



Mortality rate and clinical profile of patients with sepsis admitted at the Department of Medicine, National Referral Hospital of Bhutan, 2021: A cross-sectional study

Sonam Dema¹, Kesang Namgyal²

¹Department of Medicine, Eastern Regional Referral Hospital, Mongar, Bhutan

² Department of Intensive Care Unit, Jigme Dorji Wangchuk National Referral Hospital, Thimphu, Bhutan

ABSTRACT

Introduction: Sepsis is a leading cause of death globally, particularly in low and middle-income countries. However, data on adult sepsis in Bhutan remains limited. This study aimed to determine the mortality rate and clinical profile of sepsis patients admitted to the medical ward of the National Referral Hospital in Bhutan. **Methods:** A cross-sectional study was conducted at the Jigme Dorji Wangchuck National Referral Hospital in 2022. All adult patients with sepsis admitted to the Department of Medicine were included. Data was collected using a structured pro forma and analyzed using Epi Data Analysis version 2.2.2.183 and STATA version 12.1. **Results:** Among 278 patients with sepsis, the in-hospital mortality rate was 26.6%. Mortality was significantly higher in patients aged over 60 years ($p < 0.001$). Pneumonia was the most common source of infection (39.2%) while spontaneous bacterial peritonitis and bloodstream infections were more strongly associated with mortality ($p < 0.001$). Gram-negative bacteria, particularly *Escherichia coli* and *Klebsiella* species were the predominant pathogens. Independent predictors of death included mechanical ventilation (adjusted OR 23.5, 95% CI 11.2–49.2, $p < 0.001$), vasopressor support (adjusted OR 9.78, 95% CI 4.02–23.8, $p < 0.001$), spontaneous bacterial peritonitis (adjusted OR 3.85, 95% CI 1.43–10.3, $p = 0.007$), and bloodstream infections (adjusted OR 3.62, 95% CI 1.25–10.5, $p = 0.018$). **Conclusion:** Mortality was reported in one quarter of patients admitted with sepsis, particularly in the critically ill. Strengthening early recognition, prompt treatment, microbiological diagnostics, and critical care infrastructure are essential to reduce sepsis mortality and improve patient outcomes.

Keywords: Intensive care unit; Mortality; Pneumonia; Sepsis

INTRODUCTION

Sepsis is a life-threatening condition resulting from a dysregulated host response to infection, ultimately leading to organ dysfunction. It is recognized as a global health priority, with the World Health Organization (WHO) estimating that sepsis affects approximately 49 million people each year and contributes to 11 million deaths. This represents nearly one in five global deaths annually¹. Despite being preventable and treatable in many cases, sepsis remains one of the most underrecognized and underreported health threats, especially in low and middle-income countries (LMICs), where nearly 80% of the cases occur^{1,2}.

Sepsis disproportionately affects individuals with underlying health conditions such as diabetes, cardiovascular disease and immunosuppression. Common sources of infection leading to sepsis include respiratory tract infections, urinary tract infections, abdominal infections, and skin or soft tissue infections^{2,3}. The predominant microbial agents vary between regions. Usually, gram-positive bacteria are more frequently identified in high-income settings, while gram-negative organisms

dominate in LMICs, although increasing use of invasive medical procedures has begun to shift this distribution^{4,6}.

In Bhutan, there is a significant lack of comprehensive epidemiological data on sepsis, particularly among the adult population. Existing studies are limited, focusing primarily on neonatal sepsis, where gram-negative organisms were identified as the predominant pathogens⁷. This lack of data represents a critical gap in understanding the burden, clinical characteristics, and outcomes of sepsis in the Bhutanese adult population. Therefore, this study aims to address this gap by determining the mortality rate and clinical profile of patients with sepsis admitted to Department of Medicine at the Jigme Dorji Wangchuck National Referral Hospital (JDWNRH).

METHODS

Study Design

A cross-sectional study was conducted in the Department of Medicine at the JDWNRH in Thimphu, Bhutan. It was conducted over a year long period, spanning 1st January 2021 to 31st December 2021.

Study setting

The JDWNRH, located in Thimphu is Bhutan's tertiary care center

Corresponding author:

Sonam Dema

sodragon0389@gmail.com

and functions as a teaching hospital. It offers a comprehensive range of services, which includes emergency care, inpatient and outpatient services, specialized clinics, and rehabilitative care. The hospital houses departments such as Medicine, Surgery, Paediatrics, Obstetrics and Gynaecology, Psychiatry, and others.

In 2021, the Department of Medicine had 36 in-patient medical beds and medical out-patient clinics (OPD) that operated six times a week. The Intensive Care Unit (ICU) had 10 beds, and the High Dependency Unit (HDU) had 4 beds. The department was staffed by a multidisciplinary team including 15 consultants, 10 internal medicine residents and 42 nurses.

Study participants

All patients with sepsis admitted to the Department of Medicine at the JDWNRH were eligible participants.

Inclusion Criteria: All patients >18 years diagnosed with sepsis based on the System Inflammatory Response Syndrome (SIRS) and quick Sequential Organ Failure Assessment (qSOFA) criteria.

SIRS criteria: At least two of the following four criteria must be present to diagnose sepsis: temperature <36 °C or > 38 °C; heart rate >90/min; respiratory rate >20/min; white blood cell (WBC) count < 4000 cells/mm³ or > 12000 cells/mm³ or > 10% immature band forms⁸.

qSOFA criteria: At least two of the following three criteria must be present for sepsis and it indicates organ dysfunction: systolic BP <100 mmHg; respiratory rate >22/min; altered mental status characterised by GCS <15⁹.

Exclusion Criteria: Post-operative sepsis, surgical site infections and cases without consent.

Sample size calculation

In 2017, 544 cases of sepsis were recorded among patients aged 15 and above in Bhutan¹⁰. Data from JDWNRH was not available. A 50% prevalence was assumed for the study using the equation $[Np(1-p)] / [(d^2/Z^2(1-\alpha/2)^2(N-1)+p*(1-p))]$ available online (OpenEpi.com). The following inputs were utilised: hypothesized % frequency of outcome factor in the population (p) of 50%; population size (for finite population correction factor fpc) of 544; confidence limits as % of 100 (absolute +/-) (d) of 5% and the design effect of 1. The sample size (n) obtained was 241 at 95% confidence interval.

Sampling method

A convenience sampling method was used to include all patients with sepsis meeting the inclusion criteria.

Study variables

Sociodemographic variables (age and sex), underlying comorbidities (chronic kidney disease, diabetes mellitus, hypertension, heart disease, malignancy, chronic obstructive pulmonary disease, etc...), causes of infections (gram positive, gram negative, others), and outcome of the patient (alive or dead) were collected for the study.

Study tool

A structured interviewer-administered research questionnaire was used for collecting the data.

Data Management

The nurses of the Medicine Ward were trained as data collectors. They were trained on the study instrument, consent form, and the data collection procedure. The collected data were checked for completeness daily by the investigator to monitor the overall quality of the data collection process. Completed questionnaires were stored under lock and key by the investigator.

Data Analysis

The demographic and clinical data collected via the paper-based questionnaire was later securely digitized in EpiData (version 3.1, EpiData Association, Odense, Denmark) software with double data entry to minimize errors. Statistical analysis was conducted using EpiData Analysis (version 2.2.2.183, EpiData Association, Odense, Denmark). The adjusted analysis was done using STATA (version 12.1, copyright 1985–2011 StataCorp LP USA, serial number: 30120504773). Descriptive statistics were used to summarize patients' clinical characteristics, microbiological profile and outcomes. Chi-square test was used to identify associations between independent variables and mortality with a p-value < 0.05 being considered statistically significant. Binary logistic regression was used to calculate crude odds ratio and adjusted odds ratio to estimate the strength of association between potential risk factors and mortality.

Ethical Considerations

Ethical clearance was obtained from the Interim Institutional Review Board (INTERM IRB/P020/015/449), Khesar Gyalpo University of Medical Sciences of Bhutan. Informed written consent was obtained from eligible participants or their primary guardian, after they received detailed information about the study's purpose, procedures, risks, and benefits. Participation was voluntary, with the option to withdraw without affecting medical care. Patients were anonymized using unique identification numbers. Data confidentiality and protection were maintained, and the study concluded either at patient discharge or upon death.

RESULTS

Of the 3002 patients admitted to the Department of Medicine at JDWNRH, there were 278 patients with sepsis. Amongst them, 74 (26.6%) died during hospitalization (Figure 1). As shown in Table 1, more than half (52.1%, 145) were female; and most of the patients with sepsis were aged over 60 years (38.5%).

Hypertension was the most prevalent comorbidity, present in 33.1% of patients, followed by autoimmune diseases, stroke, neurological disorders, HIV and immunosuppressed states collectively accounting for 18.8%, and diabetes mellitus observed in 15.5% of patients (Table 2). As shown in Table 2, pneumonia was the most common source of sepsis (39.2%), followed by urinary tract infections (12.6%) and meningoencephalitis (9.0%).

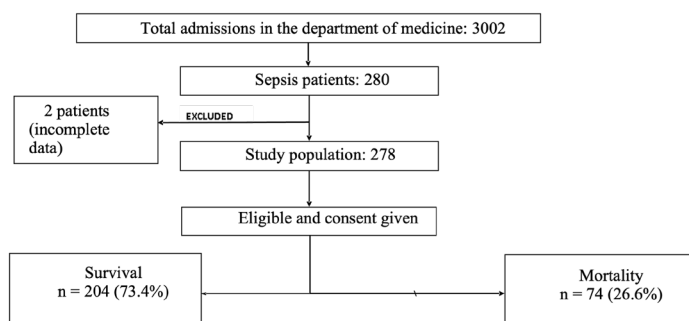


Figure 1. Patients with sepsis at the Department of Medicine, Jigme Dorji Wangchuck National Referral Hospital, 2021

The study revealed that 78.1% of patients required intensive care measures, 24.8% required mechanical ventilation and 53.2% required pressor support.

As shown in Table 3, gram-negative bacteria were the most frequently identified pathogens, particularly *Escherichia coli* (34.5%) and *Klebsiella* species (18.5%), followed by gram-positive *Staphylococcus* species (12.8%).

Table 1: Profile of patients with sepsis admitted to the Department of Medicine at the National Referral Hospital, 2021

	Total	Sur- vived	Died	
Characteris- tics	n(%)	n(%)	n(%)	p-value
Sex				
Male	133 (47.8)	93 (45.6)	40 (54.1)	0.266
Female	145 (52.2)	111 (54.4)	34 (45.9)	
Age (years)				
18-40	82 (29.5)	68 (33.3)	14 (18.9)	<0.001
41-60	89 (32.0)	59 (28.9)	30 (40.5)	
>60	107 (38.5)	77 (37.7)	30 (40.5)	

There were no significant sex-based differences in mortality. However, advancing age was associated with higher mortality, wherein patients aged >60 years had significantly worse outcomes compared to those aged 18–40 years ($p<0.001$). While co-morbidities did not have statistically significant differences between survival and death, specific conditions such as malignancy ($p=0.045$) were linked to increased mortality (Table 4).

Table 2: Clinical profile of patients with sepsis admitted to the Department of Medicine at the National Referral Hospital, 2021

Characteristics	Total n(%)	Survived n(%)	Died n(%)	p-value
Co-morbidities				
CKD	26 (14.4)	22 (17.5)	4 (7.3)	0.244
COPD	15 (8.3)	11 (8.7)	4 (7.3)	1.000
DM	28 (15.5)	19 (15.1)	9 (16.4)	0.637
Hypertension	60 (33.1)	48 (38.1)	12 (21.8)	0.252
Heart disease	12 (6.6)	9 (7.1)	3 (5.4)	1.000
Malignancy	6 (3.3)	2 (1.6)	4 (7.3)	0.045
Others	34 (18.8)	15 (11.9)	19 (34.5)	<0.001
Causes of sepsis				
Pneumonia	109 (39.2)	83 (40.7)	26 (35.1)	0.485
UTI	35 (12.6)	30 (14.7)	5 (6.8)	0.118
Meningo-encephalitis	25 (9.0)	19 (9.3)	6 (8.1)	0.942
SBP	24 (8.6)	10 (4.9)	14 (18.9)	<0.001
Infective endocarditis	7 (2.5)	6 (2.9)	1 (1.3)	0.679
GI sepsis	12 (4.3)	10 (4.9)	2 (2.7)	0.526
Line infection	6 (2.1)	6 (2.9)	0 (0.0)	0.347
Bloodstream infection	21 (7.6)	9 (4.4)	12 (16.2)	<0.001
Skin infection	8 (2.9)	3 (1.4)	5 (6.8)	0.033
Others*	31 (11.1)	28 (13.7)	3 (4.1)	0.029
Intensive care requirement				
Mechanical ventilation	69 (24.8)	16 (23.1)	53 (76.8)	<0.001
Pressor requirement	148 (53.2)	82 (55.4)	66 (44.6)	<0.001

CKD: Chronic kidney disease; COPD: Chronic obstructive pulmonary disease; DM: Diabetes mellitus; HIV: Human immunodeficiency virus; UTI: Urinary tract infection; SBP: Spontaneous Bacterial Peritonitis; GI sepsis: gastrointestinal sepsis; *Others include autoimmune, HIV, organ transplant, patient of immunisuppression

There were no significant sex-based differences in mortality. However, advancing age was associated with higher mortality, wherein patients aged >60 years had significantly worse outcomes compared to those aged 18–40 years ($p<0.001$). While co-morbidities did not have statistically significant differences between survival and death, specific conditions such as malignancy ($p=0.045$) were linked to increased mortality

Table 3: Microbiological profile of patients with sepsis admitted to the Department of Medicine at the National Referral Hospital, 2021

Characteristics of culture reports	Total n(%)	Survived n(%)	Died n(%)	p-value
Gram negative bacteria				
<i>Acinetobacter</i>	4 (3.9)	3 (4.9)	1 (4.0)	0.576
<i>Escherichia coli</i>	36 (34.5)	10 (16.4)	6 (24.0)	0.706
<i>Klebsiella</i>	19 (18.5)	15 (9.2)	4 (16.0)	0.419
<i>Pseudomonas</i>	12 (11.7)	8 (13.1)	4 (16.0)	0.738
Gram positive bacteria				
<i>Staphylococcus</i>	13 (12.6)	10 (16.4)	3 (12.0)	0.524
<i>Enterococcus</i>	5 (4.9)	4 (6.6)	1 (4.0)	0.329
<i>Streptococcus</i>	2 (1.9)	2 (3.3)	0 (0.0)	1.000
Others				
Tuberculosis	4 (3.9)	3 (4.9)	1 (4.0)	0.576
Scrub typhus, Dengue, or Leptospirosis	8 (7.8)	6 (9.8)	2 (8.0)	0.685

(Table 4).

As shown in Table 4, Spontaneous Bacterial Peritonitis (SBP) and bloodstream infections were strongly associated with death ($p<0.001$), while culture reports showed no statistically significant association with mortality. Intensive care measures were notably linked to poor outcomes, with intubation (76.8% in deaths, $p<0.001$) and pressor use ($p<0.001$) being particularly significant.

After adjustment, SBP (adjusted OR 3.85, 95% CI 1.43 - 10.3, $p=0.007$), bloodstream infections (adjusted OR 3.62, 95% CI 1.25 - 10.5, $p=0.018$), the need for intubation (adjusted OR 23.5, 95% CI 11.2 - 49.2, $p<0.001$) and pressor support (adjusted OR 9.78, 95% CI 4.02 - 23.8, $p<0.001$) remained independent predictors of death (Table 4).

DISCUSSION

The study found a notably high in-hospital mortality rate of 26.6% among patients with sepsis admitted to the Department of Medicine at the National Referral Hospital. This underscores the significant burden of sepsis in the country and aligns with mortality rates reported in other low and middle-income countries, which often ranges between 20% and 40% depending on healthcare access, time of intervention, and availability of intensive care

facilities^{4,11,12}. Studies in India have reported mortality rates ranging from 51.6% to 65.2%^{13,14}. This finding is particularly significant given that Bhutan provides free healthcare suggesting that high mortality may be attributed more to late presentation, underlying comorbidities, and limited critical care capacity than to economic barriers alone.

Intensive care interventions, specifically intubation ($p<0.001$) and pressor support ($p<0.001$), emerged as independent predictors of mortality. A study from Vietnam reported similar results, highlighting that the invasive therapies are often used and offered to critically ill patients with severe sepsis or shock, who already have a low chance of survival¹⁵. While these interventions are vital to support and possibly save lives, the underlying fragility of the patients means that the outcomes can often still be poor.

Advancing age is a well-established independent risk for sepsis. Consistent with this, this study found that patients over 60 years experienced significantly higher mortality rates ($p<0.001$). Similar findings were reported from studies conducted in Bangladesh and Northeast India, where the mean age of patients with sepsis was 55.82 ± 19.19 years, with the 61-70 year age group being the most affected^{11,16}. The increased vulnerability of older adults to sepsis is likely attributable to age related immune decline, reduced physiological reserves, and a higher prevalence of comorbidities^{17,18}. These findings underscore the importance of aggressive management of sepsis for elderly patients with sepsis.

This study found that hypertension and diabetes mellitus were the most prevalent comorbidities among patients with sepsis, though neither showed a significant association with mortality. The presence of malignancy and other immunocompromised states was associated with poor outcomes. Malignancy, in particular, was significantly associated with mortality, likely due to immunosuppression and thus, a delayed recognition of infection. These findings align with previous studies suggesting that immunocompromised states, rather than common chronic illnesses such as hypertension or diabetes, are stronger predictors of adverse outcomes in sepsis^{11,19}.

While sex difference was not significantly associated with mortality, a slight female predominance was observed, consistent with global data published in 2020¹. Females with autoimmune diseases accounted for 18.8% of the sepsis cases, which may partly explain this trend. It is worth highlighting that the scoring system used for sepsis identification does not incorporate sex as a variable. While physiological and biological differences exist between males and females, the scoring criteria primarily focuses on clinical indicators such as heart rate, respiratory rate and blood pressure^{9,11,20,21}. These parameters may be altered during autoimmune disease flares, potentially resulting in the slight female preponderance in this study.

The microbiological culture profile in this study demonstrated a predominance of gram-negative organisms, with *Escherichia coli* (34.5%) and *Klebsiella* species (18.5%) being the most frequently isolated pathogens. This pattern aligns with

Table 4: Factors associated with mortality in patients with sepsis admitted to the Department of Medicine at the National Referral Hospital, 2021

Characteristics	OR (95% CI)	p-value	Adjusted OR (95%CI)	p-value
Age (>40 vs 18- 40)	2.14 (1.12 – 4.10)	0.020	1.57 (0.85 – 2.91)	0.140
Sex (Male)	1.40 (0.82 – 2.41)	0.220	1.30 (0.75 – 2.26)	0.331
Co-morbidities				
Malignancy	5.77 (1.01 – 32.9)	0.045	4.90 (0.89 -27.1)	0.067
Other comorbidities	2.36 (1.17 – 4.76)	0.015	1.94 (0.92 – 4.11)	0.082
Cause of sepsis				
Pneumonia	0.78 (0.43 – 1.41)	0.450	4.45 (1.02-19.45)	1.000
UTI	0.42 (0.15 – 1.17)	0.960	2.37 (0.65 – 8.67)	1.000
SBP	4.53 (1.78 – 11.5)	0.001	3.85 (1.43 -0.103)	0.007
Blood stream infection	4.19 (1.51 -11.6)	0.002	3.62 (1.25 – 10.5)	0.018
Skin infections	5.67 (1.28 – 25.0)	0.03	4.30 (0.95 – 19.3)	0.059
Others (combined)*	0.26 (0.07 – 0.95)	0.411	1.52 (0.35 – 6.65)	1.000
Culture reports				
Gram-negative bacteria	0.66 (0.22 – 2.01)	0.554	1.18 (0.29 – 4.08)	0.816
Gram-positive bacteria	1.04 (0.26- 4.08)	1.000	0.85 (0.21 -3.44)	1.000
Others**	2.03 (0.48 – 8.48)	3.900	2.10 (0.48 – 9.11)	0.322
Intensive care treatment				
Intubation required	29.66 (15.0 – 58.7)	<0.001	23.5(11.2-49.2)	<0.001
Pressors required	12.27 (5.5 – 27.2)	<0.001	9.78 (4.02 – 23.8)	<0.001

CI: confidence interval

SBP: Spontaneous bacterial peritonitis; UTI: Urinary tract infection.

*Others include tuberculosis, autoimmune diseases, scrub typhus, dengue, leptospirosis

**Others include tuberculosis, dengue, scrub typhus, leptospirosis, detected via Gene Xpert and serology tests

findings from other South Asian countries, where gram-negative pathogens are frequently implicated in sepsis^{6,11,22}. However, no statistically significant association was observed between culture positivity and mortality, which may be attributed to factors such as prior antibiotic use, low sensitivity of conventional culture methods, or delayed sample collection. Furthermore, a substantial proportion of sepsis cases were culture-negative, a phenomenon also documented in other studies, which poses challenges for targeted antimicrobial therapy^{23,24}.

Pneumonia was the most common cause of sepsis (39.2%), followed by urinary tract infections (12.6%) and meningococcalitis (9%). This finding aligns with studies from India, which reported respiratory infections as the most common source of sepsis (37.2%), followed by urinary tract infections (10.3%) and intra-abdominal infections (9.5%)¹³. Similarly, studies in the United States also identified pneumonia as the primary cause of sepsis and the leading contributor to mortality²³. While pneumonia was the most frequent cause, spontaneous bacterial peritonitis (SBP) and bloodstream infections were significantly associated with higher mortality. These findings suggest that while pneumonia remains a key contributor to sepsis burden, intra-abdominal and hematogenous infections may carry a more severe clinical course, likely due to delayed diagnosis, multidrug-resistant pathogens, or rapid progression to organ failure. Patients with SBP are noted to have a higher progression rate to death or liver transplantation within one month compared to others²⁵. Furthermore, patients with SBP due to extensively drug-resistant bacteria have a 30-day mortality rate of 69.2%²⁶.

LIMITATIONS

This study has few limitations. Firstly, as single-centre study, the findings may not be generalizable to other healthcare settings in Bhutan. Secondly, the reliance on microbiological cultures may have underestimated pathogen prevalence, particularly in cases where antibiotics were administered prior to sample collection. Similarly, culture-negative sepsis also contributes to underestimating pathogen prevalence. Finally, small sample sizes for certain conditions like malignancy and specific infections may have reduced the power to detect statistically significant associations.

CONCLUSIONS

One-quarter of patients admitted with sepsis at the Department of Medicine at the JDWNRH had in-hospital mortality with significant associations observed for advanced age, SBP, bloodstream infections, and the need for mechanical ventilation and vasopressor support. To reduce the burden of sepsis and its associated mortality, national clinical guidelines on early recognition and timely administration of antibiotics must be developed. There is also a need to improve microbiological diagnostics, expand critical care capacity and train healthcare workers on sepsis management and enhance infection prevention strategies to improve outcomes.

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AUTHORS CONTRIBUTION:

Following authors have made substantial contributions to the manuscript as under:

SD: Concept, design, data collection, manuscript writing, editing and review.

KN: Concept, design, data collection, manuscript writing, editing.

Authors agree to be accountable for all respects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST

None

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