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Analysis of clinical management and outcomes of sepsis in ICU and HICU: A prospective observational study in a tertiary care hospital

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ABSTRACT

Background: Sepsis is one of the most common causes of morbidity and mortality in critical care units. It is essential to understand the clinical patterns of sepsis, various causes, and complications in the ICU and HICU settings. This study aims to understand the causes and analyse the different treatment approaches that affect the clinical outcomes in the management of sepsis.

Methods: In this prospective observational study, 60 patients admitted to the ICU and HICU with a diagnosis of sepsis were included. Patients' demographic details, comorbidities, laboratory parameters, sources and complications of sepsis were collected and analyzed.

Results: In our study, 71.6% of patients received broad-spectrum antibiotics, among which the most frequently used agents were meropenem (46.7%) and colistin (20%). The most common sources of sepsis were the genitourinary tract (40%) and respiratory tract (23.3%). Acinetobacter sp. (17.2%), Klebsiella sp. (14.1%) and Escherichia coli (14.8%) were the most regularly isolated pathogens. Septic shock (70% of patients, 45.2% death) and acute renal injury (50% incidence, 40% mortality) were the most common complications. The mean SOFA score was 10.1, indicating substantial organ failure, and there was no correlation with mortality. The overall mortality rate was 45%, and the median hospital stay was 14.5 days.

Conclusions: The study focuses on managing sepsis in critical patients with comorbidities at a tertiary care hospital. Respiratory and genitourinary tract infections were the leading cause of death, whereas septic shock and acute renal injury were the most common complications. Early identification, appropriate antimicrobial therapy, and intensive management are crucial to improve patient outcomes.

INTRODUCTION

Sepsis is a serious condition that occurs when the body shows an excessive response to an infection, leading to tissue damage, impaired organ function, and possibly septic shock. If not identified early and treated immediately, it progresses to MODS and death. The management includes various antimicrobial therapies, intravenous fluids and different supportive measures.

Sepsis presents a significant challenge to global health, causing a substantial number of illnesses and deaths worldwide. In 2017, around 48.9 million cases and 11 million fatalities occurred, representing approximately 20% of global mortality. The impact of sepsis is especially pronounced in low- and middle-income countries, with about 85% of cases occurring in these regions, notably in Sub-Saharan Africa and Southeast Asia (1).

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Sepsis can occur in patients with infections (such as pneumonia, UTIs, bloodstream infections, skin infections, abdominal infections, infections of the liver or gallbladder, and brain or spinal cord infections). Non-infectious sources, such as trauma, burns, or pancreatitis, can also trigger the body's immune responses and cause sepsis, similar to how infections do. In some cases, it can be challenging to determine the cause, especially when a bacterial agent is involved, and the patient has been treated with antibiotics. This can make it difficult to identify the underlying cause of sepsis. It affects both healthy and ill individuals, without regard to age, race, or geography. The factors influencing survival are poorly understood. (2)

The signs and symptoms of sepsis are not specific and can differ from person to person. They may encompass a change in mental state, tachypnea, unexplained sweating, feeling dizzy, shivering, and symptoms specific to the type of infection, such as painful urination from a urinary tract infection or a worsening cough from pneumonia. Sepsis can progress to septic shock, which involves a severe drop in blood pressure. Symptoms of septic shock include the inability to stand up, extreme drowsiness, or difficulty staying awake, and a significant change in mental state, such as extreme confusion. (3)

The diversity of sepsis makes it difficult to identify high-risk patients, diagnose the condition early, and provide disease-specific treatments. Delay in administering appropriate treatment, especially potent antibiotics, significantly increases the risk of mortality. The clinical characteristics of septic patients can vary widely due to factors such as age, gender, underlying health conditions, infection site, and the specific pathogen involved, making them challenging to identify and classify.

Although standardised treatments like broad-spectrum antibiotics, fluid therapy, and vasopressors have reduced mortality, there is still a need for improved efficacy. (4)

Current professional recommendations include several actions ("bundles") to be followed as soon as possible after diagnosis. Within the first three hours, patients should receive antibiotics and intravenous fluids if there is evidence of either low blood pressure or other evidence for inadequate blood supply to organs (as evidenced by a raised level of lactate); blood cultures also should be obtained within this time period. After six hours, the blood pressure should be adequate, close monitoring of blood pressure and blood supply to organs should be in place, and the lactate should be measured again if initially it was raised. (5)

Sepsis starts with an infection triggering an inflammatory response. It's vital to intervene early before health problems worsen. Standard treatments aim to support organ function, control infection, and moderate the body's response. Current sepsis care bundles may not work for all patients due to diverse profiles and genetic differences. Understanding patient responses to treatments is crucial. (6)

The SOFA Score can be used to determine the level of organ dysfunction and mortality risk in ICU patients. It is the most widely used prognostic score for patients with sepsis, which evaluates the partial pressure of oxygen or fraction of inspired oxygen for ventilated patients, the GCS, platelets, bilirubin, creatinine, and mean arterial pressure (MAP), or administration of vasoactive agents. (7)

METHODS

The following data was recorded using a pre-designed structured format for all new adults admitted to the HICU and ICU.

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This includes demographic data of the patients, the source of infection, comorbid diseases, clinical laboratory data, hospital stay, and complications of sepsis. The data was collected prospectively from patient charts, MIS, or other suitable sources. The pathogen responsible for the infection was also identified.

In addition, details of the management of sepsis were analyzed. This includes data on the use of antibiotics (both empirical use and pathogen-specific use). Management of secondary complications of sepsis such as AKI (HD), metabolic acidosis (sodium bicarbonate), shock (inotropes), etc., were recorded and analyzed. Furthermore, patients were followed up until death or hospital discharge, whichever occurs earlier, to identify any mortality associated with sepsis.

Study procedure

The research procedure involved a comprehensive approach, starting with the collection of detailed patient demographics, diagnosis, and lab investigations, including microbiological cultures. The study also encompasses the different treatments administered to patients, including empirical and pathogen-specific treatments, as well as the identification and management of any complications that arise.

The initial step in the study was to identify patients with sepsis who meet specific inclusion criteria, such as being over 18 years old and being admitted to the ICU or HICU with sepsis. Data was gathered from various sources, including patient profiles, doctors' and nurses' notes, management information systems, medical records, and medication charts. This data was then used to identify the causative pathogen responsible for the sepsis and determine the appropriate treatment.

In addition to identifying and treating the primary infection, the study also assessed secondary complications of sepsis such as acute kidney injury, metabolic acidosis, and shock, and focused on their management. The prognosis of the sepsis was assessed using the SOFA score of first 24 hour of admission using a SOFA score calculator from mdcal. Follow-up observations were conducted until the patient was discharged or passed away, allowing for an assessment of morbidity and length of hospital stay.

Statistical analysis

The data obtained were entered in a Microsoft Excel sheet, and statistical analysis was performed using Jeffrey's amazing statistics program 0.19.1v.

The results are presented as Mean ± SD, counts, or percentages. A comparison of two variables was performed using one sample t-test for laboratory data, if the variables were normally distributed parametric test was performed; if the data were not normally distributed non-parametric test was performed. An association between two variables was also performed using the chi-square test. For all tests, significance was achieved at $p < 0.05$.

RESULTS

The total number of patients included in this study, their age and comorbidities are represented in Table 1. A total of 60 participants were included, with 60% males and 40% females.

The age range was 27 to 94 years, with a median age of 68.5 years. The most prevalent comorbidity was chronic cardiovascular disease, affecting 70% of the participants.

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Table 1: Baseline demographics of the study population (N = 60)

Gender	N (%)
Male Female	36(60) 24(40)
Age (27-94) years	**Median**
All Male Female	68.5 60.5 69
Comorbidities	**N (%)**
Chronic pulmonary disease Chronic renal disorder Chronic cardiovascular disease Endocrine disorder	36(60) 35(58.3) 42(70) 40(66.7)
LOS	**N (%)**
2-7days 8-14 days 14-21 days >21 days	15(25) 15(25) 15(25) 15(25)
Management	**N (%)**
MV Inotropes HD	39 (65) 54(90) 20(33.3)
SOFA Prediction	**N (%)**
95.20% 33.30% 50% 21.50% 20.20% 6.40%	21(35) 16(26.6) 11(18.3) 10(16.6) 1(1.6) 1(1.6)

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Endocrine disorders affected 66.7%, chronic pulmonary disease 60%, and chronic renal disorder 58.3% of the participants. The length of hospital stays (LOS) was evenly distributed across four time ranges: 2-7 days, 8-14 days, 14-21 days, and over 21 days, with 15 patients (25%) in each category. In terms of management interventions, 39 patients (65%) required mechanical ventilation (MV), 54 patients (90%) needed inotropes, and 20 patients (33.3%) underwent haemodialysis (HD). This indicates that while the duration of hospital stays was similar across the population, most patients required significant interventions, particularly ionotropic support.

Table 2 illustrates the different sources of sepsis in the study population and their respective outcomes. The sources include genitourinary tract (40%), lower respiratory tract (23.3%), gastrointestinal tract (10%), skin (8.3%), wound contamination (6.6%), intravenous catheter (5%), and biliary tract and bloodstream infections, each affecting less than 2% of the population. The outcomes for sepsis sources are divided into three categories: Discharge, Death, and DAMA. Out of 33 participants, 55% were discharged, 36.6% died, and 8.3% left against medical advice.The complications and outcomes in participants with sepsis are represented in Table 3. Shock occurred in 42 participants, with 21 patients discharged, 19 deaths, and 2 leaving against medical advice. AKI affected 30 participants, with 15 discharged, 12 deaths, and 3 left against medical advice. Other complications and outcomes are also listed.

Table 4 shows the distribution of microorganisms isolated from different sample types. Acinetobacter species had 28 isolates (17.2%), mainly from sputum (12 isolates). E. coli had 24 isolates (14.8%), primarily from urine (12 isolates).

Table 2: Sources of sepsis and patient outcomes in the study population

S.no.	Source of sepsis	Outcome			N (%)
		Discharge	Death	DAMA	
1	Genitourinary tract	14	7	3	24(40)
2	Lower respiratory tract	9	5	0	14(23.3)
3	GIT	3	2	1	6(10)
4	Skin	3	2	0	5(8.3)
5	Wound contamination	2	2	0	4(6.6)
6	Intravenous catheter	1	2	0	3(5)
7	lower respiratory tract/ genitourinary tract	0	1	1	2(3.3)
8	Biliary tract	1	0	0	1(1.6)
9	Bloodstream infection	0	1	0	1(1.6)
	Total No. (%)	**33(55)**	**22(36.7)**	**5(8.3)**	**60(100)**

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Table 3: Complications of sepsis and outcomes in the study population

S.no	Complications	Outcome			N	(%)
		Discharge	Death	DAMA		
1	Shock	21	19	2	42	70
2	Acute kidney injury	15	12	3	3	50
3	Respiratory failure	12	6	2	20	33.3
4	Encephalopathy	6	11	2	1	31.7
5	Metabolic acidosis	11	15	1	27	45
6	Coagulopathy	5	10	0	15	25
7	Thrombocytopenia	6	5	0	11	18.3
8	Diabetic ketoacidosis	4	3	3	10	16.7
9	MODS	1	7	0	8	13.3
10	Lactic acidosis	2	5	0	7	11.7
11	Hyperkalaemia	2	3	2	7	11.7
12	ARDS	2	4	1	7	11.7

The total number of isolates was 162, distributed as follows: blood 37 (22.8%), sputum 32 (19.75%), urine 34 (20.98%), tissue 22 (13.58%), pus 19 (11.72%), and other sources 18 (11.11%).

In this study of 60 sepsis patients, the statistical analysis showed no significant association between receiving pathogen-specific therapy and health status (p=0.618). However, there was a significant association between the need for mechanical ventilation and patient outcomes (p=0.008), with patients requiring MV having a higher mortality rate.

The chi-square result for inotropic support was $\chi^2 = 1.148$ with a p-value of 0.284, suggesting no significant association (NS) between the need for inotropic support and health status. The chi-square analysis found no significant association between gender and health status (chi-square value: 0.191, p-value: 0.662), length of stay and health status (chi-square value: 3.158, p-value: 0.368), and SOFA score predictions and health status (highest predicted probability: 95.20%, chi-square value: 2.436, p-value: 0.786). (Table 5)

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Table 4: Microorganisms isolated from cultures in the study population

M.O	BLOOD	SPUTUM	URINE	TISSUE	PUS	OTHER	TOTAL	
							N	(%)
ACINETOBACTER SP.	5	12	1	3	3	4	28	17.2
E. COLI	6	2	12	1	2	1	24	14.8
KLEBSIELLA SP.	0	9	4	3	3	4	23	14.1
ENTEROCOCCUS SP.	0	0	1	10	6	3	20	12.3
CONS	14	0	1	0	1	1	17	10.4
CANDIDA ALBICANS	0	1	0	4	0	1	6	3.7
MRSA	1	1	1	0	1	1	5	3.08
OTHER	11	7	14	1	3	3	39	24.07
GRAND TOTAL (N)	37	32	34	22	19	18	162	100

Table 5: Chi-square analysis of health outcomes in sepsis patients based on various clinical factors

Variables	Health status		Chi-Square X2	P Value	Remark
	Alive	Dead			
Pathogen-specific therapy					
Received	29	18	0.249	0.618	NS
Not received	9	4			
Need for MV					
Yes	20	19	6.969	0.008	S
No	18	3			
Need for inotrope					
Yes	33	21	1.148	0.284	NS

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Gender					
Male	22	14	0..191	0.662	NS
Female	16	8			
LOS					
1-7days	11	4	3.158	0.368	NS
8-14 days	11	4			
14-21 days	7	8			
>21 days	9	6			
SOFA prediction					
95.20%	11	10	4.007	0.548	NS
33.30%	11	5			
50%	6	5			
21.50%	8	2			
20.20%	`1	0			
6.40%	1	0			
NS: Not significant, S: Significant					

DISCUSSION

In this study, we aimed to analyse the management, complications, and outcomes of sepsis in a tertiary care hospital. A total of 60 participants were enrolled in the study, among them 60% were male, and the ages ranged broadly from 27 to 94, with a median age of 68.5 [Table 1]. It was similar to a study conducted by ....., which also shows sepsis predominantly affects older individuals due to age-related immune decline and the higher prevalence of comorbidities in this population.

Management of Sepsis

In our research, we found that a variety of antibiotics were commonly used, both as empiric and pathogen-specific treatments. For empiric therapy, Piperacillin-Tazobactam (PIPTAZ) was the most frequently used, with 43 instances, followed by Meropenem (28 instances), Azithromycin (22 instances), Metronidazole (17 instances), and Colistin (16 instances). This demonstrates the frequent reliance on broad-spectrum antibiotics in the early stages of sepsis management before the specific pathogen is identified.

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After the causative pathogen was identified, the treatment was tailored to target the specific pathogen, outlining the pathogen-directed therapy.Meropenem was administered 19 times, followed by Colistin 18 times and Cotrimoxazole DS 12 times, whereas both Teicoplanin and Tigecycline were administered 10 times, and the least administered agent was Amikacin for 7 times. All these different antimicrobial therapies were used to treat a variety of infections. The high usage of Meropenem, particularly as pathogen-specific therapy, aligns with findings from Abe et al. (2018), where 51.5% of cases required Meropenem due to the presence of multidrug-resistant organisms. Similarly, in Mulatu et al. Similarly, in a study conducted by Mulatu et al. (2021), for an early treatment, 62.5% of patients received broad-spectrum antibiotics, but drugs like colistin were restricted due to some limitations. (8) (12)

Source of Sepsis and Causative Microorganisms

In our study, the genitourinary tract (n=24, 40%) and lower respiratory tract (n=14, 23.3%) were the most common sources of sepsis [Table 2]. This finding is consistent with the study conducted by Abe et al. (2018) and Mulatu et al. (2021), as their study also revealed that urinary tract and respiratory tract infections are the most common sources of sepsis. (8,12).

In terms of pathogens, our study found Klebsiella sp. in 28.1% of respiratory infections and Escherichia coli (E. coli) in 28.2% of urine cultures, closely matching the 27.4% and 30.5% of cases, respectively, reported by Rahat Ullah et al. (2020) and Mulatu et al. (2021). (8) (9) The high frequency of these pathogens emphasizes the need for targeted antibiotic therapies in these patient populations.

Complications and Mortality

It was found that septic shock was one of the most common complications, affecting 70% of the patients, with a mortality rate of 45.2% [Table 3]. It was consistent with a study conducted by Abe et al. (2018), which revealed that 66.5% of patients experienced septic shock, with a mortality rate of 42.7%.12. However, in a study conducted by Rahat Ullah et al. (2020), the mortality rate was 51.5% which is slightly higher than our study; this may be due to delayed interventions. (9)

The second most common complication was AKI, which was seen in 50% of the study population, with a mortality rate of 40% [Table 3]. In comparison, Abe et al. (2018) and Mulatu et al. (2021) reported AKI in 42.3% and 48.5% of patients, respectively, with similar mortality rates of 39.4% and 41%. (12) (8)

MODS (multi-organ dysfunction syndrome) was present in 16.6% of our patients, with a mortality rate of 87.5% [Table 3]. Abe et al. (2018) found MODS in 18.4% of their study, with a comparable mortality rate of 85%, underscoring the severe prognosis associated with multi-organ failure. Whereas, in a study conducted by Rahat Ullah et al. (2020) and Mulatu et al. (2021), MODS was relatively infrequent but showed similar mortality risks. (12) (8) (9) Our study also revealed that 31.6% of the study population developed encephalopathy [Table 3], with a mortality rate of 57.9%, similar to the study of Abe et al. (2018). (12)

SOFA Score and Outcome Prediction

The mean SOFA score in our study during the first 24 hours was 10.1, indicating significant organ dysfunction. In a similar study conducted by Abe et al. (2018), the mean score was 7.4, which is slightly lower than our study, which had a clear correlation with higher mortality.

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However, our chi-square analysis revealed no significant association between SOFA scores and mortality with a chi-square value: of 2.436 and a p-value: of 0.786 [Table 5] (12). This may be because we only assessed the SOFA score for the worst value in the first 24 hours. Gender differences in SOFA scores in septic patients were also analyzed. It was observed that, on average, females (9.29 ± 2.74) had a lower SOFA score at admission for sepsis compared to males (10.75±3.21). It's probably a uniform threshold in the laboratory component that accounts for the sum of the observed difference. Despite this, there is no difference in mortality as observed. A previous study conducted by Zimmermann et al. also found that women have lower SOFA scores at ICU admission for sepsis compared to men and differences in ICU mortality or length of stay (LOS) were observed between the sexes. According to the current and previous studies, the SOFA score's standard laboratory thresholds might not accurately represent physiological changes, particularly gender-specific ones, which could account for score disparities without affecting the end outcome. (15)

Length of Hospital Stay and Mortality

The median length of hospital stay in our study was 14.5 days (IQR 7.5-21) [Table 1], which is consistent with the 15-day stay reported by Abe et al. (2018). However, the overall mortality rate in our study was 36.7%, but in a study conducted by Abe et al (2018) (12), the mortality rate was observed to be 29.5%. These differences may be due to comorbidities or the severity of patients in ICU care. The results of this study are consistent with international studies on sepsis, because in both studies, the study pathogen prevalence, complications, and treatment approaches are the same. The use of broad-spectrum antibiotics and early aggressive management are recurring themes in all of the research, but the results differ greatly depending on the quality of healthcare and the availability of resources. Notably, outcomes vary between high- and low-resource settings, and comorbidities, including septic shock, AKI, and MODS, continue to be important predictors of mortality.

DECLARATIONS

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Abbreviations
ICU (Intensive Care Unit), HICU (High Intensive Care Unit), GCS (Glasgow Coma Scale), SOFA (Sequential Organ Failure Assessment), MAP (Mean Arterial Pressure), MO (Microorganism), LOS (Length of Stay), MV (Mechanical Ventilator), HD (Haemodialysis), DAMA (Discharge Against Medical Advice), UTIs (Urinary Tract Infections), AKI (Acute Kidney Injury), GIT (Gastrointestinal Tract), MODS (Multiple Organ Dysfunction), ARDS (Acute Respiratory Distress Syndrome), MRSA (Methicillin-Resistant Staphylococcus Aureus), and CONS (Coagulase-Negative Staphylococcus).

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Conflicts of Interest

The authors declare that there are no conflicts of interest related to this study. The research was conducted independently, and the findings represent the unbiased results and interpretations of the authors.

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Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request. The data will be made available to qualified researchers for non-commercial purposes only, subject to ethical and privacy considerations. Due to privacy restrictions, participant data cannot be publicly shared, but can be accessed by contacting the corresponding author.

Protection of humans and animals.

The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval

The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence.

The authors declare that no generative artificial intelligence was used in the writing of this manuscript