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Epidemiology, Clinical Features, Management, and Outcomes of ICUs Sepsis in Adult in Lubumbashi, DRC: A Prospective Multicenter Study

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Abstract

Background: Sepsis is a leading cause of ICU mortality, disproportionately affecting low- and middle-income countries (LMICs). However, prospective data from Central Africa, particularly the Democratic Republic of Congo (DRC), remain scarce. This study aimed to describe the epidemiology, clinical characteristics, microbiological profile, management practices, and outcomes of adult patients with sepsis in the intensive care units (ICUs) of Lubumbashi, DRC.

Methods: A prospective multicenter observational study was conducted between January 2021 and December 2023 in three ICUs in Lubumbashi. All adult patients (≥16 years) admitted with suspected infection and meeting Sepsis-3 criteria (acute organ dysfunction) were included. Organ dysfunction was assessed using available Sequential Organ Failure Assessment (SOFA) score components. Data on demographics, comorbidities, clinical severity, microbiological findings, therapeutic interventions, and ICU mortality were collected and analyzed descriptively.

Results: A total of 76 patients were enrolled (mean age 49.1 ± 22.3 years; 52.6% male). Comorbidities were frequent, notably hypertension (46.7%) and diabetes (20.6%). The primary sources of infection were pulmonary (28.6%) and urinary tract (26.0%). Microbiological cultures were positive in 40% of patients; Gram-negative bacteria predominated (66.1% of bacterial isolates), with *Escherichia coli* (28.3%) and *Klebsiella pneumoniae* (22.7%) being most common. Fungal organisms, mainly *Candida* species, were isolated in 39% of patients, though colonization could not be excluded. Only 24% of patients received antibiotics within the first hour of ICU admission, and 68.4% required vasopressors, with adrenaline used more frequently than norepinephrine. ICU mortality was 80.3%, with 63.2% of deaths occurring within the first five days. Mortality was uniformly high regardless of ICU length of stay.

Conclusion: Sepsis in this resource-limited ICU setting was characterized by delayed presentation, advanced organ dysfunction at admission, significant constraints in therapeutic capacity, and extremely high early mortality. These findings underscore the urgent need for context-adapted sepsis strategies that prioritize early recognition at peripheral levels, streamlined referral pathways, improved access to essential diagnostics and treatments (including first-line vasopressors and antifungals), and locally informed antimicrobial stewardship programs. Addressing socioeconomic barriers to care is equally critical to improving outcomes.

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Introduction

Sepsis, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, remains a leading cause of ICU admission and mortality worldwide [1,2]. Global estimates from the Global Burden of Disease Study indicate that approximately 49 million cases of sepsis occur annually, accounting for nearly 11 million deaths, or about 20% of all global mortality [3]. The burden of sepsis is disproportionately concentrated in low- and middle-income countries (LMICs), where the high prevalence of severe infectious diseases, delayed presentation to care, limited diagnostic capacity, and restricted access to advanced organ support result in patients being admitted with advanced disease severity and multiple organ dysfunction [4,5]. These disparities underscore sepsis as a critical unmet clinical need in resource-limited health systems.

In recognition of its substantial clinical and public health impact, sepsis has been formally acknowledged by the World Health Organization as a global health priority, with emphasis on early recognition, timely treatment, and strengthening of health systems [6,7]. In this context, the Surviving Sepsis Campaign (SSC) has developed evidence-based international guidelines and standardized care bundles, including the Hour-1 bundle, aimed at optimizing early antimicrobial therapy, hemodynamic resuscitation, and organ support [8]. While implementation of these strategies has been associated with improved outcomes in high-resource settings, their application in LMICs remains inconsistent due to contextual limitations related to infrastructure, workforce, and resource availability [9]. Regional initiatives and professional networks in Africa have sought to promote sepsis awareness and training adapted to local contexts; however, systematic implementation and outcome evaluation remain limited.

In sub-Saharan Africa, the clinical management of sepsis is shaped by a convergence of diagnostic, microbiological, and health system constraints that collectively delay recognition and compromise effective treatment. Limited access to timely laboratory investigations, including microbiological cultures and essential biomarkers, often necessitates empirical management and restricts early etiological identification. Within this context, the growing burden of antimicrobial resistance further complicates therapeutic decision-making, particularly in settings with limited access to second-line antimicrobials and insufficient antimicrobial stewardship capacity [10]. These challenges are intrinsically linked to structural barriers such as delayed referral pathways, shortages of trained critical care personnel, limited ICU bed capacity, and substantial financial barriers to care. Together, these interconnected factors contribute to advanced organ dysfunction at presentation and constrain the effective implementation of evidence-based sepsis protocols, positioning sepsis as a single, system-level clinical challenge rather than a collection of isolated problems in resource-limited African settings. In the Democratic Republic of Congo (DRC), these challenges are particularly acute due to decades of health system underfunding and infrastructure deficits. However, contemporary data on sepsis epidemiology and outcomes from Congolese ICUs are virtually nonexistent, hindering the development of evidence-based, locally adapted policies

Despite the substantial burden of sepsis, contemporary data from Congolese ICUs are virtually nonexistent, hindering the development of evidence-based, locally adapted policies. Therefore, this prospective multicenter study was conducted to address this knowledge gap. The primary objective was to describe the epidemiological characteristics, clinical features, microbiological profiles, and outcomes of adult patients with sepsis admitted to ICUs in Lubumbashi, DRC. The secondary objectives were to evaluate current management practices and to identify key health system and contextual constraints influencing care delivery and outcomes in this resource-limited setting.

Methods

Study Design, Setting, and Period

This study was conducted as a prospective multicenter observational investigation between January 2021 and December 2023 in three tertiary-level intensive care units (ICUs) in Lubumbashi, Democratic Republic of Congo. The participating institutions included the Cliniques Universitaires de Lubumbashi(211 beds; 7 ICU beds, 3.3%), a university-affiliated tertiary referral hospital; the SNCC Hospital(7 ICU beds, 3.1%), the healthcare facility of the Société Nationale des Chemins de Fer du Congo (SNCC) and the Centre Médical Diamant(65 beds; 12 critical care beds, 8 ICU and 4 high-dependency), a private tertiary medical center with ICU capacity. These ICUs operate under significant structural constraints, including intermittent availability of essential drugs and consumables, limited numbers of mechanical ventilators, and the absence of on-site continuous renal replacement therapy (CRRT), a characteristic feature of resource-limited urban critical care environments in sub-Saharan Africa.

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Study Population

Patients were included if they were aged ≥16 years, admitted to the ICU or continuous care unit of the participating hospitals, and presented with suspected sepsis or septic shock at admission or during the ICU stay. Patients were excluded if they were younger than 16 years, died within 24 hours of hospital admission, were pregnant, were readmitted for sepsis or septic shock during the study period (in which case only the first admission was considered), or lacked informed consent for study participation. Based on hospital admission records, 76 eligible patients with complete data were identified over the study period.

Operational Definitions

Sepsis and Organ Dysfunction: Sepsis was defined according to the Sepsis-3 consensus criteria as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction was operationalized as an acute increase in the Sequential Organ Failure Assessment (SOFA) score of ≥ 2 points from baseline [2]. In settings where immediate calculation of the full SOFA score was not feasible due to laboratory constraints, the quick SOFA (qSOFA) score was used for initial bedside screening. Definitive classification required subsequent documentation of infection and retrospective SOFA calculation.

Microbiological Interpretation: Microbiological confirmation was attempted for all included patients. Positive cultures were interpreted as causative pathogens only when consistent with clinical signs of infection and organ dysfunction. Isolation from non-sterile sites (e.g., sputum, urine) was considered indicative of infection only in the presence of corresponding clinical severity, acknowledging the potential for colonization. Specifically for *Candida* species, isolation was interpreted cautiously; fungemia was considered definitive, whereas isolation from other sites required strong clinical correlation to distinguish colonization from invasive candidiasis.

Socioeconomic Status (SES): SES was classified as **low** when the patient had an average monthly income of less than the equivalent of 100 US dollars, lived in precarious housing conditions, and was unable to cover direct healthcare costs. This threshold aligns with poverty benchmarks used in the Demographic and Health Survey of the DRC (INS & ICF, 2022). Patients not meeting these criteria were classified as having higher SES.

Data collection and quality assurance

Data were collected prospectively using a standardized case report form across all participating centers by trained ICU physicians and senior residents, under the supervision of the principal investigator. Data completeness and consistency were ensured through prior training on variable definitions, regular supervision, weekly coordination meetings, and cross-checking of case report forms against medical records. All data were entered into a secure database using Microsoft Excel 365®.

Collected variables included demographic characteristics (age, sex, socioeconomic status, insurance coverage), clinical data (source of ICU admission, comorbidities, vital signs at admission, severity scores, suspected source of infection), laboratory and microbiological findings, therapeutic interventions, and clinical outcomes. Socioeconomic status was assessed using a composite pragmatic classification adapted to the local context, based on health insurance coverage, employment status, and ability to afford ICU-related expenses. Patients were categorized into low or higher socioeconomic status for descriptive analyses.

Microbiological investigations were performed whenever feasible using standard culture and biochemical methods. Clinical samples were collected under aseptic conditions, and antimicrobial susceptibility testing followed conventional procedures. Fungal isolates were identified using microscopy, germ tube testing for Candida albicans, and standardized biochemical panels, with laboratories adhering to internal quality control procedures compliant with ISO 15189 standards.

The primary outcome was ICU mortality, defined as death occurring during the ICU stay. Secondary outcomes included length of ICU stay and microbiological profiles. Missing data were infrequent and mainly related to unavailable laboratory investigations due to resource constraints; no data imputation was performed, and analyses were conducted using available-case data only.

Data analysis

Data were analyzed using SPSS (version 26). Continuous variables are presented as mean ± standard deviation or median (interquartile range) based on their distribution. Categorical variables are presented as frequencies and percentages. Group comparisons were performed using Student's t-test or Mann-Whitney U test for continuous variables, and chi-square or Fisher's exact test for categorical variables, as appropriate. Given the modest sample size and the descriptive nature of the study, all inferential statistical results should be interpreted cautiously. No adjustment for multiple comparisons was performed. Missing data were not imputed; analyses were conducted on available-case data. Survival was analyzed using the Kaplan-Meier method.

Ethical Considerations

The study received approval from the University of Lubumbashi Medical Ethics Committee (Ref. UNILU/CEM/030/2021), with written authorization from participating hospitals. Informed consent was obtained from patients or legal representatives, and all data was anonymized and securely stored. The study complied with the Declaration of Helsinki, ensuring confidentiality, privacy, and the right to withdraw.

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Results

Participant Flow and Epidemiological Characteristics

During the study period, 800 patients were admitted to the participating ICUs. After excluding 132 patients aged <16 years, 668 adult ICU admissions remained for screening. Among these, 505 patients without suspected or confirmed infection were excluded, leaving 163 patients with suspected/confirmed infection. Of these, 80 did not meet Sepsis-3 criteria and 7 had incomplete SOFA data. Finally, 76 patients were included in the final analysis (Figure 1).

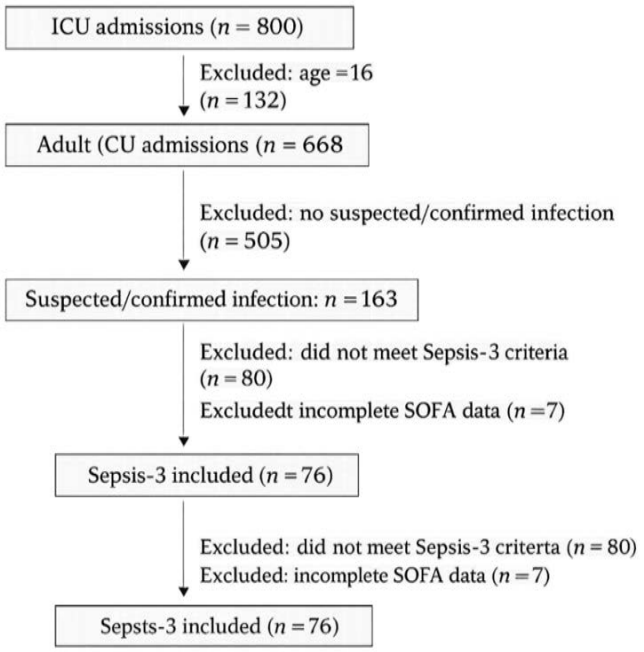

Figure 1: Study Flow Diagram showing patient screening, exclusion criteria, and final inclusion

Epidemiological Characteristics of the Study Population

A total of 76 adult patients with sepsis admitted to the participating intensive care units (ICUs) were included in the final analysis. Most patients were aged 41-60 years (n=42; 55.3%), followed by those aged ≥61 years (n=20; 26.3%) and 16-40 years (n=14; 18.4%). The sex distribution was relatively balanced, with males representing 52.6% (n=40) and females 47.4% (n=36) of the cohort. Marked socioeconomic vulnerability was observed: 67.1% (n=51) of patients were classified as having low socioeconomic status, and 63.2% (n=48) had no health insurance coverage. Medical admissions accounted for the largest proportion of cases (73.7%; n=56), followed by surgical (14.5%; n=11) and obstetric-gynecological admissions (11.8%; n=9). Baseline sociodemographic characteristics are summarized in Table 1.

Most patients (68.4%; n=52) presented with one or more comorbidities at admission. The most frequently observed comorbidity was the puerperal context (20.0%; n=15), followed by hypertension and diabetes mellitus, each present in 7.9% (n=6) of patients. Other comorbidities included HIV infection, chronic kidney disease, and malignancy, though these were less prevalent.

Sex Distribution Across Age Groups

Analysis of sex distribution across age strata revealed an age-dependent variation (Figure 2). Males predominated in the youngest (16-20 years) and oldest (>60 years) age groups, while females were more frequently represented in the 20-40 years (62.0%) and 40-60 years (61.1%) age groups. This pattern suggests potential sex-specific vulnerabilities or healthcare-seeking behaviors across different life stages in this setting.

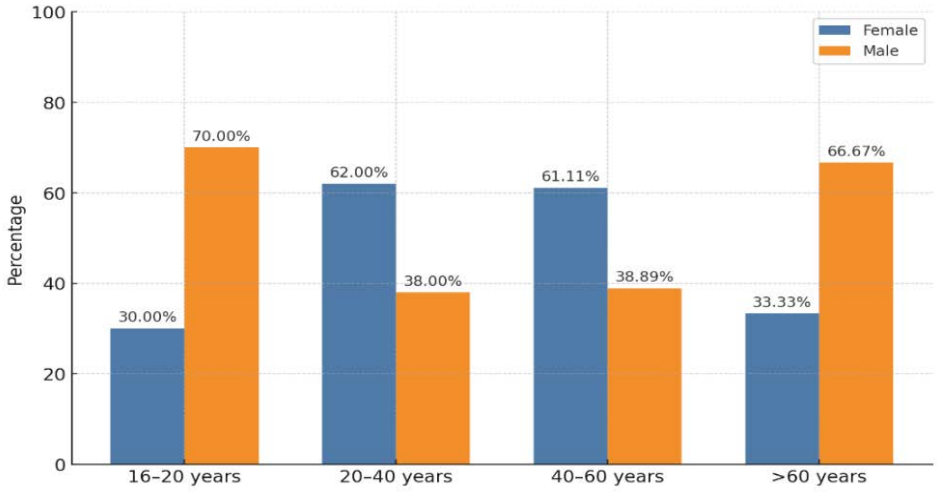

Figure 2: Gender Distribution by Age Group.

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Timing and Sources of ICU Admissions

Regarding time to ICU admission from symptom onset or initial hospital presentation, 42.1% (n=32) of patients were admitted within 5 days, while 57.9% (n=44) were admitted after 5 days, with a mean delay of 5.0 ± 4.2 days. Most patients were transferred to the ICU from the emergency department (76.3%; n=58). Other sources of admission included surgery (5.3%; n=4), gynecology and obstetrics (6.6%; n=5), internal medicine (5.3%; n=4), and neurology (6.6%; n=5). Detailed distribution by admission source and timing is presented in Table 2.

Clinical Features

Clinical Severity, Severity Scores, and ICU Mortality at Admission

At ICU admission, most patients presented with advanced disease severity, as reflected by elevated organ dysfunction scores. The mean SOFA score was 10.1 ± 3.1, and the mean APACHE II score was 25.4 ± 6.2, indicating severe illness. Bedside clinical indicators of severity were frequent: 47.4% (n=36) had respiratory dysfunction (SpO_2 < 90%), 32.9% (n=25) presented with neurological impairment (Glasgow Coma Scale ≤ 8), and 25.0% (n=19) exhibited hemodynamic instability (systolic blood pressure < 90 mmHg). The qSOFA score was ≥2 in 97.3% (n=74) of patients, and all three qSOFA criteria were fulfilled in 36.8% (n=28).

Early ICU mortality was substantial. The overall ICU mortality rate was 80.3% (n=61), with a large proportion of deaths (63.2%; n=48) occurring within the first five days of admission. Clinical severity indicators and outcomes are detailed in Table 3.

Sex-Based Differences in Laboratory Parameters

Sex-stratified analysis of laboratory parameters at ICU admission revealed several statistically significant differences (Table 4). Males had significantly higher hemoglobin levels (11.4 ± 2.2 g/dL vs. 9.9 ± 2.3 g/dL; p=0.002), hematocrit (33.8 ± 7.9% vs. 30.1 ± 8.6%; p=0.01), and white blood cell counts (20.1 ± 3.5 ×10³/mm³ vs. 18.7 ± 3.1 ×10³/mm³; p=0.048) compared to females. These differences likely reflect physiological norms and potentially more pronounced inflammatory responses in males. However, other critical indicators of illness severity—including serum lactate, creatinine, mean arterial pressure, respiratory rate, and SOFA scores—did not differ significantly between sexes, suggesting comparable overall disease severity at presentation regardless of gender.

Table 1: Sociodemographic Characteristics of Patients Admitted to the ICU for Sepsis (n=76).

Variable	Category	Frequency (n)	Percentage (%)
Age Groups	16–40 years	14	18.4
	41–60 years	42	55.3
	≥61 years	20	26.3
Sex	Male	40	52.6
	Female	36	47.4
Socioeconomic Status	Higher	25	32.9
	Low	51	67.1
Health Insurance Coverage	Yes	28	36.8
	No	48	63.2
Type of Patients	Medical	56	73.7
	Surgical	11	14.5
	Obstetrics and Gynecology	9	11.8

Table 2: Time to Admission and Source of ICU Transfer (n=76).

Admission delay (days)	Surgery	Gyneco-obstetrics	Internal Medicine	Neurology	Emergency Room	Total
≤ 5 days	1	3	2	2	24	32
> 5 days	3	2	2	3	34	44
Total	4	5	4	5	58	76
Mean time to ICU admission					**5.0 ± 4.2 days**	

Abbreviations: *ICU, Intensive Care Unit; SD, Standard Deviation. Data are presented as n (%), except mean time to admission (mean ± SD).*

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Table 3: Clinical Severity Indicators, Severity Scores, and ICU Mortality at Admission (n=76).

Severity domain	Indicator / Threshold	n	%
Clinical severity (bedside)			
Neurological dysfunction	GCS ≤ 8	25	32.9
Respiratory dysfunction	SpO_2 < 90%	36	47.4
Hemodynamic instability	SBP < 90 mmHg	19	25.0
qSOFA score			
≥ 2 criteria fulfilled	74	97.3	
All 3 criteria fulfilled	28	36.8	
Organ dysfunction score			
SOFA score (mean ± SD)	—	10.1 ± 3.1	—
APACHE II score (mean ± SD)	—	25.4 ± 6.2	—
Outcomes			
ICU mortality	61	80.3	
Deaths within first 5 days	48	63.2	

***Abbreviations**: GCS, Glasgow Coma Scale; ICU, Intensive Care Unit; qSOFA, quick Sequential Organ Failure Assessment; SBP, Systolic Blood Pressure; SD, Standard Deviation; SOFA, Sequential Organ Failure Assessment; SpO_2, Peripheral Oxygen Saturation. Data are presented as n (%) or mean ± SD as appropriate. Statistical comparisons used chi-square test for categorical variables.*

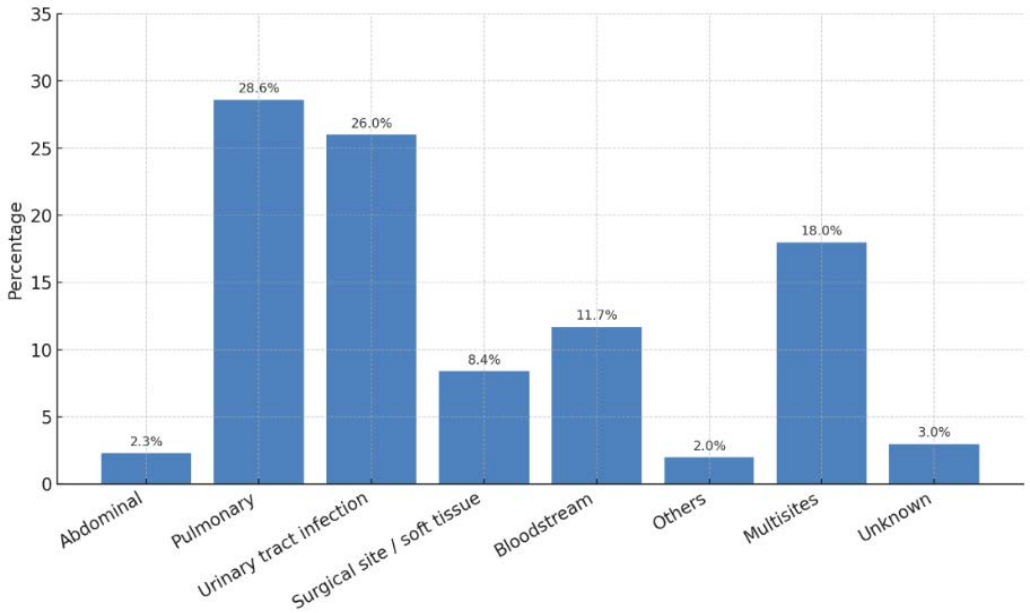

Figure 3: Sources of infection among adult ICU patients with sepsis.

Sources of Infection and Microbiological Profile

Sources of Infection

The distribution of infection sources among the 76 sepsis patients is illustrated in Figure 3. Pulmonary infections (28.6%; n=22) and urinary tract infections (26.0%; n=20) were the most frequently identified sources. Multisite infections accounted for 18.0% (n=14) of cases, followed by primary bloodstream infections (11.7%; n=9) and surgical/soft tissue infections (8.4%; n=6). Less common sources included abdominal infections (2.3%; n=2), infections of unknown origin (3.0%; n=2), and other focal infections such as central nervous system or catheter-related infections (2.0%; n=2). These findings underscore the predominance of pulmonary and urinary sources in this population and highlight the clinical severity associated with multisite involvement.

Microbiological Profile

Microbiological cultures were obtained from 76 patients. A pathogenic or potentially pathogenic organism was isolated in 40% (n=30) of patients. Polymicrobial growth was observed in 21% of positive cultures.

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Bacterial Pathogens

Bacterial isolates: Among patients with positive cultures, bacteria were isolated in 40% (n=30). Gram-negative bacteria accounted for 66.1% of bacterial isolates, with Escherichia coli (28.3%, 15/53 isolates) and Klebsiella pneumoniae (22.6%, 12/53) being the most frequent. Gram-positive bacteria represented 33.9% of isolates, predominantly Coagulase-negative staphylococci (15.1%, 8/53) and Enterococcus species (13.2%, 7/53). The distribution is shown in Figure 4.

Fungal Pathogens

Fungal organisms were isolated from cultures of 39% (n=30) of patients. *Candida* species were predominant, with *C. albicans* accounting for 50.2% of fungal isolates, followed by various non-albicans *Candida* species (Figure 5). It is important to note that, in the absence of specific fungal biomarkers and histopathological evidence, these isolates may represent colonization rather than invasive fungal infection, and these findings should be interpreted with caution.

Antimicrobial susceptibility testing revealed extensive resistance among bacterial isolates. Among Gram-negative bacteria, *E. coli* and *K. pneumoniae* demonstrated high resistance rates to third-generation cephalosporins (83.0–92.0%), with extended-spectrum beta-lactamase (ESBL) production detected in approximately 65.0% of isolates. Carbapenem resistance was observed in 17.0% of *K. pneumoniae* and 9.0% of *P. aeruginosa* isolates. Amikacin (~80.0% susceptibility) and fosfomycin (~75.0% susceptibility) retained the highest in vitro activity against Gram-negative pathogens. Among Gram-positive isolates, *Staphylococcus aureus* was the predominant species, with methicillin-resistant *S. aureus* (MRSA) representing approximately 28.0% of cases. All Gram-positive isolates remained susceptible to vancomycin and linezolid, and most (>80.0%) were susceptible to clindamycin.

Regarding fungal isolates, *Candida albicans* was the most frequently isolated species, followed by various non-albicans *Candida* species. In the absence of fungal biomarkers, these isolates may represent colonization rather than invasive infection. Fluconazole resistance reached approximately 70.0%, primarily among non-*albicans Candida* species. *C. albicans* isolates remained largely susceptible to amphotericin B (86.0%), nystatin (77.0%), and caspofungin (64.0%). These findings highlight extensive antimicrobial resistance among both bacterial and fungal pathogens, supporting the need for carbapenem-sparing, minimum inhibitory concentration (MIC)-guided treatment strategies and strengthened local antimicrobial stewardship programs.

Therapeutic Management

Adherence to international guideline-recommended sepsis management bundles was limited in this cohort. Delays in antibiotic initiation were frequent: only 24.0% (n=18) of patients received antibiotics within the first hour of recognition, 30.3% (n=23) within 1–3 hours, and 46.1% (n=35) after more than 3 hours. Fluid resuscitation was administered to only 36.8% (n=28) of patients, while 63.2% (n=48) did not receive protocolized fluid management, largely due to resource constraints. Vasopressor therapy was initiated in 68.4% (n=52) of patients requiring hemodynamic support. However, adrenaline was the predominant agent used (42.3% of those receiving vasopressors), whereas norepinephrine, the recommended first-lineagent, was utilized in only 13.5%.

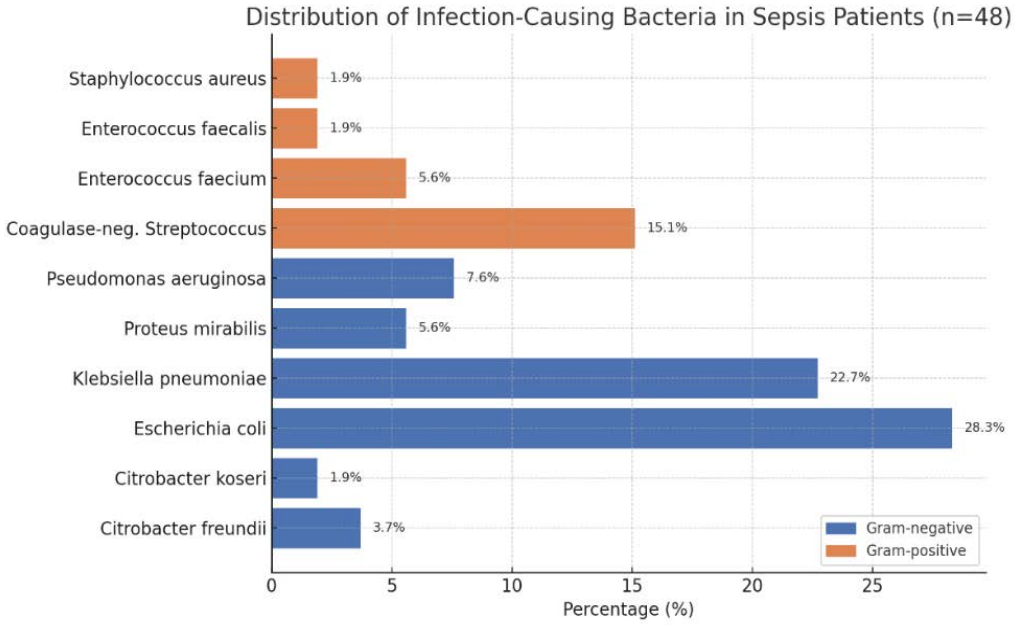

Figure 4: Distribution of infection-causing bacteria in patients with sepsis (n=48 isolates).

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Corticosteroid therapy (hydrocortisone) was administered in 9.2% (n=7) of cases. Mechanical ventilation was required in 35.5% (n=27) of patients, and renal replacement therapy (hemodialysis) was performed in only 3.9% (n=3), reflecting limited access to advanced organ support modalities.

All patients received empirical broad-spectrum antibiotic therapy, with adjustments made when microbiological results became available. Ceftriaxone was the most frequently prescribed agent in monotherapy (28.6%), followed by piperacillin-tazobactam (13.9%). Among dual-therapy regimens, the combination of ceftriaxone and metronidazole was prescribed in 15.4% of cases, followed by ciprofloxacin and metronidazole. Triple-antibiotic therapy (ceftriaxone, metronidazole, and gentamicin) was utilized in select severe cases (Figure 6). Surgical source control interventions were required in a subset of patients for complications such as peritonitis or necrotizing soft tissue infections. Key therapeutic interventions are summarized in Table 5.

All patients received empirical broad-spectrum antibiotic therapy, with adjustments made when microbiological results became available. Ceftriaxone was the most frequently prescribed agent in monotherapy (28.6%), followed by piperacillin-tazobactam (13.9%). Among dual-therapy regimens, the combination of ceftriaxone and metronidazole was prescribed in 15.4% of cases, followed by ciprofloxacin and metronidazole. Triple-antibiotic therapy (ceftriaxone, metronidazole, and gentamicin) was utilized in select severe cases. Surgical source control interventions were required in a subset of patients for complications such as peritonitis or necrotizing soft tissue infections.

Clinical Outcomes and Survival Analysis

Overall ICU mortality was 80.3% (n=61 deaths). The median length of ICU stay was 3 days (interquartile range: 2 days; range: 0–37 days). Mortality rates remained persistently high across all durations of ICU stay: 78.6% for stays ≤5 days, 77.8% for 6–10 days, and 83.3% for stays >10 days. Corresponding survival rates were 21.4%, 22.2%, and 16.7%, respectively. A chi-square test found no statistically significant association between ICU length of stay and mortality ($\chi^2 = 0.21$; df = 2; $p = 0.902$), indicating that mortality remained uniformly high regardless of duration of care (Figure 7).

Kaplan–Meier survival analysis demonstrated a steep decline in survival probability during the initial days following ICU admission (Figure 8). Survival probability fell to 21.4% by Day 5, 22.2% by Day 10, and 16.7% by Day 15, with no survivors observed beyond Day 20. Kaplan-Meier survival curve for ICU patients with sepsis (log-rank test, $p < 0.001$). The steep early decline indicates high early mortality, with most deaths occurring within the first week of admission.

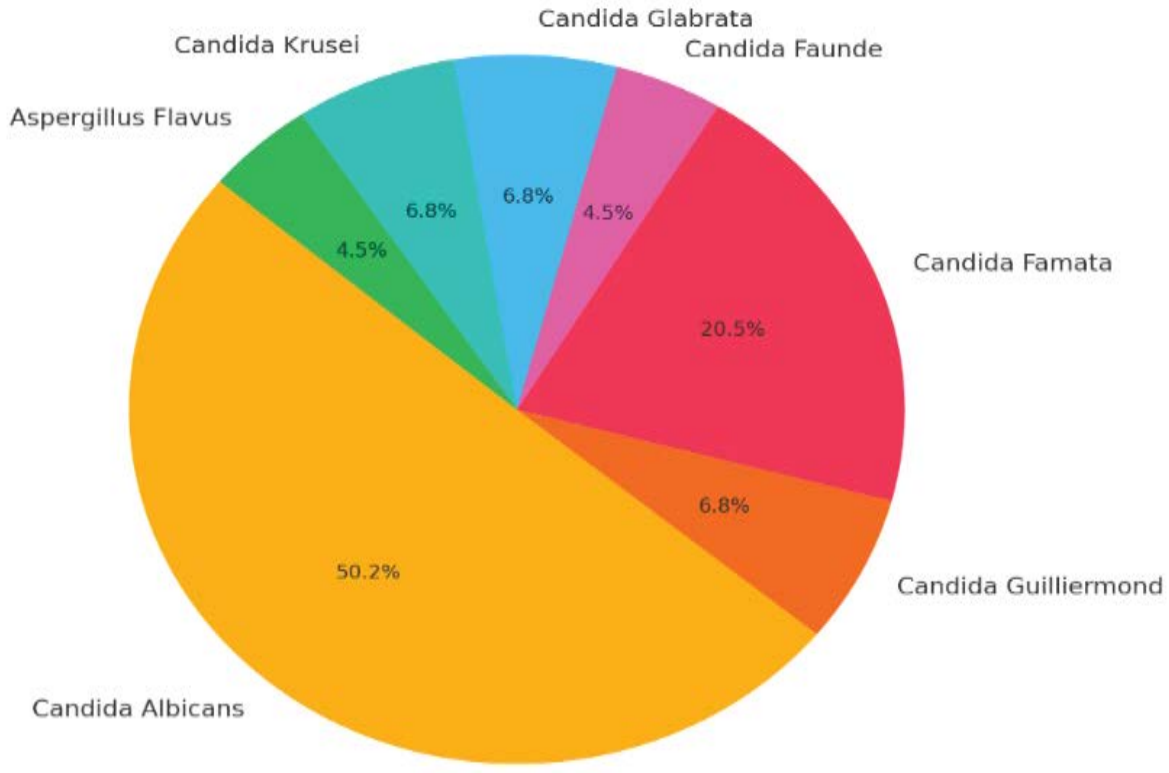

Figure 5: Fungal isolates from microbiological samples of ICU patients with sepsis **Antimicrobial Susceptibility Patterns.**

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Discussion

Summary of Principal Findings

This prospective multicenter study provides a comprehensive description of adult sepsis in ICUs in Lubumbashi, DRC. The principal findings reveal: (1) substantial delays in ICU admission (mean 5 days); (2) extreme illness severity at presentation (mean SOFA 10.1); (3) an overall ICU mortality of 80.3%, with most deaths occurring within five days; (4) major therapeutic gaps, including delayed antibiotics and predominant use of adrenaline over norepinephrine; and (5) a microbiological profile dominated by resistant Gram-negative bacteria, alongside fungal isolates requiring cautious interpretation. Rather than reflecting isolated clinical failures, these findings illustrate the cumulative impact of systemic, organizational, and socioeconomic constraints characterizing sepsis care in many LMICs [3,9,11].

Table 5: Therapeutic Management Variables Among Sepsis Patients.

Therapeutic intervention	n	%
Time to antibiotic initiation		
≤ 1 hour	18	24
1–3 hours	23	30
> 3 hours	35	46
Fluid resuscitation administered		
Yes	28	37
No	48	63
Vasopressor therapy		
Any vasopressor	52	68
└ Adrenaline	22	42
└ Norepinephrine	7	14
Corticosteroid therapy (hydrocortisone)	7	9.2
Mechanical ventilation required	27	36
Renal replacement therapy (hemodialysis)	3	3.9

Delayed Presentation and Illness Severity at ICU Admission

The prolonged delay between symptom onset and ICU admission likely contributed to the advanced clinical severity observed at presentation and may have influenced early mortality. Similar patterns have been described in sub-Saharan African settings, where delayed referral is associated with worse outcomes [12,13]. Prior studies, including those from Malawi, have demonstrated the relationship between late ICU admission and increased mortality [12]. In our cohort, most patients exhibited significant physiological derangements and established organ dysfunction at ICU admission. These findings suggest that disease progression prior to ICU transfer may play an important role in determining outcomes in resource-limited environments [9,14].

The mean age of our cohort (49 years) contrasts sharply with that of high-income countries (HICs), where sepsis predominantly affects older adults over 60 years of age

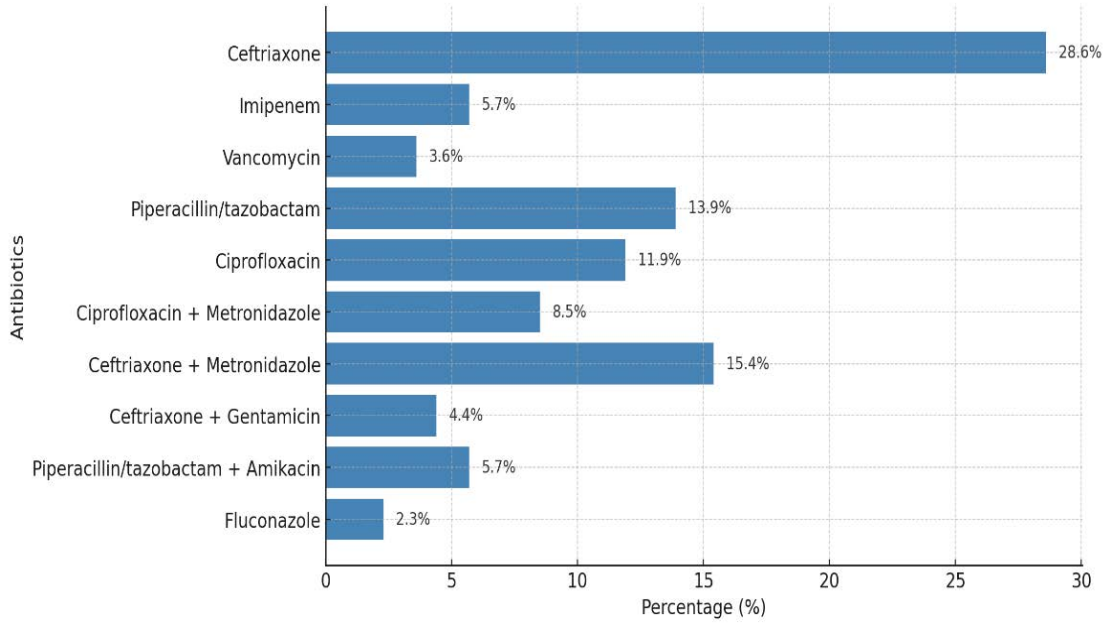

Figure 6: Distribution of prescribed antibiotics.

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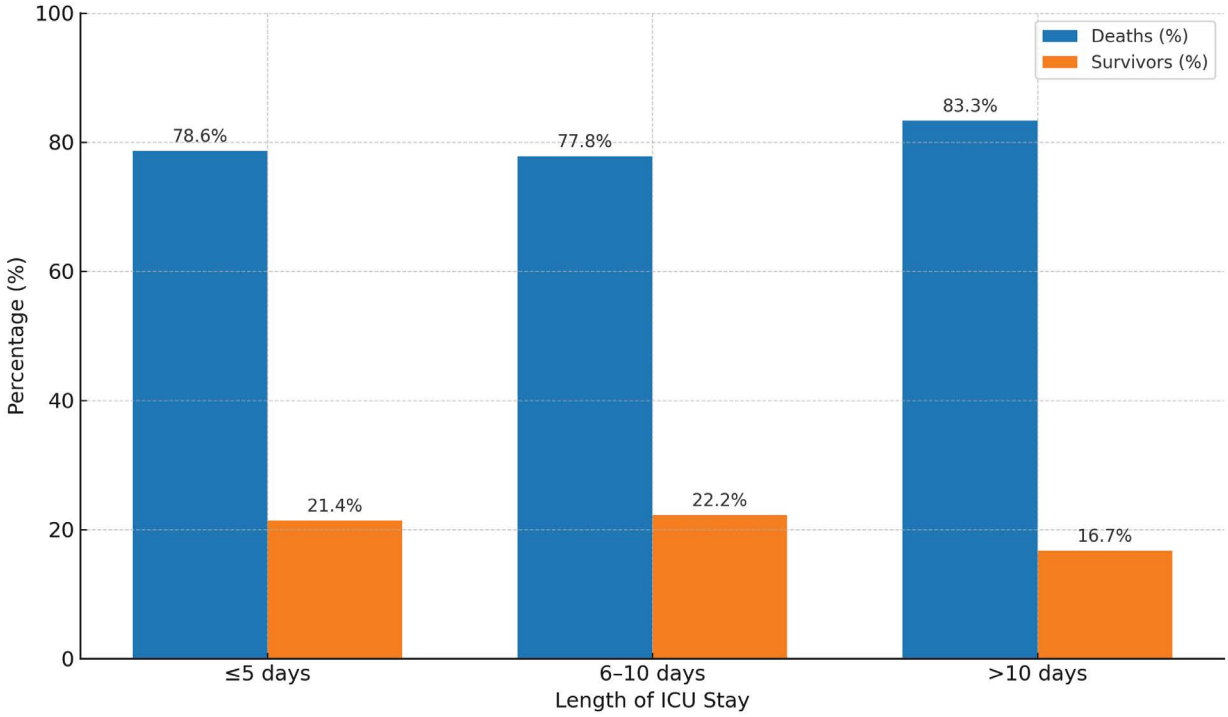

Figure 7: Association Between Hospital Length of Stay and Patient Mortality.

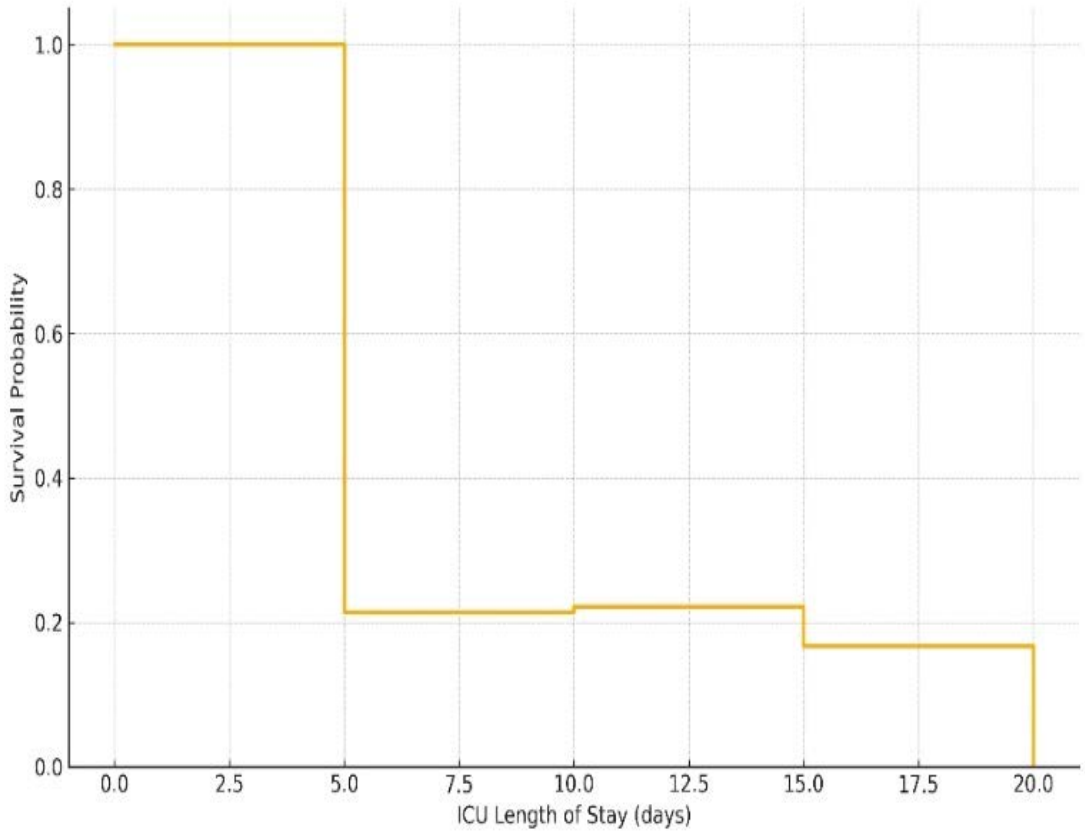

Figure 8: Kaplan–Meier Survival Curve of ICU Patients with Sepsis.

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[1,15,16]. This demographic profile is consistent with other studies from sub-Saharan Africa and Asia, where community-acquired, obstetric, and trauma-associated infections affect a younger, working-age population [15,16]. A recent prospective study from Tanzania reported a median age of 48 years (IQR 33-62) among sepsis patients, closely mirroring our findings and reinforcing the distinct epidemiological pattern of sepsis in the region [17]. This younger age distribution likely reflects the epidemiological context of LMICs, characterized by a high burden of community-acquired, obstetric-related, and trauma-associated infections affecting working-age adults [18-20]. Nevertheless, older adults accounted for more than one quarter of the cohort, highlighting their increased vulnerability due to immunosenescence and multimorbidity, well-recognized contributors to sepsis severity and mortality [21,22].

Microbiological Profile and Antimicrobial Resistance

Pulmonary (28.6%) and urinary tract infections were the predominant sources of sepsis, aligning with reports from other sub-Saharan African and LMIC settings [1,13,23]. Delayed diagnosis, limited access to microbiological testing, and late initiation of antimicrobial therapy likely facilitate progression of these common infections to advanced organ dysfunction [9]. The relatively high proportion of multisite infections (18%) further indicates advanced disease at ICU admission and has been consistently associated with greater organ failure and poorer outcomes in resource-limited settings, where early source control is often delayed [13].

The microbiological landscape was dominated by Gram-negative bacteria, comprising 66.1% of bacterial isolates, with *Escherichia coli* (28.3%) and *Klebsiella pneumoniae* (22.6%) being the most frequently identified pathogens. This distribution is consistent with profiles reported from ICUs across Africa, Asia, and Latin America [23-25]. The high prevalence of resistance to third-generation cephalosporins (83-92%) and extended-spectrum beta-lactamase (ESBL) production in approximately 65% of isolates mirrors alarming trends documented globally in LMICs [9,13,23]. The emergence of carbapenem resistance, observed in 17% of *K. pneumoniae* and 9% of *Pseudomonas aeruginosa* isolates, poses a critical threat in settings where reserve antimicrobial options are severely limited. These findings underscore the urgent need for sustained microbiological surveillance and the implementation of antimicrobial stewardship programs adapted to local epidemiological and resource realities [26].

Cautious Interpretation of Fungal Data

An equally notable finding requiring careful interpretation was the high proportion of patients with fungal isolates. Fungal organisms were isolated from clinical samples in 39% of patients, predominantly *Candida* species, with *C. albicans* accounting for 50.2% of fungal isolates. Fluconazole resistance was high (≈70%), particularly among non-albicans species. This prevalence exceeds that reported in most international ICU cohorts [1,27], but is consistent with findings from other resource-limited settings. A recent study from Kenya reported that non-albicans *Candida* species constituted 86.7% of isolates from critically ill patients [28], while an Indian ICU cohort found 82% non-albicans species with fluconazole resistance in 54% of isolates [29]. Similarly, a 10-year study from Kuwait documented a marked shift toward non-albicans species, with *C. auris* exhibiting 97% fluconazole resistance [30].

In the absence of fungal biomarkers (e.g., beta-D-glucan, mannan antigen) and histopathological evidence, it is impossible, based solely on culture results, to definitively distinguish between invasive fungal infection, colonization, or contamination [31]. This diagnostic limitation is well-recognized in critical care, where *Candida* colonization is highly prevalent, affecting 10-56% of mechanically ventilated patients [32]. Consequently, this signal should be regarded as hypothesis-generating rather than as definitive evidence of a high burden of invasive fungal infections in this setting. This cautious interpretation is particularly warranted in the African context, where access to essential fungal diagnostics remains critically limited across more than 40 countries [33]. Future prospective studies incorporating standardized diagnostic criteria—including biomarkers, imaging, and, where feasible, histopathology—are urgently needed to accurately determine the true incidence of invasive fungal infections in African ICUs [34]. Several factors may contribute to the high proportion of fungal isolates observed, including prolonged broad-spectrum antibiotic exposure prior to ICU admission, malnutrition, immunosuppression, widespread use of invasive devices, and referral bias toward more severely ill patients [35]. However, in the absence of definitive diagnostic criteria, these associations remain speculative and require confirmation through appropriately designed prospective studies.

Therapeutic Constraints and Organ Support

Therapeutic management in this cohort was profoundly constrained by structural barriers. Only 24% of patients received antibiotics within the first hour of ICU admission, and 46% experienced delays exceeding three hours. Such delays, consistently associated with increased mortality in global sepsis cohorts [8,13,35], do not reflect a lack of awareness of Surviving Sepsis Campaign recommendations, but rather systemic constraints: diagnostic uncertainty due to the absence of rapid testing, intermittent drug availability at hospital pharmacies, administrative inefficiencies, and financial barriers requiring out-of-pocket purchase of medications by families. These observations are consistent with reports from other African and Asian ICUs operating under similar resource limitations [9,36].

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Vasopressor utilization patterns serve as a stark illustration of supply-side constraints. While norepinephrine is unequivocally recommended as the first-line vasopressor in septic shock [8], it was used in only 13.5% of patients requiring vasopressors. Adrenaline, employed in 42.3% of cases, was used predominantly due to its more consistent availability on the local market. This substitution, driven by drug availability rather than clinical choice, may have implications for outcomes, although direct comparative data from resource-limited ICU settings remain sparse.

Access to advanced organ support was severely limited. Mechanical ventilation was utilized in only 35.5% of patients, and renal replacement therapy in a mere 3.9%, despite a high prevalence of severe hypoxemia and acute kidney injury. These rates, substantially lower than those reported in HICs [1,3], reflect chronic shortages of equipment, consumables, and trained personnel, rather than the absence of clinical indication. These cumulative therapeutic gaps constitute a "second hit" following the initial septic insult, directly contributing to the failure to reverse organ dysfunction and the observed high early mortality.

Socioeconomic and Systemic Determinants of Outcomes

Socioeconomic vulnerability was a defining characteristic of this cohort: 67% of patients were classified as having low socioeconomic status, and 63% lacked any form of health insurance coverage. This profile reflects the reality of the Congolese healthcare system, which is predominantly financed through out-of-pocket payments. Multiple studies across sub-Saharan Africa have demonstrated that poverty and the absence of social protection mechanisms constitute major barriers to accessing emergency and critical care services [12,13,37].

In the present study, low socioeconomic status was associated with prolonged care-seeking delays, difficulties in procuring medications and consumables during hospitalization, and, plausibly, implicit therapeutic limitations. These observations align with findings from Malawi [35] and a meta-analysis by Galiatsatos et al. [38] examining racial and socioeconomic disparities in sepsis outcomes [38]. They reinforce the concept that social determinants of health are independent prognostic factors in sepsis, operating beyond biological disease severity [12,14,35,39]. In the Congolese context, the absence of effective health insurance mechanisms and the predominance of out-of-pocket payments likely magnify these disparities.

Implications for Clinical Practice and Health Policy

These findings have important implications for sepsis care in resource-limited settings. Mortality reduction requires extending interventions beyond the ICU to address upstream failures through a systemic approach.

First, strengthening early recognition at peripheral levels using simple tools like qSOFA is paramount [39,40]. Second, establishing structured referral pathways is essential to reduce treatment delays. Third, context-adapted sepsis bundles—prioritizing rapid antibiotics, protocolized fluid resuscitation, reliable access to first-line vasopressors (norepinephrine), and basic organ support—should be implemented within existing constraints [8,41,42]. Fourth, diagnostic capacity, particularly microbiology, requires investment in blood cultures, antimicrobial susceptibility testing, and selected biomarkers to guide therapy and monitor resistance [10,43]. Fifth, reducing financial barriers through progress toward universal health coverage (UHC) and publicly financed critical care is indispensable for improving equity and outcomes.

Limitations

This study has several limitations. First, conduct in three urban tertiary ICUs limits generalizability to rural or district settings, where constraints are even more severe. Second, the modest sample size (n=76), though one of the largest from the DRC, reflects limited ICU capacity (27 beds across three centers) and a high exclusion rate due to incomplete data. This precluded robust multivariable modeling; all inferential analyses are exploratory. Third, incomplete data for full SOFA score calculation required pragmatic use of available components and estimation of the respiratory sub-score from SpO_2/FiO_2 ratios—though validated—potentially introducing misclassification bias. Fourth, microbiological data are limited by the absence of molecular diagnostics and fungal biomarkers (e.g., procalcitonin, beta-D-glucan), preventing reliable differentiation between colonization and invasive infection. The high prevalence of fungal isolates should therefore be considered hypothesis-generating. Fifth, as an observational study, residual confounding cannot be excluded; unmeasured variables (e.g., time from symptom onset to antibiotics, end-of-life decisions, post-ICU outcomes) were not captured. Sixth, the study was not designed or powered to test intervention effectiveness, and no adjustments were made for multiple comparisons.

Despite these limitations, this study provides unique empirical data from a severely understudied region and highlights actionable targets for health system strengthening.

Conclusions

This prospective multicenter study demonstrates that the extremely high sepsis-related mortality in Lubumbashi ICUs is driven primarily by systemic failures across the care continuum rather than by ICU-level management alone. Delayed recognition, fragmented referral pathways, advanced organ dysfunction at admission, severe diagnostic and therapeutic constraints, high antimicrobial resistance, and profound socioeconomic vulnerability collectively shaped outcomes in this resource-limited setting.

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Mortality was largely determined upstream of the ICU, where delayed care-seeking, financial barriers, and fragmented systems limited access to timely interventions. Common infections progressed to advanced sepsis, while therapeutic gaps reflected structural constraints rather than isolated clinical decisions. Socioeconomic vulnerability emerged as a critical determinant of poor outcomes, reinforcing the central role of social determinants of health in sepsis prognosis.

From a global health perspective, reducing sepsis mortality in LMICs requires a paradigm shift from ICU-centered interventions to a comprehensive, system-wide approach. Priority strategies include: strengthening early recognition and triage at peripheral levels; establishing efficient referral pathways; ensuring reliable access to essential diagnostics, medications (including norepinephrine), and equipment; implementing locally informed antimicrobial stewardship programs based on real-time resistance surveillance; and reducing financial barriers through progress toward universal health coverage. Addressing sepsis as both a health system and equity challenge is essential to achieving sustainable improvements in outcomes in low- and middle-income countries.

Authors' contributions

MMM, IFR, SN-TH, TKA and KKL designed the study and revised the manuscript. MMF andKIE supervised the laboratory examinations. TMI, MNY, WME, NKN curated data and KKAW, MKS and KNC contributed to the analysis and interpretation of the data and the revision of the manuscript. The all contributed to the writing of the manuscript and the revision.

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Availability of Data and Materials

The datasets generated and analyzed during the current study are not publicly available due to local data protection regulations and institutional restrictions. However, anonymized data may be made available from the corresponding author upon reasonable request and with approval from the Ethics Committee of the University of Lubumbashi.

Declarations: Conflict of Interest

The authors declare that they have no competing interests.

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