMR prevalence complicates empiric choices
Empiric antimicrobials	Rapid administration with broad formulary access; stewardship programs embedded	Delays due to recognition, access, or cost; empiric therapy must cover endemic pathogens (eg, malaria) despite diagnostic uncertainty
Fluid resuscitation	Guideline-driven early bolus strategies (often 30 mL/kg), with ICU backup	Cautious, physiology-guided small boluses; large boluses associated with harm when ventilatory/ICU support is limited
Hemodynamic monitoring	Invasive monitoring, frequent laboratories, and vasopressors via central access	Clinical surrogates (blood pressure, heart rate, and capillary refill); minimal invasive monitoring
Vasopressor use	Early norepinephrine via central line and infusion pumps	Peripheral vasopressors used pragmatically with protocols; dopamine or epinephrine used when norepinephrine unavailable
Oxygen therapy	Reliable oxygen supply; HFNC, NIV, mechanical ventilation readily available	Supplemental oxygen often scarce or unreliable; concentrators, cylinders, and pulse oximetry limited; triage of oxygen may be common
Advanced organ support	Broad access to RRT, invasive ventilation, ECLS	RRT often unavailable or unaffordable; peritoneal dialysis used as alternative; ECLS extremely rare
Source control	Timely surgical/interventional radiology access	Delayed or unavailable due to workforce, anesthesia, blood bank, or infrastructure limitations
Workforce	High density of ICU-trained staff	Severe shortages of trained staff; care often delivered on wards or EDs
Guidelines & evidence base	SSC-based protocols derived from HRS trials	Need for context-specific adaptations; some HRS-derived strategies may be harmful if applied uncritically
System resilience	Surge capacity, redundancy in supplies	Highly vulnerable to disruptions (eg, disasters, supply chain failure)

Abbreviations: ECLS, extracorporeal life support; HFNC, high-flow nasal cannula; RRT, renal replacement therapy.

triage pathways, decentralizing basic emergency surgical capability, scaling up anesthesia and surgical workforces, and ensuring perioperative and postoperative infection control are critical steps to reduce sepsis mortality from surgically treatable causes.[31–34]

Fluid Resuscitation

In HRS, volume resuscitation with isotonic fluids has been associated with improved outcomes in observational studies, with 30 mL/kg of a balanced crystalloid solution (eg, lactated Ringer's) recommended by current guidelines.[4] The precise volume of fluid to administer remains unclear when evaluated in clinical trials, however, with more restrictive fluid volumes of less than 1.5 L showing equivalent outcomes as larger volumes.[35,36]

These findings, however, may not necessarily apply to LRS. The FEAST trial, evaluating the role of fluid therapy in African children with severe infections, showed an increase in 48-hour mortality in participants randomized to rapid bolus resuscitation (albumin or normal saline) versus maintenance fluids in settings without ready access to advanced respiratory or critical care support.[37] This highlighted that aggressive early boluses could be harmful where downstream supportive care (oxygen, ventilation, and transfusion) is limited. It is important to observe, however, that the excess mortality in these children appeared to be related to cardiovascular collapse rather than directly due to hypervolemia, that is, pulmonary or cerebral edema. This suggests that the harm from fluid therapy in the LRS context may not solely be due to volume overload but possibly related to reperfusion injury following delayed rather than early resuscitation.[38] This phenomenon does not appear to be confined to children; subsequent studies in adults in Africa have shown similar lack of benefit and possible harm with early fluid resuscitation for sepsis.[39,40]

There is growing recognition that the timing, volume, and context (patient population, baseline anemia or malaria, and availability of ventilatory support, among others) matter greatly in LRS. Although guidelines continue to recommend volume resuscitation for patients with sepsis in LRS, cautious, physiology-guided initial resuscitation (administering small boluses and closely reassessing the response) is recommended, along with earlier consideration of vasopressors when available.[41] Particular caution is advised regarding large, repeated boluses late in the disease course when critical care support is limited. In the absence of advanced monitoring or lactate testing, responses to fluid resuscitation may be monitored using decreases in heart rate, increases in systolic blood pressure may be used as surrogates for improvement in intravascular volume status. Changes in pulse pressure and systolic arterial pressure through a brachial cuff can be used to assess a fluid-induced increase in cardiac output, although all these methods are limited.[42,43] Decreases in capillary refill time with resuscitation have been validated as equivalent to, if not superior to, lactate-guided measures.[44]

Vasopressor Support

In LRS, the choice of vasopressors must weigh drug availability, nursing ratios, monitoring capacity, and the logistics of safe peripheral infusion. Guidelines recommend norepinephrine as the first-line vasopressor for septic shock, but norepinephrine infusion requires medications, reliable IV access, monitoring, and often central venous access.[4] Where central access or pumps are unavailable, well-structured protocols for short-term peripheral norepinephrine infusion (peripheral lines, protocolized site

checks, short durations, and early plan for escalation) have shown low-complication rates and can be lifesaving.[45,46]

If norepinephrine is not available, epinephrine is an acceptable alternative, particularly in children.[47,48] Although dopamine has been shown to have higher adverse effects in randomized trials (such as higher risks of arrythmia), randomized trials have not shown a clear difference in mortality between norepinephrine and dopamine, and dopamine is presumably superior to no vasopressor support in the absence of other agents.[49,50]

Oxygen Therapy

Oxygen is the most commonly required form of organ support in sepsis, spanning modalities from nasal cannula and simple masks to noninvasive ventilation (NIV) and mechanical ventilation. Oxygen availability became a critical scarce resource in many regions, including parts of the United States, during the COVID-19 pandemic.[51,52] In many regions, oxygen supply is chronically unreliable; in a survey across 39 low- and middle-income countries, only 24.5% of primary, 52.4% of secondary, and 66.8% of tertiary facilities reported reliable oxygen availability, with inadequate levels of availability of critical equipment such as cylinders, concentrators, delivery devices, and monitoring equipment such as pulse oximetry.[51] Limited oxygen availability in LRS may lead to the need to triage, resulting in restricted access for vulnerable patients. Oxygen concentrators can expand access but require reliable power sources.[53,54] Solar-powered systems and low-pressure storage mechanisms have shown promise as a way to improve access to oxygen therapy in LRS, particularly when electricity is unreliable.[55–57]

Basic monitoring with pulse oximetry may be unavailable or unreliable in LRS, with equipment reliability, batteries, maintenance, and staff training serving as barriers.[58,59] Clinical signs such as tachypnea, tachycardia, or cyanosis may be helpful in the absence of oximetry but tend to be evident only in severe illness, and reliance on such markers will likely lead to delays in treatment.[60–62] (63) Interventions to strengthen oxygen systems, such as routine pulse oximetry, reliable supplies, and maintenance programs have demonstrably reduced pediatric pneumonia mortality and improved quality of care.[63,64] Nonetheless, significant gaps in access persist. Advanced respiratory support remains out of reach for many facilities, leaving a substantial unmet need.

Extracorporeal Support

Advanced extracorporeal support for patients with sepsis includes renal replacement therapy for acute kidney injury, extracorporeal membrane oxygenation (ECMO) for refractory respiratory or cardiac failure, and durable mechanical cardiac support. Acute kidney injury (AKI) is common in sepsis, but a substantial proportion of patients who meet indications for dialysis in LRS never receive it due to lack of equipment or trained staff, consumable costs, or inability to pay.[65] Peritoneal dialysis may be a feasible, lower-resource alternative in many settings and has been promoted by international nephrology bodies as part of a pragmatic strategy.[66]

ECMO and other high-cost extracorporeal supports are largely absent outside high-income regions because of cost, staff, and volume requirements; targeted regionalization and careful case selection are the realistic near-term models where these technologies exist. In Africa, there are only 5 centers registered with the Extracorporeal Life Support Organization, despite the continent containing over 16% of the world's population.[67] Before and during the COVID-19 pandemic, new ECMO centers established in South Africa, India, and the Middle East have reported mortality rates

higher than, but comparable to, those in higher-resource settings. However, access to these centers remains limited by distance and capacity.[68–70] These limited extracorporeal options mean that clinicians must prioritize early prevention, basic organ support, and timely transfer when appropriate.

ADVANCING SEPSIS CARE IN LOW-RESOURCE SETTINGS

Given both the high burden of disease and resource limitations in LRS, we propose that sepsis care must first focus on the areas of highest potential impact, specifically in recognition, diagnostics, and acute management. While advanced technologies such as ECMO will eventually play a role, the costs, incremental effects on outcomes, and challenges with patient selection and transport make such interventions unlikely to make a major impact on public health in the immediate-term.

We suggest the following steps:

Triage tools and triggers. Broad sepsis screens from electronic systems in HRS often lead to excessive alerts and alarm fatigue in busy wards.[71] Clear, physiology-based triggers (mental status change, hypotension, tachypnea, hypoxemia, and oliguria) plus a low threshold for empiric antibiotics when severe illness is evident may be ideal, particularly when using locally-derived severity scoring systems.[16–19] The updated 2024 guidelines from the National Institute for Health and Care Excellence in the United Kingdom explicitly tie early antibiotics to severity of illness, striking a balance between benefit and stewardship.[71] This could serve as a model for similar guidelines in LRS.

Diagnostic testing. Although physiology-based clinical assessments are the critical first step in identifying sepsis, diagnostic testing is necessary to provide specific therapy. Unfortunately, major gaps in diagnostic testing remain in most LRS. A survey of hospitals in Africa and Asia revealed that ultrasound was available in only half of the hospitals, basic radiography in 61.5%, and the ability to perform routine Gram staining in 45.8%.[72] Improving access to these core capabilities would have a significant impact on care. Expanding access to point-of-care ultrasound (POCUS) specifically may reduce the need for many forms of more expensive imaging modalities, for example, computed tomography (CT) scanners and portable radiography, although training, cost, and the need for reliable electricity could remain barriers.[73] Point-of-care, handheld lactate meters are increasingly affordable and speed risk stratification, guide initial resuscitation, and improve bundle adherence where other assays are slow or absent.[74]

Expanding access to essential clinical microbiology is also necessary, given the high burden of AMR in LRS. Automated blood culture systems, common in HRS, may not be sufficiently robust for LRS, but traditional, manual blood culture methods are comparatively inexpensive and perform acceptably.[75] A *mini-lab*, designed by Médecins Sans Frontières and implemented in selected field sites, consists of 6 boxes that unfold into a fully equipped and ready-to-use workstation, permitting the performance of bacterial culture, identification, and susceptibility testing, and can be operated by nonspecialist technicians; similar ruggedized and portable solutions may be generalizable across LRS.[76]

Hemodynamic support. The paradox seen in fluid resuscitation in patients with sepsis between LRS and HRS suggests that the importation of Surviving Sepsis Campaign (SSC)-based fluid protocols in LRS may be inappropriate, at least for now. This paradox may arise from different reasons between children and adults, that is, reperfusion injury versus hypervolemia and respiratory failure.[37–40] For adults, balanced crystalloids are weakly favored over saline when available, with moderate boluses and frequent reassessment. In children, smaller aliquots, earlier reassessment, antipyretics, glucose

if needed, and appropriate antimicrobial therapy may be preferred over routine aggressive boluses.[41] POCUS may be a useful adjunct to fluid resuscitation, permitting avoidance of hypervolemia, and POCUS training models set in LRS are continuing to mature.[77] In patients with ongoing hypotension despite fluids, norepinephrine can be administered peripherally in controlled settings; epinephrine is an acceptable alternative. Capillary refill time as a surrogate for perfusion is a zero-cost test and compares favorably to lactate testing in its impact on outcomes.[44]

Oxygen as a first-line therapy. Pulse oximetry-guided oxygen saves lives but has historically been underused in curricula and guidelines. The recent oxygen utilization guidance and work on closing the global oxygen gap by the World Health Organization (WHO) highlight scalable approaches: robust concentrators, basic distribution systems, and routine pulse oximetry monitoring in EDs, maternity, and pediatric wards.[63,64] If invasive ventilation is available and required, the standardized use of lung-protective settings (6 mL/kg predicted body weight, plateau <30 cm H_2O) is recommended.[78,79] When invasive ventilation is unavailable, high-flow nasal cannula oxygenation, NIV, awake proning (when safe), and conservative fluids may represent the best available strategies.[80]

Antimicrobial therapy and source control. Seriously ill patients, particularly those in shock, can benefit from the early administration of broad-spectrum antibiotics (ideally within an hour); when severity is uncertain, a brief focused assessment is appropriate.[4,41] Awareness of local antibiograms is likely to improve the impact of empiric therapy, as will expanding clinical microbiology capabilities as described earlier. Source control, ideally with 6 hours, is similarly likely to improve patient outcomes. POCUS may be a useful adjunct to the physical examination to identify foci of infection, for example, abscess and empyema, and guide drainage when radiology capacity is limited. Early referral to a center with core surgical capabilities will be necessary if bedside source control cannot be obtained.[34]

SUMMARY

Identifying gaps and strategies in sepsis care in LRS is easy; filling those gaps is hard. There is a marked shortage of intensivists, critical care nurses, respiratory therapists, and biomedical technicians in many, if not most, LRS. Many of these staff members are concentrated in tertiary care centers, which leaves the district hospitals (where many septic patients first present) with limited staff.[81,82] International guidelines and clinical trials may not reflect the populations, diseases, and needs of LRS, highlighting a marked need for research and protocols that incorporate local epidemiology and resource profiles.[81–83]

The year 2025 has seen major cuts in global health funding by wealthy countries, notably including but not limited to the United States and the United Kingdom. The termination of funding by the United States Agency for International Development alone may contribute to over 14 million additional deaths by 2030, including nearly 4.5 million children less than the age of 5 years, with notable increases in deaths due to malaria, human immunodeficiency virus (HIV), tuberculosis, and other neglected diseases.[84] Similarly, the United Kingdom has reduced funding for international health development assistance by more than 30% since 2021.[85] In this context, any improvements in sepsis care in LRS will require new forms of support, including national governments, nongovernmental organizations, and academic institutions, including professional societies. Research and guidelines produced in Africa, Latin America, and Asia have the potential to make significant strides in sepsis care, provided the necessary resources are available to implement these advances.[41,86–89]

CLINICS CARE POINTS

- Sepsis causes nearly 50 million cases and 11 million deaths annually, with ~ 80% occurring in low-resource settings (LRS).
- Early recognition is limited by diagnostic scarcity; context-specific tools (eg, Universal Vital Assessment score, bedside signs, and point-of-care lactate) may improve detection.
- Antimicrobial therapy is lifesaving but challenged by delayed recognition, high antimicrobial resistance, and limited microbiology capacity.
- Source control is often delayed due to surgical workforce and infrastructure shortages; decentralizing emergency surgical care is vital.
- Fluid resuscitation strategies from high-income settings may cause harm in LRS; cautious, physiology-guided boluses with early vasopressors are recommended.
- Oxygen therapy remains the most common support needed; concentrators, solar power, and improved oximetry access are crucial to reducing mortality.
- Advanced extracorporeal support (eg, extracorporeal membrane oxygenation and dialysis) is largely unavailable; lower-cost alternatives like peritoneal dialysis may be feasible.
- Sustainable improvement requires health system strengthening, workforce training, context-appropriate guidelines, and global funding support.

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