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Unraveling Sepsis Epidemiology in a Low- and Middle-Income Intensive Care Setting Reveals the Alarming Burden of Tropical Infections and Antimicrobial Resistance: A Prospective Observational Study (MARS-India)

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Background. Our study addresses the sepsis research gap in lower- and middle-income countries, notably India. Here, we investigate community-acquired sepsis comprehensively and explore the impact of tropical microbiology on etiology and outcomes.

Methods. MARS-India was a prospective observational study from December 2018 to September 2022 in a tertiary-care hospital in South India. Adult patients within 24 hours of intensive care unit (ICU) admission meeting the Sepsis-3 definition were enrolled, with 6 months of follow-up.

Results. More than 4000 patients were screened on ICU admission, with 1000 unique patients meeting the inclusion criteria. Median age was 55 (interquartile range, 44–65) years, with a male preponderance (66%). Almost half the cohort resided in villages (46.5%) and 74.6% worked in the primary sector. Mortality in-hospital was 24.1%. Overall, about 54% had confirmed microbiological diagnosis and >18% had a viral cause of sepsis. Surprisingly, we identified leptospirosis (10.6%), scrub typhus (4.1%), dengue (3.7%), and Kyasanur forest disease (1.6%) as notable causes of sepsis. All of these infections showed seasonal variation around the monsoon. In community-acquired infections, we observed substantial resistance to third-generation cephalosporins and carbapenems.

Conclusions. In India, sepsis disproportionally affects a younger and lower-socioeconomic demographic, yielding high mortality. Tropical and viral sepsis carry a significant burden. Analyzing local data, we pinpoint priorities for public health and resources, offering valuable insights for global sepsis research.

Clinical Trials Registration. NCT03727243.

Keywords. sepsis; LMIC; tropical infection; AMR; ICU.

The Third International Consensus Definition for Sepsis (Sepsis-3) definition has for the first time included dysregulated host response to infection as the cause of organ dysfunction [1]. However, sepsis remains a highly heterogenous syndrome with new guidelines ignoring the role of pathogens and antimicrobial resistance (AMR), especially in lower-socioeconomic settings where 85% of the sepsis burden resides [2]. This heterogeneity is an impediment to both research and clinical practice, with the recent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic further illustrating the critical importance of adopting global approaches to foster more comprehensive and equitable discoveries [3, 4].

In 2017, the Global Burden of Diseases study estimated 48.9 million cases of sepsis and 11 million deaths worldwide, with

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India contributing 26.4% of global sepsis-related deaths [2]. Despite these figures, no data from South Asia or Africa were used in modeling. Hence, improving understanding of patient demographics, causative pathogens, and treatment outcomes is crucial for developing region-specific approaches to combat sepsis [5].

So far, studies on the causes of sepsis among patients admitted to Indian intensive care units (ICUs) are limited, with some 56.4% of patients admitted to Indian ICUs experiencing sepsis [6]. However, most are point prevalence studies, potentially underestimating certain causative agents due to seasonal variations [6–8]. Furthermore, many studies only focus on bacterial sepsis, providing limited data on community-acquired causes and AMR [6–9]. This skews our understanding of the true sepsis burden.

Here, the Molecular Diagnosis and Risk Stratification of Sepsis in India (MARS-India) study provides an in-depth description of a large cohort of patients with sepsis, prospectively recruited in a tertiary-care academic hospital in South India, and gives insights into patient characteristics, causative agents, outcomes, seasonal variation, and AMR.

METHODS

Study Design and Population

The present study was conducted as part of the MARS-India project (ClinicalTrials.gov identifier NCT03727243), a prospective longitudinal observational study undertaken at a tertiary-care academic hospital in Manipal, Karnataka, India. The study focused on patients admitted to mixed ICUs of Kasturba Medical College, spanning the period from December 2018 to November 2022. The cohort included 1000 adult patients (>18 years) with patients. For inclusion, patients were identified based on the Sepsis-3 criteria [1]. Specifically, individuals suspected of infection within 24 hours of admission to the ICU, accompanied by an increased Sequential Organ Failure Assessment (SOFA) score of ≥2, were categorized as having sepsis.

Exclusion criteria included pregnant/breastfeeding women, "withdrawal of care" decision at enrollment, anticipated ICU stay <24 hours, extracorporeal circulation in the preceding month, restricted liberty or under legal protection, expected lifespan of <3 months due to comorbidities, blood transfusion >4 units in the past week, inability to consent by the patient or next of kin, previous enrollment, or transfer from another hospital ICU (stay >24 hours) or ward (stay >72 hours). This study conformed to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (Supplementary Appendix, pages 12–14). The study was approved by the local ethics committee (Kasturba Medical College and Kasturba Hospital Institutional Ethics Committee: IEC: 371/2018; approval date: 12/06/2018), Institutional Biosafety Committee, and Health Ministry Screening Committee, Ministry of Health and Family Welfare, Government of India (project approval number 2020–9817). Written informed consent was obtained from all patients or their legal representative.

Data Collection and Definitions

Dedicated and trained personnel prospectively collected patient data. Demographic, clinical, radiological, microbiological, and therapeutic data were collected from ICU to hospital discharge. Patients had telephone follow-up at 3 and 6 months after ICU admission. SOFA scores were calculated for the day of inclusion. Outcomes at discharge, such as length of stay, organ supportive therapy, nosocomial infections, and mortality, were recorded. Data were collected using premade case report forms in the online Castor electronic data capture system.

Prospective data collection resulted in limited missing data. Patients lost to follow-up after hospital discharge were still analyzed for earlier time points but excluded for analyses at 3 months. When calculating the SOFA and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, we assumed that the absence of measurement indicated an optimal condition, implying no evident clinical suspicion of failure.

According to the Sepsis-3 criteria, sepsis was defined as a clinical suspicion of infection and ΔSOFA score ≥2, while shock was defined as a serum lactate >2 mmol/L and vasopressor requirement. The primary infection site was established through a comprehensive assessment of discharge summaries, clinical observations, and microbiological and radiological findings. Causative microorganisms were classified based on all microbiology results [10, 11]. Diagnosis and identification of the causative pathogen were determined based on the opinion of the attending physician in the discharge letter and an investigator. In cases where the investigator encountered uncertainty after evaluating the clinical, laboratory, and radiological data, consensus was reached between clinical infectious disease and microbiology study physicians (J. J. B., H. S. V., W. J. W., and C. M.). Causative pathogens were defined as positive microbiology <48 hours, or a positive test from agents not typically contracted in the hospital (*Leptospira* sp, *Orientia tsutsugamushi*, Kyasanur forest disease virus (KFDV), or *Burkholderia pseudomallei*). Hospital-acquired infections were defined as an infection that was not present at hospital admission and developed at least 48 hours thereafter. Reactivation of latent infections and colonization were excluded [12]. Systemic infection was defined as a bloodstream infection without a primary focus or infectious syndrome without a clear singular focus or origin of infection.

Microbiological Processing

Microbiological investigations were requested at the discretion of the attending physician. All specimens and blood cultures

were taken and handled by experienced personnel. A range of specific serological and polymerase chain reaction testing was performed for certain pathogens (Supplementary Table 1).

Statistical Analysis

Statistical analyses were performed using R software (4.1.0). Differences between groups were tested using Mann-Whitney *U* test, Fisher exact test, and χ^2 test, as appropriate. Details of missingness of clinical variables and routine laboratory values as well as differences between patients lost to follow-up and patients with a known mortality status at 3 months are described in Supplementary Tables 2 and 3. We used Benjamini-Hochberg correction for multiple testing. All results are presented as median and interquartile range (IQR) or number and percentage, as appropriate. All statistical tests were 2-tailed, with $P < .05$ considered statistically significant.

Role of the Funding Source

The funders of the study had no role in study design, data collection, data analysis, interpretation, or writing of the report. Only the primary study investigator and study coordinator had access to the entire database. All authors had full access to all anonymized summary study data and take final responsibility for the decision to submit for publication.

RESULTS

Within 24 hours of ICU admission, screening was conducted for >4000 patients. Among these, 1446 were found to be eligible, and 1122 (77.6%) were subsequently enrolled (Supplementary Figure 1). Of these 1122 enrolled patients, 1000 unique patients (89.1%) fulfilled the Sepsis-3 criteria at ICU admission (Supplementary Figure 1). The 122 other patients were ICU patients without a clinical suspicion of infection and included as a control group for future studies. Median age was 55 (IQR, 44–65) years, with a male preponderance (663 [66.3%]) (Table 1). The majority of patients lived outside urban areas, with 23.7% living in towns and 46.5% residing in villages. Approximately half of the patients exhibited minimal to no formal education (Supplementary Table 4). The majority of patients worked in the primary sector (74.6%) (Supplementary Table 4). The median duration of symptoms before ICU admission was 4 (IQR, 3–7) days. Two-thirds of patients had a comorbidity, with median Charlson Comorbidity Index score of 2.0 (IQR, 0–3). The most common comorbidities included hypertension (n = 367 [36.7%]), diabetes mellitus type 2 (n = 352 [35.2%]), and cardiovascular disease (n = 140 [14.0%]). Human immunodeficiency virus (HIV) prevalence in this cohort was 1.8%. The median APACHE II score of patients on ICU admission was 13 (IQR, 9–19), and the median SOFA score was 6 (IQR, 4–9). Septic shock, defined as lactate >2 mmol/L and necessity of inotropic support, was present in 389 patients (38.9%) [1]. One hundred eighty-one patients (18.1%) had a prior hospital admission within the year of their current admission, with 106 patients (58.6%) admitted due to infections (Supplementary Table 5).

Table 1. Baseline Characteristics of Patients With Sepsis on Intensive Care Unit Admission (N = 1000)

Baseline Characteristics	No. (%)
Age, y, median (IQR)	55 (44–65)
Male sex	663 (66.3)
Duration of symptoms, d, median (IQR)	4 (3–7)
Comorbidities	
Any comorbidities	593 (59.3)
Hypertension[a]	367 (36.7)
Type 2 diabetes mellitus	352 (35.2)
Cardiovascular disease[b]	140 (14.0)
Chronic lung disease	98 (9.8)
Chronic kidney disease	64 (6.4)
Chronic liver disease	65 (6.5)
Immunocompromised	52 (5.2)
Malignancy	23 (2.3)
HIV	18 (1.8)
Autoimmune disorder	11 (1.1)
Psychiatric disorder	14 (1.4)
CCI score, median (IQR)	2 (0–3)
Severity	
APACHE II score, median (IQR)	13 (9–19)
SOFA score, median (IQR)	6 (4–9)
Arterial lactate within 24 h of admission[c]	
>2 mmol/L	564 (56.4)
<2 mmol/L	325 (32.5)
Mechanical ventilation on admission	401 (40.1)
Inotropic support on admission	560 (56.0)
Septic shock	389 (38.9)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; CCI, Charlson Comorbidity Index; HIV, human immunodeficiency virus; IQR, interquartile range; SOFA, Sequential Organ Failure Assessment.

[a]Hypertension only included patients using anti-hypertensive medication.

[b]Includes ischemic heart disease, past cerebrovascular accident, arrhythmia, congestive heart failure, and peripheral vascular disease.

[c]In 111 patients, arterial lactate was not measured within 24 hours of hospital admission.

The median length of ICU stay was 4 (IQR, 2–8) days, and the median length of hospital stay was 8.7 (IQR, 4.8–13.9) days (Table 2). Surgery during ICU stay was performed in 62 patients (6.2%). In-hospital mortality reached 24.1%, and 11.9% of patients were discharged against medical advice. Of the 668 patients (66.8%) with known follow-up status after 3 months, 270 patients (40.4%) had died. Three months after hospitalization, 59 of the 391 known surviving patients (15.5%) were readmitted to a hospital.

Most patients had a systemic infection (n = 494 [49.4%]), followed by respiratory (n = 301 [30.1%]), urinary tract (n = 106 [10.6%]), skin and soft tissue infection (SSTI) (n = 94 [9.4%]), abdominal (n = 59 [5.9%]), and central nervous system (n = 25 [2.5%]) (Figure 1; Supplementary Table 6). Multiple sources of infection at ICU admission were found in 76

Table 2. Treatment, Disease Course, and Outcome of Sepsis Patients After Intensive Care Unit Admission (N = 1000)

Outcomes	No. (%)
Organ supportive therapy	
Supplementary oxygen therapy	780 (78.0)
Received noninvasive ventilation	236 (23.6)
Received mechanical ventilation	456 (45.7)
Length of mechanical ventilation, d, median (IQR)	2.3 (1.1–5.1)
Received vasopressor therapy	579 (57.9)
Received renal replacement therapy	170 (21.3)
Surgery while in ICU[a]	62 (6.2)
Outcomes	
Length of ICU stay, d, median (IQR)	4.09 (2.1–7.6)
Length of hospital stay, d, median (IQR)	8.73 (4.8–13.9)
Nosocomial infections	139 (13.9)
Hospital mortality	241 (24.1)
3-mo mortality (missing: n = 225)	287 (37.0)
Hospital readmissions[b] in 90 d (missing: n = 378)	59 (15.5)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: ICU, intensive care unit; IQR, interquartile range.

[a]This included debridement of necrotic tissue, stent placement, kidney stone removal, and surgery due to injuries prior to hospital admission.

[b]Percentage of readmissions was calculated on the entire cohort that survived initial hospitalization.

(7.6%) patients. Twenty-seven patients (34.2%) had a systemic and respiratory infection, 12 patients (15.8%) had a systemic infection and SSTI, 8 patients (10.5%) had a respiratory infection and urinary tract infection, and 8 patients (10.5%) had respiratory infections and SSTI.

A causative agent could be identified in 54% of patients. Sepsis was caused by bacteria in 382 patients (70.7%), viruses in 188 patients (34.8%), or fungi in 5 patients (0.9%). No cases of malaria were detected. Eighty-two (15.2%) presented with multiple causative agents, among which bacterial–bacterial coinfections were detected in 43 patients (52.4%), viral–bacterial coinfections in 33 cases (40.2%), and viral–viral in only 4 cases (4.9%). Of the 431 detected bacteria, 82 (19.0%) were gram-positive and 189 (43.9%) were gram-negative. *Escherichia coli* was the most frequently isolated gram-negative bacterium (n = 99 [52.3%]), followed by *Klebsiella pneumoniae* (n = 44 [23.3%]), *Pseudomonas aeruginosa* (n = 10 [5.3%]), and *Burkholderia pseudomallei* (n = 7 [3.7%]). Among the 82 gram-positive cultures, *Staphylococcus aureus* (n = 25 [30.5%]), *Streptococcus pyogenes* (n = 17 [20.7%]), *Enterococcus faecalis* (n = 10 [12.2%]), and *Streptococcus pneumoniae* (n = 9 [11.0%]) were most commonly isolated. *Leptospira* sp and *Orientia tsutsugamushi* were highly prevalent, with 106 (24.6%) and 41 (9.5%) positive bacterial cases, respectively. Viral sepsis was caused by influenza (n = 75 [37.9%]) and SARS-CoV-2 (n = 52 [25.8%]). Interestingly, tropical viruses such as dengue virus and KFDV had a significant impact on the case load of viral sepsis with 37 (18.7%) and 16 (8.1%) cases, respectively. Five cultures were positive for fungi (Supplementary Table 7). Of the 82 cases with multiple causative agents, *Leptospira* sp (n = 31 [37.8%]) and *E coli* (n = 22 [26.8%]) were the most frequently detected in patients with mixed infections.

Since ICUs are major foci of AMR within the hospital, we next determined the antibiotic resistance rates. *Escherichia coli*, *K pneumoniae*, and *P aeruginosa* were the most important gram-negative bacteria in community-acquired infections. Analysis of these bacteria showed high levels of resistance with 75.8% of *E coli* (n = 75), 47.7% of *K pneumoniae* (n = 21), and 30% of *P aeruginosa* (n = 3) being resistant to third-generation cephalosporins and 10.1% (n = 10), 13.6% (n = 6), and 10.0% (n = 1) to carbapenems, respectively (Table 3). Additionally, 36.0% (n = 9) of *S aureus* were methicillin resistant.

Showing seasonality of tropical infections, *Leptospira* sp, *O tsutsugamushi*, dengue, and KFDV exhibited annual correlations with precipitation. First, *Leptospira* sp cases increased throughout the monsoon, which spans from July until September. Scrub typhus cases seemed to spike post-monsoon, while dengue peaked in the middle of the monsoon, with cases dropping to almost none for the rest of the year. In contrast, KFDV cases mainly spiked in March and April, the driest months of the year in this region (Supplementary Figure 2).

DISCUSSION

In this large prospective observational cohort, we provide novel insights into several aspects of ICU care for patients with sepsis in a low- and middle-income country (LMIC) setting. Notably, sepsis disproportionally affects a younger and lower-socioeconomic demographic population, who are faced with a substantial mortality risk. Our study highlights the burden of tropical infections, such as leptospirosis, scrub typhus, dengue, and KFDV, which significantly impact ICU case load and show distinct seasonal variation.

To our knowledge, this is one of the first studies in South Asia thus far to provide an in-depth description of the causes, patient characteristics, and outcomes of primarily community-acquired sepsis. Our study underscores the notable distinctions in both patient characteristics and microbiological profiles when compared to cohorts in high-income countries (HICs) and emphasizes the importance of observational studies to highlight and recognize these differences in this population. The finding that approximately 50% of our cohort is either illiterate or has only primary education, compared to the regional rate of 43.3%, further emphasizes the burden placed on the lower-socioeconomic demographic in society [13].

Comorbidities in our cohort differ from those in HIC sepsis cohorts. For example, HIC cohorts show lower prevalence of diabetes and higher prevalence of immunosuppression and malignancies [14, 15]. Our findings are in accordance with other studies on sepsis in Indian ICUs with a similar low prevalence of

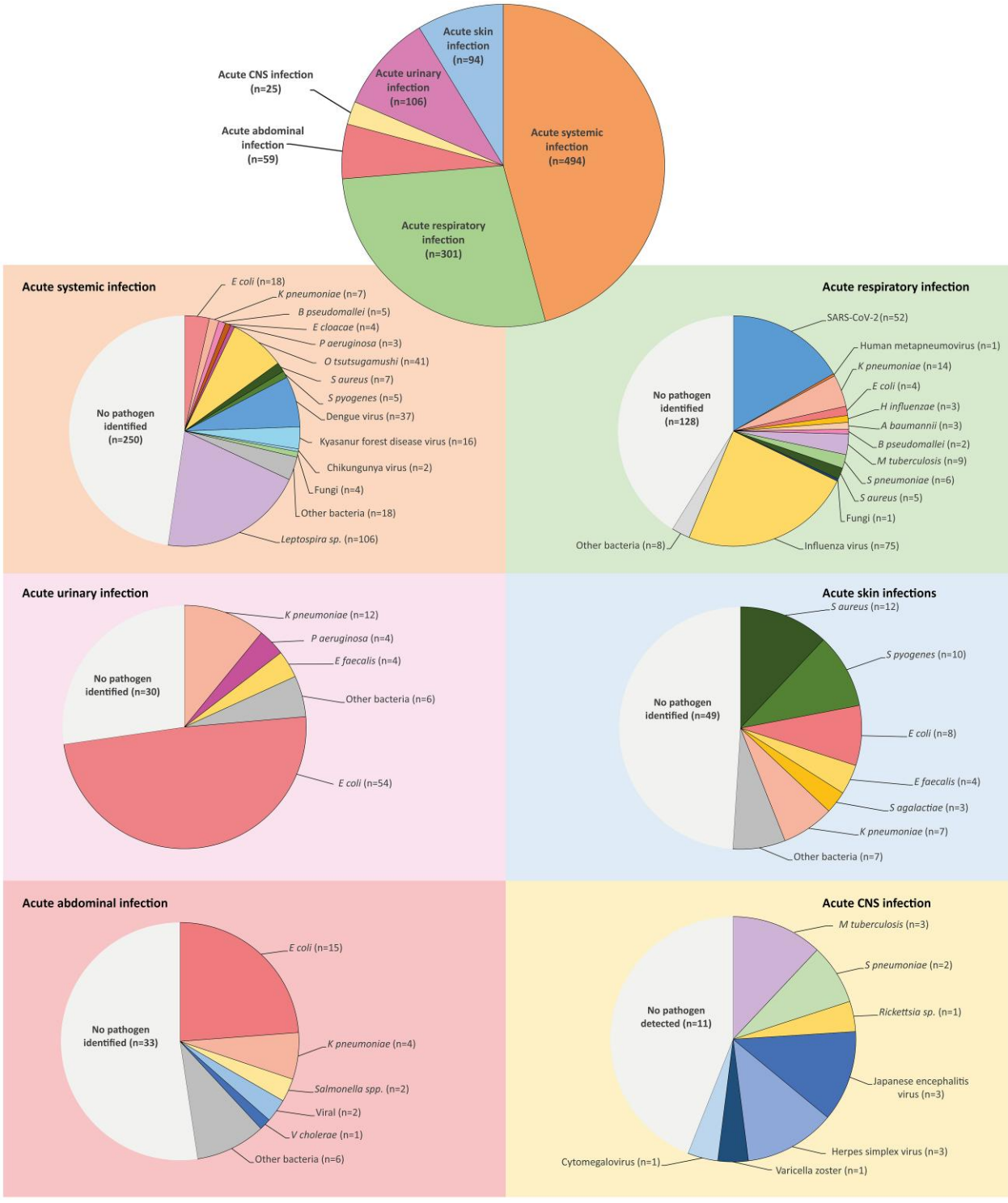

Figure 1. Distribution of clinical presentation and pathogens identified in 1000 patients with sepsis. Numbers in parentheses are number of clinical presentations of each pathogen identified. In some patients, >1 clinical presentation or >1 pathogen was identified. Abbreviations: *A. baumannii*, *Acinetobacter baumannii*; *B. pseudomallei*, *Burkholderia pseudomallei*; CNS, central nervous system; *E. cloacae*, *Enterobacter cloacae*; *E. faecalis*, *Enterococcus faecalis*; *E. coli*, *Escherichia coli*; *H. influenzae*, *Haemophilus influenzae*; *K. pneumoniae*, *Klebsiella pneumoniae*; *M. tuberculosis*, *Mycobacterium tuberculosis*; *O. tsutsugamushi*, *Orientia tsutsugamushi*; *P. aeruginosa*, *Pseudomonas aeruginosa*; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; *S. aureus*, *Staphylococcus aureus*; *S. agalactiae*, *Streptococcus agalactiae*; *S. pneumoniae*, *Streptococcus pneumoniae*; *S. pyogenes*, *Streptococcus pyogenes*; *V. cholerae*, *Vibrio cholerae*.

Table 3. Resistance Data of Common Bacterial Causative Agents

Community-Acquired Infection	No. (%) of Resistant Isolates
Gram-negative	
Escherichia coli (n = 99)	
Third-generation cephalosporins	75/93 (75.8)
Carbapenems	10/54 (10.1)
Klebsiella pneumoniae (n = 44)	
Third-generation cephalosporins	21/40 (47.7)
Carbapenems	6/13 (13.6)
Pseudomonas aeruginosa (n = 10)	
Third-generation cephalosporins	3/10 (30.0)
Carbapenems	1/5 (10.0)
Gram-positive	
Staphylococcus aureus (n = 25)	
Methicillin resistant	9/25 (36.0)

The numbers presented in this table denote the count of pathogens resistant to third-generation cephalosporins, carbapenems, methicillin, and vancomycin, respectively. Percentages indicate the proportion of known resistance relative to the entire group. It is important to note that certain samples have not undergone testing.

malignancies, ranging from 2.7% to 12.8%, while the prevalence of diabetes is varied throughout these cohorts, ranging from 13.7% to 59.2% [6–9]. In addition, a large cross-sectional study in 22 different Asian countries reported a high prevalence of diabetes among septic ICU patients of 33.5%, highlighting the importance of diabetes as a comorbidity in sepsis across Asia [16]. This warrants attention given that the prevalence of diabetes in South Asia is predicted to increase by 69% by 2045 [17]. In contrast, sepsis studies from sub-Saharan Africa report diabetes as comorbidity in <10% of cases, compared with a higher HIV prevalence, which can be present in >50% of cases [18–20]. The HIV prevalence in our study is a reflection of the low HIV prevalence in Karnataka, where only 0.46% of adults suffer from HIV [21], which likely explains the low incidence of tuberculosis causing sepsis.

Our findings underscore the heightened significance of gram-negative bacteria in sepsis, surpassing the contribution of gram-positive bacteria in this Indian cohort. This aligns with the Management of Severe sepsis in Asia's Intensive Care unitS II study (MOZAICS II) and Extended Prevalence of Infection in Intensive Care II study (EPIC II), where gram-negative bacteria caused 51.4% and 76.4% of Asian sepsis cases, compared to 43.9%–61.0% in Japan, Australia, North America, and Western Europe [14, 15, 22, 23]. In 2019, the World Health Organization introduced a novel Sustainable Development Goal indicator to monitor AMR. Our sepsis cohort exceeded global median rates for methicillin-resistant *S aureus* (12.11%) and multidrug-resistant *E coli* (36%) [24].

Our findings highlight the substantial presence of tropical infections within the septic cohort, reflecting the extensive microbiological workup at the study site. Earlier reports on the causative agents of sepsis in India reported that 2.5%–7.2% of patients had a tropical agent [8, 25]. A targeted cohort of 456 patients with tropical fevers from 34 ICUs coordinated by the Indian Society of Critical Care Medicine identified dengue, scrub typhus, malaria, and leptospirosis in 23%, 18.2%, 8.1%, and 1.5%, respectively [26]. A large multinational cross-sectional study of hospitalized patients in Southeast Asia found that 8% had dengue, 6% had leptospirosis, and 6% had scrub typhus [27]. The collective evidence from these studies, coupled with our own findings, indicates underreporting of tropical sepsis within Indian and other LMIC ICUs. Our findings demonstrate a strong correlation between tropical diseases and the monsoon, or the dry season for Kyasanur forest disease, consistent with existing literature [26, 28–30]. In endemic regions, clinicians should be mindful of their high incidence and weather-dependent spikes. Implementing systemic screening and considering empirical treatment that encompasses leptospirosis and scrub typhus may be advisable, supporting clinical guidelines that advocate for a syndromic approach to management [31].

This study highlights the large contribution of viruses as causative agents of sepsis in the ICU. Prior to the advent of coronavirus disease 2019 (COVID-19), viruses only contributed approximately 1% of documented sepsis cases in some studies [32]. Our findings shift this paradigm with almost 1 in 5 cases of community-acquired sepsis being of viral etiology. A recent Southeast Asian study also documented that viruses accounted for 33% of adult sepsis (Sepsis-2 definition) [27]. We partially included from the COVID-19 pandemic period. If we had continued enrolling patients, the percentage of viral infections would likely have been even higher. Viral infections might therefore be overstated due to this large time-dependent effect. Excluding patients with COVID-19, the percentage of septic patients with a viral cause drops to 28%, still emphasizing the significant burden of viruses in sepsis.

Our study has limitations. First, due to its monocentric nature, although it provides an in-depth perspective on sepsis in India and highlights significant differences from other regions globally, the observed trends should not be uniformly applied across all regions of India, given the country's diverse geography. Second, being conducted in an academic hospital, it may preclude generalizability. Nevertheless, since more than half of patients originate from rural areas and many work in the primary sector, there still is reasonable representation from outside urban settings. Third, a significant part of the cohort was discharged against medical advice or lost to follow-up after hospital discharge, potentially misrepresenting early disease mortality and overrepresenting mortality after 3 months. Finally, like most studies during this time, we faced temporary recruitment disruptions during the SARS-CoV-2 pandemic.

This study provides a detailed examination of sepsis in South India and fills important knowledge gaps of the real burden of sepsis in LMICs. South Indian sepsis patients are young and mostly from rural areas. Gram-negative bacteria, viral sepsis, and tropical diseases significantly contribute to the overall case load. High multidrug resistance in community-acquired infections coupled

with rising burden of chronic diseases, particularly diabetes, makes for a potent convergence. These findings provide critical groundwork for strengthening capacity, optimizing resource allocation, and formulating evidence-based treatment guidelines specifically tailored to South India, underscoring the importance of regional epidemiological sepsis research in LMICs.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

Author Contributions. H. S. V., J. J. B., and V. A. E. were involved in data collection, data analysis, and manuscript drafting. S. C., R. I. F., S. M. K., R. V. A., and V. S. were involved in the data collection and manuscript review. J. J. B. performed statistical analysis. H. S. V., J. M. B., S. R., V. K. E., M. D. V., T. v. d. P., W. J. W., and C. M. were involved in the study conception, design, and supervision. H. S. V., V. A. E., and C. M. were involved in obtaining ethical and legal authorizations. W. J. W. and C. M. had full access to all the data in the study; take responsibility for the integrity of the data and the accuracy of the data analysis; and were involved in the study conception and design, data analysis, and manuscript review. All authors confirm that they have had full access to all study data, accepted responsibility for submitting for publication, and read and approved the final manuscript.

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Data availability. A cleaned and finalized database will be stored in a secure institutional archiving system. Access to the data will adhere to the regulations and procedures established by the institution and the Health Ministry Screening Committee, Ministry of Health and Family Welfare, Government of India. Requests for data access should be submitted to the corresponding author. The final decision regarding the sharing of this study data will be made by the Kasturba Medical College–Manipal Academy of Higher Education independent review panel.

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Potential conflicts of interest. The authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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