

**MICROBIAL EPIDEMIOLOGY OF SEPSIS AND SEPTIC SHOCK: WORLDWIDE, SOUTH ASIA, AND CENTRAL ASIA****Sharma Namrata**

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<https://doi.org/10.5281/zenodo.20279762>

**Abstract:** Sepsis and septic shock remain leading causes of illness and death worldwide and represent final pathways of severe infection by diverse pathogens. The microbial causes of sepsis are continually evolving, driven by patterns of antibiotic use, health-care practices, vaccination coverage, and socio-economic conditions. Gram-negative bacilli, Gram-positive cocci, fungi, and, in some settings, viral and parasitic pathogens all contribute, with an increasing share of cases associated with multidrug-resistant (MDR) organisms. This review outlines current concepts and definitions of sepsis and septic shock, summarizes global epidemiology with a focus on South Asia and Central Asia, and examines principal microbial etiologies and resistance profiles. It also reviews key principles of diagnosis, empiric treatment, antimicrobial stewardship, and prevention.

**Keywords:** Microbial Epidemiology of Sepsis and Septic Shock

**Introduction**

Sepsis is currently defined as life-threatening organ dysfunction resulting from a dysregulated host response to infection.<sup>1</sup> Septic shock is considered a more severe subset of sepsis, characterized by profound circulatory, cellular, and metabolic abnormalities and a substantially higher risk of death.<sup>1</sup>

According to the Sepsis-3 adult consensus:<sup>1</sup>

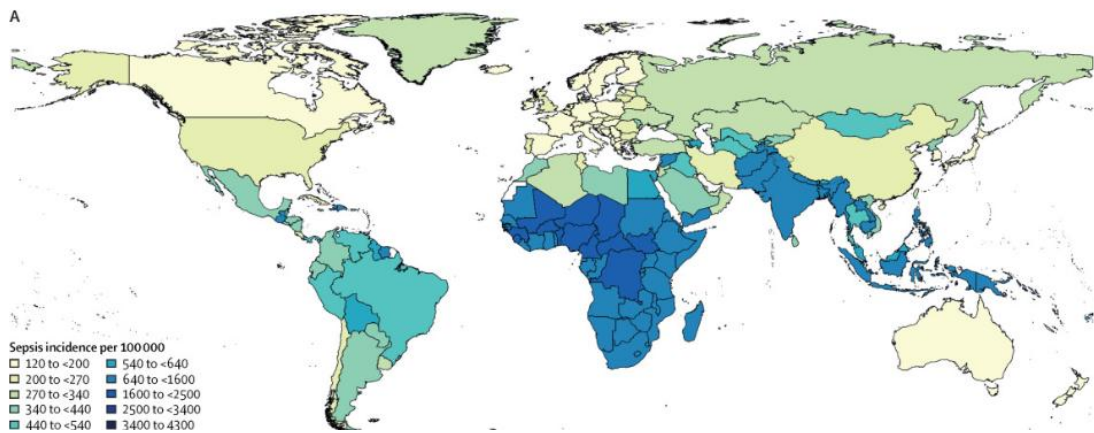
- **Sepsis** is suspected or documented infection accompanied by an acute increase of  $\geq 2$  points in the Sequential Organ Failure Assessment (SOFA) score.
- **Septic shock** is sepsis with persistent hypotension requiring vasopressors to maintain a mean arterial pressure  $\geq 65$  mmHg and a serum lactate level  $> 2$  mmol/L despite adequate fluid resuscitation.

In neonates and children, age-adapted definitions and scores are used, but the underlying concept—organ dysfunction triggered by an abnormal host response to infection—is the same.<sup>2,3</sup> From a microbiological standpoint, sepsis represents invasive infection by a broad array of organisms, with the spectrum varying by geography, age, and health-care context.

**Global Epidemiology of Sepsis and Septic Shock****Incidence and mortality**

Global estimates are hampered by heterogeneous definitions, coding practices, and health-system capacity. Using Global Burden of Disease data, a large modelling study estimated for 2017:<sup>4</sup> Approximately **48.9 million** episodes of sepsis. Around **11.0 million** sepsis-related deaths, corresponding to nearly **one in five** deaths worldwide.

The highest incidence and mortality rates are observed in sub-Saharan Africa, Oceania, South Asia, and parts of East and Central Asia, where infectious diseases are common and access to critical care is constrained.<sup>4,5</sup>



**Vulnerable groups;** Neonates, infants, older adults, and immunocompromised individuals have the highest risk of sepsis and death.<sup>2,5</sup> In many low- and middle-income countries (LMICs), neonatal and pediatric sepsis remain leading causes of preventable mortality.<sup>2,5,6</sup>

**Community-acquired versus health-care-associated sepsis,** Sepsis may originate in the community or within health-care facilities:<sup>5,7</sup> Community-acquired sepsis commonly arises from pneumonia, urinary tract infections, intra-abdominal infections, or skin and soft-tissue infections.

**Hospital-acquired and ICU-associated sepsis** is frequently related to invasive devices (central venous catheters, urinary catheters, ventilators), surgery, and prior broad-spectrum antibiotic exposure, and is more likely to involve resistant organisms.

In low-resource settings, community-acquired infections predominate because many patients never reach advanced hospital care.

**Microbial Etiology of Sepsis and Septic Shock;** The organisms that cause sepsis differ across regions and over time, but several consistent patterns have been described.<sup>5,7-9</sup>

**Gram-negative bacteria** Common Gram-negative pathogens include:

*Escherichia coli*, *Klebsiella* species, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Enterobacter* species

These organisms frequently cause sepsis originating from the urinary tract, abdomen, lungs, and hospital-acquired infections. High rates of extended-spectrum  $\beta$ -lactamase (ESBL) production and carbapenem resistance—especially in *Klebsiella* and *Acinetobacter*—are a major concern in many regions.<sup>9-11</sup>

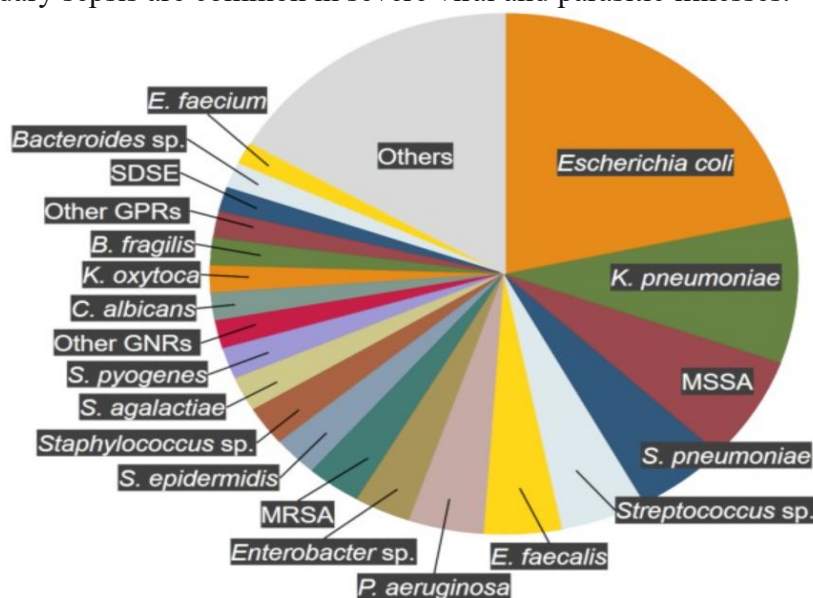
**Gram-positive bacterial**

- *Staphylococcus aureus* (including methicillin-resistant *S. aureus* [MRSA])
- Coagulase-negative staphylococci (notably in catheter-related and neonatal sepsis)
- *Streptococcus pneumoniae*,  $\beta$ -haemolytic streptococci (e.g. group A *Streptococcus*), *Enterococcus* species (including vancomycin-resistant *Enterococcus* [VRE])

Gram-positive organisms remain important causes of community-acquired pneumonia-related sepsis and of bloodstream infections associated with health care. Pneumococcal vaccination has modified *S. pneumoniae* disease patterns in many high-income countries, though substantial global burden persists.<sup>8,12</sup>

**Fungal sepsis;** Invasive fungal infections, particularly due to *Candida* and *Aspergillus* species, are important causes of sepsis in ICU patients and in those with significant immunosuppression.<sup>13</sup> Non-albicans *Candida* species and azole-resistant strains are increasingly reported, including in LMICs. *Candida auris* has emerged as a multidrug-resistant pathogen responsible for nosocomial outbreaks in several regions, notably in South Asia.<sup>13,14</sup>

**Viral and parasitic infections,** Severe viral infections (e.g. influenza, SARS-CoV-2, dengue) can lead to sepsis or sepsis-like syndromes characterized by systemic inflammation and multi-organ failure.<sup>15</sup> In malaria-endemic areas, severe *Plasmodium falciparum* malaria may present with features fulfilling sepsis or septic shock criteria.<sup>16</sup> Bacterial co-infection and secondary sepsis are common in severe viral and parasitic illnesses.



### Antimicrobial Resistance and Its Impact on Sepsis

Antimicrobial resistance (AMR) is central to sepsis outcomes because it delays appropriate therapy and is associated with increased mortality.<sup>9–11</sup> ESBL-producing Enterobacterales, carbapenem-resistant *Klebsiella* and *Acinetobacter*, MRSA, and VRE are prominent threats. In many LMICs, widespread empiric use of broad-spectrum antibiotics, over-the-counter availability, and weak stewardship measures fuel resistance. Data from the Global Antimicrobial Resistance Surveillance System (GLASS) and other surveillance networks demonstrate particularly high burdens of AMR in South Asia and parts of Central Asia.<sup>10,11,17</sup>

### South Asia: Epidemiology and Microbial Patterns

South Asia (India, Pakistan, Bangladesh, Nepal, Sri Lanka, Bhutan, Maldives) carries a heavy burden of infection-related sepsis, with large populations, variable sanitation, limited intensive care capacity, and high AMR prevalence.<sup>10,11,18</sup>

**Burden of sepsis;** Comprehensive population-level sepsis data are scarce, but hospital and ICU studies from India, Pakistan, and Bangladesh show high sepsis and septic shock rates, with ICU mortality often exceeding 30–40%.<sup>18–20</sup> Neonatal sepsis is a major cause of mortality,

particularly where home deliveries, suboptimal cord care, and delayed presentation are common.<sup>6, 21</sup>

**Microbial spectrum;** Frequently identified pathogens in South Asian sepsis include:<sup>10, 11, 18–22</sup>. Gram-negative bacilli: *K. pneumoniae*, *E. coli*, *P. aeruginosa*, *Acinetobacter* spp. Gram-positive cocci: *S. aureus* (including MRSA), coagulase-negative staphylococci, *Enterococcus* spp. Neonatal sepsis organisms: *Klebsiella*, *E. coli*, *S. aureus*, *Acinetobacter*, and in some settings *Streptococcus agalactiae*. Fungi: *Candida* spp., including *C. tropicalis* and *C. auris*, especially in intensive care units. Notably, ESBL-producing Enterobacterales, carbapenem-resistant *Klebsiella* and *Acinetobacter*, and MDR *P. aeruginosa* are widely reported.<sup>10, 11, 18–20</sup>

### **Contributing factors and system constraints**

Extensive use and misuse of broad-spectrum antibiotics in human medicine, animal production, and agriculture. Easy access to antibiotics without prescription and weak regulatory enforcement. Overcrowded facilities and gaps in infection prevention and control (IPC). Limited microbiology infrastructure and delayed or incomplete culture results. These factors complicate empirical therapy and, together with late presentation, contribute to high mortality.

### **Central Asia: Epidemiology and Microbial Features**

Central Asia (Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, Uzbekistan) has experienced significant political and health-system changes since the early 1990s. Systematic sepsis surveillance is limited, but available data provide some insight.<sup>17, 23</sup>

**Pathogens and resistance patterns;** Hospital-based studies indicate:<sup>17, 23–25</sup>

- Predominant roles for Gram-negative bacilli (*E. coli*, *Klebsiella*, *P. aeruginosa*, *Acinetobacter*) and Gram-positive cocci (*S. aureus*, coagulase-negative staphylococci, *Enterococcus* spp.).

- High frequencies of ESBL-producing Enterobacterales and rising carbapenem resistance among *Klebsiella* and *Acinetobacter* spp.

- Variable but concerning levels of MRSA and VRE.

Microbiology and IPC capacity differ widely across and within countries, with some tertiary centres equipped with modern laboratories and stewardship programs, and others operating with limited infrastructure.

### **Diagnosis: Microbiology and Biomarkers**

Prompt identification of the causative organism and its susceptibility profile is central to optimizing sepsis treatment.<sup>1, 7, 9</sup>

#### **Microbiological investigations**

- **Blood cultures** remain the primary tool for detecting bloodstream pathogens, though sensitivity is imperfect, especially in patients pre-treated with antibiotics.

- Cultures from likely infection sites (urine, respiratory secretions, cerebrospinal fluid, intra-abdominal samples, wounds) increase diagnostic yield.

• In many LMICs, challenges include limited access to reliable culture systems, lengthy turnaround times, and incomplete or absent susceptibility data.<sup>9–11</sup>

### **Rapid and molecular diagnostics**

• Automated blood culture systems and MALDI-TOF mass spectrometry shorten time from culture positivity to organism identification in settings where they are available.

• Multiplex PCR panels and other rapid molecular tests can detect multiple bacterial, viral, and fungal pathogens directly from clinical specimens, but cost and infrastructural needs limit their current use in many South and Central Asian hospitals.

### **Empirical Therapy and Antimicrobial Stewardship**

**Principles of empiric treatment;** Initial antimicrobial therapy in suspected sepsis must be:<sup>1, 7, 9</sup>

- **Rapidly initiated** once sepsis or septic shock is recognized.
- **Sufficiently broad** to cover likely organisms and regional resistance patterns.
- **Adapted** as microbiology results become available.

### **Antimicrobial stewardship**

Effective stewardship programs aim to optimize antibiotic use by:<sup>9–11, 17</sup>

- Promoting appropriate empiric choices and encouraging de-escalation based on culture results.
- Limiting treatment duration to the shortest effective course.
- Reducing unnecessary broad-spectrum or combination therapy.
- Integrating up-to-date microbiology and resistance data into clinical decision-making.

Even in resource-constrained settings, simple measures—standardized prescribing guidelines, regular audit and feedback, and restricted access to last-line agents—can have meaningful impact.

### **Prevention and Infection Control**

Reducing the incidence of sepsis and septic shock requires a combination of public health and hospital-based interventions.<sup>5, 7, 12</sup>

• **Vaccination:** Pneumococcal, Haemophilus influenzae type b, meningococcal, influenza, and COVID-19 vaccines lower the incidence of severe infections that can progress to sepsis.

• **Water, sanitation, and hygiene (WASH)** interventions decrease diarrhoeal and other infections in communities.



• **Infection prevention and control (IPC) in health facilities:** effective hand hygiene, aseptic insertion and maintenance of invasive devices, adherence to surgical bundles, environmental cleaning, and isolation precautions for MDR organisms.

### Conclusion

Sepsis and septic shock continue to pose a major global health challenge and reflect a diverse array of bacterial, fungal, viral, and parasitic infections. The pathogen profile is increasingly dominated by multidrug-resistant Gram-negative bacilli and resistant Gram-positive cocci, especially in high-burden regions such as South Asia and parts of Central Asia. Limited diagnostic resources, a high prevalence of AMR, and constrained critical-care capacity complicate timely recognition and optimal management. Improving sepsis outcomes will depend on strengthening microbiology and AMR surveillance, broadening access to rapid diagnostics, implementing context-appropriate antimicrobial stewardship, and investing in prevention through vaccination, IPC, and fundamental public health measures. Coordinated global and regional actions can yield substantial reductions in sepsis-related morbidity and mortality.

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