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The Impact of Antibiotics Timing on ICU Stay Duration in Sepsis Patients- A Retrospective Study

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ABSTRACT

Background: Timely antibiotic administration is crucial in the management of sepsis and septic shock, but the impact of timing on clinical outcomes remains controversial. This study aimed to evaluate the association between time to antibiotic administration and duration of intensive care unit (ICU) stay, as well as the relationship between Acute Physiology and Chronic Health Evaluation II (APACHE II) scores at presentation and ICU stay duration in patients with sepsis or septic shock. **Methodology**:This retrospective study included 101 patients aged ≥18 years with suspected infection and clinically diagnosed sepsis or septic shock, admitted to the ICU or high dependency unit from the emergency department between May 2022 and August 2022. Patients were divided into groups based on the time from triage to first antibiotic administration. APACHE II scores were calculated at presentation. The primary outcome was duration of ICU stay. Regression analyses were performed to evaluate the associations of interest, adjusting for potential con-founders. **Results:** The mean duration of ICU stay was 5.3 ± 3.5 days, and the mean APACHE II score was 18.95 ± 8.96. No significant association was found between time to antibiotic administration and duration of ICU stay ($p > 0.05$). Similarly, there was no significant correlation between APACHE II scores at presentation and ICU stay duration ($p > 0.05$) or mortality ($p > 0.05$). **Conclusion:** In this cohort of sepsis and septic shock patients, the timing of antibiotic administration and APACHE II scores at presentation were not significantly associated with the duration of ICU stay or mortality. These findings contribute to the ongoing discussion regarding the impact of antibiotic timing and severity scoring systems on sepsis outcomes.

INTRODUCTION

Sepsis is a common and life threatening condition requiring timely and effective antimicrobial therapy.[1]The growing number of older persons with comorbidities is contributing to a steady increase in the prevalence of sepsis.[2,3] Despite improvements in diagnosis and treatment, sepsis still has a heavy public health burden due to its high rates of morbidity, mortality, and medical expenses.[2,4]Over the years, outcome of sepsis have improved with more focus on intravenous fluids, appropriate antimicrobials, and other supportive measure.[5] Within the population, sepsis frequently manifests as the progression of common, avoidable infections, such as those affecting the skin, gastrointestinal tract, respiratory system, or urinary tract.

Antibiotics should be administered within one hour of emer-gency department (ED) triage, according to current sepsis recommendations. The supporting data, however, is of moderate quality, and research on the relationship between the timing of antibiotic administration and septic shock outcomes has produced contradictory findings. Early antibiotic therapy has been shown in several prior trials to enhance patient outcomes in cases of septic shock and severe sepsis.[6,7] Results regarding the relationship between the timing of antibiotic treatment and the course of severe sepsis and septic shock, however, vary.[8,9] The usefulness of early antibiotic therapy in patients hospitalised to the intensive care unit (ICU) due to severe sepsis and septic shock was documented in a 2009 study.[10] However, new research has indicated a decline in sepsis-related mortality as a result of improved diagnosis and management of the illness, and clinical practice has adjusted as a result.

Consequently, discussing how the timing of antibiotics affects sepsis and septic shock outcomes makes sense. It's possible that early antibiotic delivery serves as a proxy for higher standards of care rather than having a direct causal relationship with better outcomes for septic shock patients.

Many scoring systems, including the Organ Dysfunction and Infection System, the Simplified Acute Physiology Score (SAPS), the Sequential Organ Failure Assessment (SOFA), and the Acute Physiology Chronic Health Evaluation II (APACHE II), have been developed in recent years to assess the severity of illness and predict the outcomes, particularly the mortality of critically ill patients. The most widely used of these methods for classifying the severity of a condition is the APACHE II score, which assigns a point score between 0 and 71 based on age, past health status, and the initial values of 12 acute physiologic variables. Higher scores are associated with more serious illnesses and a higher chance of passing away. In this audit we used APACHE II score, and we will try to find relation between APACHE II score of the patient at presentation and their ICU stay duration.

Understanding the relationship between the time to antibiotic administration and ICU stay duration in septic shock patients is essential for optimizing clinical management strategies. By evaluating this association, healthcare providers can potentially identify opportunities to enhance patient care protocols, streamline treatment processes, and ultimately improve outcomes for individuals suffering from septic shock. Additionally, exploring the correlation between the Acute Physiology and Chronic Health Evaluation II (APACHE II) score at presentation and ICU stay duration can offer valuable insights into the prognostic value of this widely used severity scoring system. This study aims to bridge existing knowledge gaps, inform evidence-based practices, and contribute to the ongoing efforts to enhance the care provided to critically ill patients with septic shock.

With this background, we conducted this study to evaluate whether the time to antibiotic administration is associated with duration of ICU stay using data collected from an ED septic shock registry and to find relation between APACHE II score of the patient at presentation and their ICU stay duration.

MATERIALS AND METHODS

This Hospital based Retrospective record-based study was conducted at KMC hospital, Mangalore recruiting patients patients diagnosed with suspected infection received in emergency room at our hospital.

Case files of patients aged more than 18 years with suspected infection and clinically diagnosed to have possible sepsis admitted to ICU (Intensive Care Unit) or HDU (High Dependency Unit) from Emergency during May 2022 to August 2022 were all collected from MRD. We excluded case files with incomplete data, patients discharged against medical advice, trauma patients and patients who took early treatment elsewhere

Permission from the Medical superintendent of KMC hospital, Ambedkar Circle was taken to access the records. Investigator visited the medical records department to collect the data and data was filled in a structured proforma. Demographic data, comorbidities, clinical history, vitals on arrival were collected.

The sepsis definition used in our study was patients who had vasopressor requirement to maintain a mean arterial pressure of 65 mm Hg or greater and serum lactate level greater than 2 mmol/L (>18 mg/dL) in the absence of hypovolemia.[11]

These patients were divided into 4 groups by the interval from triage to first antibiotic administration: group 1 (≤1 hour), 2 (1-2 hours), 3 (2-3 hours), and 4 (>3 hours).APACHE II score was calculated for each patient at presentation and then their duration of ICU stay was noted.

Descriptive statistics was used to summarize patient demographics and clinical characteristics. Univariate and multivariate regression analyses was conducted to evaluate the association between time to antibiotic administration and duration of ICU stay, as well as the relationship between APACHE II score at presentation and ICU stay duration. The regression models were adjusted for potential confounding factors, such as patient age, sex, comorbidities, and severity of illness.

RESULTS

One hundred one patients were included in the study; 62 were males and 39 were females. The mean age of study participants was 65.97 ± 12.54, ranging from 24 to 88 years. In our patient group, the average number of days that patients spent in the intensive care unit was 5.3 ± 3.5 days (mean ± SD). The mean APACHE II score in our cohort of patients was 18.95 ± 8.96 (mean ± SD). We had 78 patients suspected with sepsis and 23 patients with septic shock.

Table 1 shows that the source of infection among suspected sepsis was mostly respiratory (74.4%) which was significantly higher compared to septic shock patients (39.1%)($p<0.05$). We found that the acute renal failure (78.3%) and mortality (30.4%) was significantly higher in septic shock patients ($p<0.05$).

Table 1: Comparison of Categorical Variables among Suspected Sepsis and Septic Shock Patients

		Suspected sepsis (N=78)	Septic shock (N=23)	P value
Gender	Males	51 (65.4%)	11 (47.8%)	0.149
	Females	27 (34.6%)	12 (52.2%)	
Co-morbidities	Diabetes	41 (52.6%)	14 (60.9%)	0.634
	CKD	16 (20.5%)	2 (8.7%)	0.233
	COPD	16 (20.5%)	5 (21.7%)	1
Source of infection	Respiratory	58 (74.4%)	9 (39.1%)	**0.003**
	Genitourinary	5 (6.4%)	5 (21.7%)	**0.046**
	Gastrointestinal	6 (7.7%)	3 (13%)	0.680
	Central Nervous System	15 (19.2%)	8 (34.8%)	0.157
	Skin and Soft Tissue	0	1 (4.3%)	0.228
Blood culture sample taken	No	25 (32.1%)	6 (26.1%)	0.621
	Yes	53 (67.9%)	17 (73.9%)	
Antibiotic indicated	No	66 (84.6%)	21 (91.3%)	0.514
	Yes	12 (15.4%)	2 (8.7%)	
Acute Renal failure	Yes	28 (35.9%)	18 (78.3%)	**<0.001**
	No	50 (64.1%)	5 (21.7%)	
Survival	Survived	72 (92.3%)	16 (69.6%)	**0.009**
	Death	6 (7.7%)	7 (30.4%)	
Time of administration of antibiotic	<1 hour	40 (51.3%)	15 (65.2%)	0.341
	1-2 hour	38 (48.7%)	8 (34.8%)	

Table 2 shows that the mean MAP, HCO3-, GCS and qSOFA was significantly higher in suspected sepsis patients compared to septic shock patients($p<0.05$). We found that the mean WBC count was significantly higher in septic shock patients compared to suspected sepsis patients ($p<0.05$).

Table 2: Comparison of Continuous Variables among Suspected Sepsis and Septic Shock Patients

	Suspected sepsis (N=78)	Septic shock (N=23)	P value
Age	66.6±11.2	63.9±16.5	0.363
Temperature	36.9±0.63	37.1±0.8	0.327
MAP	93.2±16.8	63.9±16.5	**<0.001**
HR	105.7±24.5	114.9±26.6	0.127
RR	24.5±6.9	23.3±7.3	0.462
FiO2	511.9±233.2	652.7±23.9	0.339
PaO2	88.97±11.7	91.2±8.5	0.428
Ph	7.08±0.27	7.04±0.21	0.583
HCO3-	22.85±7.7	17.1±7.1	**0.002**
Na	130.5±7.6	131.5±9.9	0.620
K	4.06±0.98	4.5±1.5	0.091
Creatinine	2.3±2.1	2.65±1.87	0.502
HCT	35.6±6.8	34.1±8.2	0.373
WBC	13.5±6.7	18.5±9.8	**0.005**
GCS	12.6±3.8	10.65±4.3	**0.04**
qSOFA	1.13±0.59	1.6±0.58	**0.001**
TTA	60.62±21.3	53.1±21.01	0.139

Table 3 and table 4shows that there was no significant association and correlation between time of administration of antibiotic and APACHE II with duration of ICU stay (p>0.05)

Table 3: Association of time of administration of antibiotic and APACHE II with duration of ICU stay

		ICU stay			P value
		≤5 days	6 -10 days	≥11 days	
Time of administration of antibiotic	**< 1 hour**	36 (54.5%)	12 (60%)	7 (46.7%)	0.764
	1 to 2 hours	30 (45.5%)	8 (40%)	8 (53.3%)	
APACHE II	**Group 1 (31–40)**	3 (4.7%)	1 (5.3%)	2 (13.3%)	0.508
	Group 2 (21–30)	16 (25%)	7 (36.8%)	3 (20%)	
	Group 3 (11–20)	37 (57.8%)	8 (42.1%)	6 (40%)	
	Group 4 (3–10)	8 (12.5%)	3 (15.8%)	4 (26.7%)	

Table 4: Correlation between length of ICU stay in days with Time of administration of antibiotic and APACHE II score using Pearson correlation coefficient.

Correlational statistical analysis		**Time of administration of antibiotic**	**APACHE II score**
Length of ICU stay in days	**Pearson correlation coefficient**	0.053	0.011
	P value (<0.05)	0.602	0.909
	Number of patients in the study	101	101

Table 5 shows that there was no statistically significant correlation between APACHE II and qSOFA in suspected sepsis and septic shock patients (p>0.05)

Table 5: APACHE II Score with qSOFA in Suspected Sepsis and Septic Shock Patients

Correlational statistical analysis		**qSOFA**	
		Suspected sepsis	**Septic shock**
APACHE II	**Pearson correlation coefficient**	0.120	0.213
	P value (<0.05)	0.296	0.328
	Number of patients in the study	78	23

Table 6 shows that there was no statistically significant association of APACHE II with mortality of patients (p>0.05)

Table 6: Group Categories as per APACHE II Scores and Patient Outcomes

Group (APACHE II scoring)	**Outcome**		**Chi-square Test**
	Discharged	**Died**	Chi-square value: 5.602 P-value: 0.108
Group 1 (31–40)	4 (4.7%)	2 (16.7%)	
Group 2 (21–30)	21 (24.4%)	5 (41.7%)	
Group 3 (11–20)	48 (55.8%)	3 (25%)	
Group 4 (3–10)	13 (15.1%)	2 (16.7%)	
Total	**86 (100%)**	**12 (100%)**	-

Figure 1: Bar graph Showing age Distribution Among Study

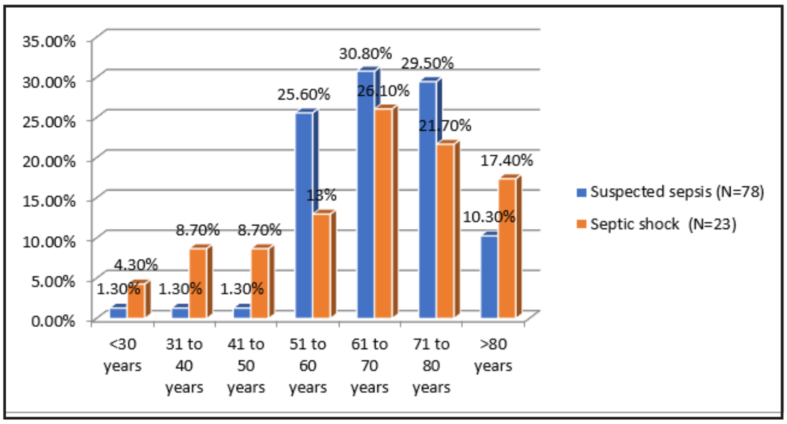


Figure 2: Bar Graph Showing Timing of Administration of Antibiotic Among Study Groups

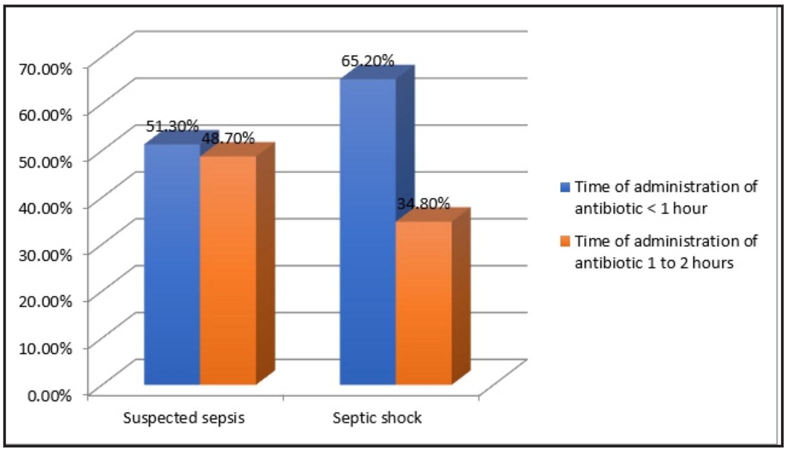


Figure 3: Bar Graph Showing ICU Stay Among Study Groups

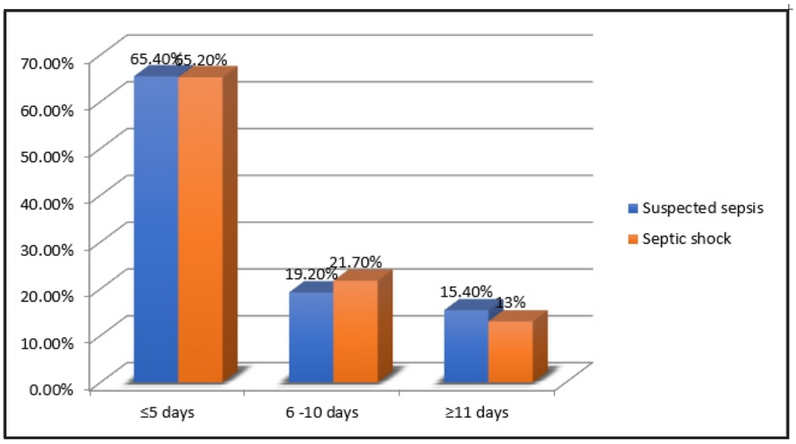


Figure 4: Bar graph showing antibiotic timing and ICU stay

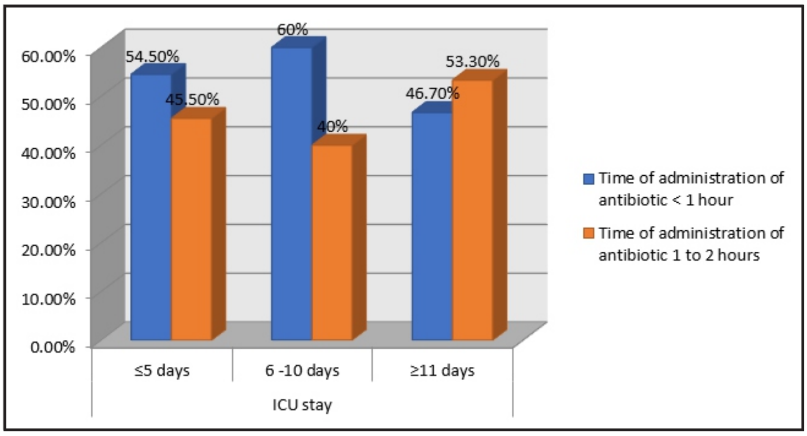


Figure 5: Bar Graph Showing APACHE and ICU Stay

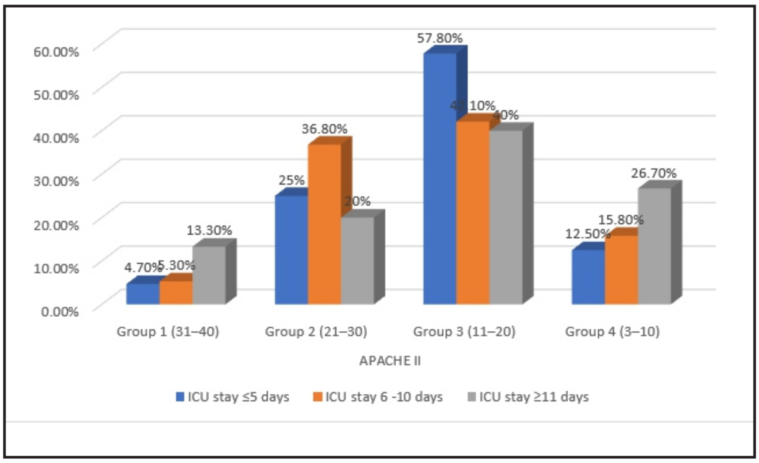


Figure 6: Bar Graph Showing Co-morbidities and ICU Stay

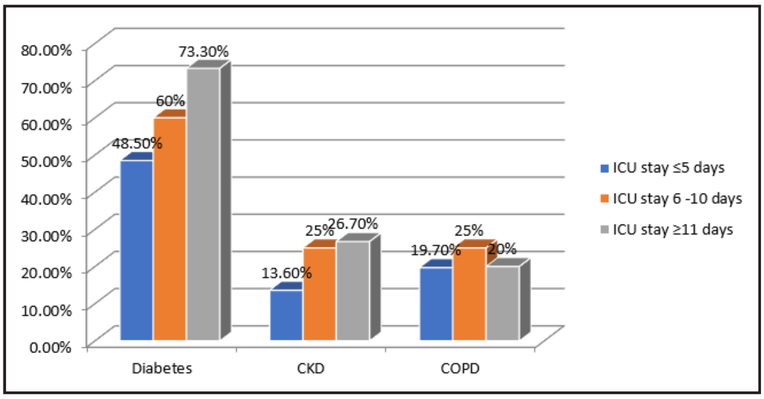


Figure 7: Bar Graph Showing Antibiotic Timing and Mortality

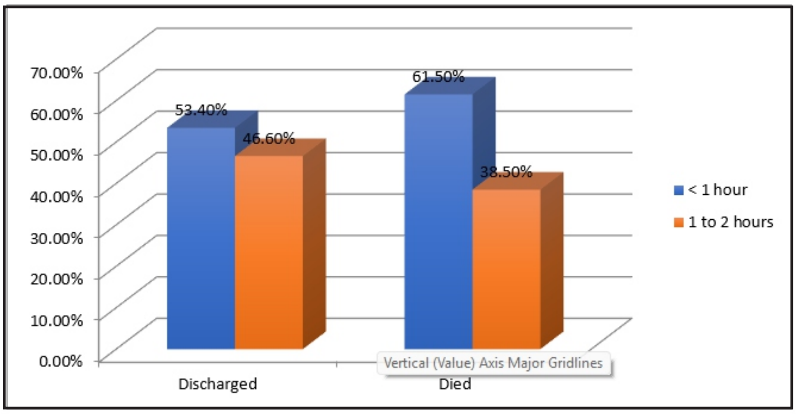


Figure 8: Bar Graph Showing APACHEII and Mortality

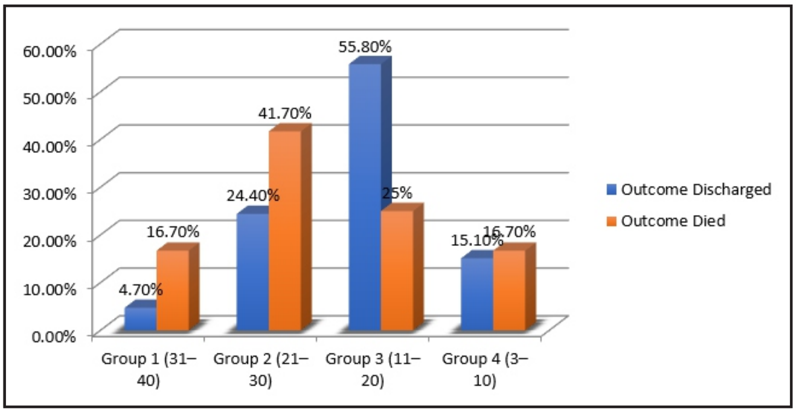
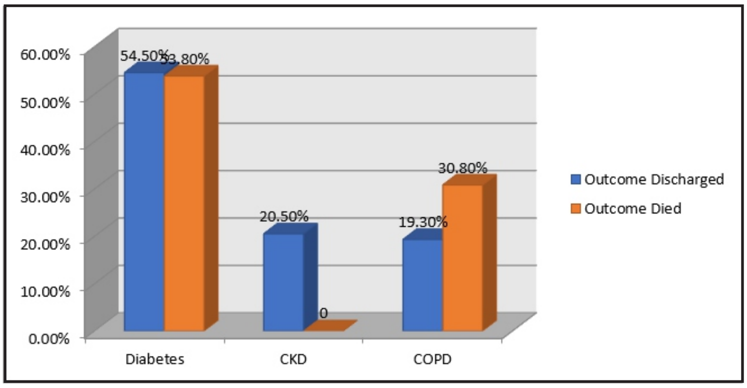


Figure 9: Bar Graph Showing Co-morbidities and Mortality



DISCUSSION

In our study, the mean length of ICU stay was 5.3 ± 3.5 days. This is in line with the findings of other studies[12, 13], which also reported similar durations of ICU stay for sepsis patients.

The length of ICU stay for patients with sepsis or septic shock was not shown to be significantly correlated with the time to antibiotic treatment in the current study. This is in line with a prospective observational study that looked at septic cases in the ED and similarly found no correlation between longer hospital stays and delayed antibiotic treatment.[14]On the other hand, prompt antibiotic administration enhanced results in patients with septic shock, according to a study titled "Time-to-antibiotics and clinical outcomes in patients with sepsis and septic shock: a prospective nationwide multicenter cohort study."[12] This suggests that while the timing of antibiotics may not impact the length of ICU stay, it could potentially influence other outcomes such as mortality. Our results contrast with some earlier studies that demonstrated improved outcomes with prompt antibiotic administration in severe sepsis and septic shock.[7,10] However, our findings align with more recent investigations reporting mixed results regarding the impact of antibiotic timing on outcomes in septic patients.[8,9]

A multicenter study by de Groot et al.[8] examined the association between time to antibiotics and relevant clinical outcomes in emergency department patients with various sepsis severities. They found no significant difference in mortality or length of stay between patients receiving antibiotics within 1 hour versus later. Similarly, Puskarich et al.[9] reported no association between timing of antibiotic administration and mortality in septic shock patients treated with a quantitative resuscitation protocol. However, another study found that timely administration of antibiotics improved outcomes in patients with septic shock.[12]This suggests that while the timing of antibiotics may not impact the length of ICU stay, it could potentially influence other outcomes such as mortality.

In terms of APACHE II scores, our study found a mean score of 18.95 ± 8.96. We found no statistically significant correlation between APACHE II and qSOFA in suspected sepsis and septic shock patients ($p>0.05$), and no statistically significant association of APACHE II with mortality of patients ($p>0.05$). A study titled "Timing of antibiotic therapy in the ICU" highlighted the importance of antibiotic timing in the ICU and provided an approach to antimi crobials that also minimizes the unnecessary use of these agents.[13] According to this study, developments in artificial intelligence and machine learning, as well as molecular microbiology testing, may make it possible to identify patients who require empirical antibiotic therapy earlier on and to determine the precise antibiotics that are needed to prevent the needless administration of broad-spectrum antibiotics.[13]

Our results contrasts with the general understanding that higher APACHE II scores correspond to greater illness severity and potentially longer hospitalizations.[15]

Additionally, our study did not find a significant association between APACHE II scores and mortality. While prompt antibiotic administration remains crucial for sepsis management, the lack of association with ICU stay echoes recent reports[8,9] suggesting that other factors, such as overall care quality, timely recognition and resuscitation, and appropriate source control, may play a more significant role in determining outcomes than antibiotic timing alone.

Discrepancies between our results and some prior studies could stem from differences in study populations, sepsis definitions, antibiotic protocols, and evolving sepsis understanding and management over time. As noted, recent years have seen improvements in sepsis-related mortality due to better comprehension and treatment.[5]

CONCLUSION

In conclusion, our study did not find a significant association between the time to antibiotic administration and duration of ICU stay or between APACHE II scores at presentation and ICU stay duration or mortality in patients with sepsis or septic shock. These findings contribute to the ongoing discussion on the impact of antibiotic timing and severity scoring systems on sepsis outcomes. Further research, potentially incorporating larger sample sizes and more diverse patient populations, may help elucidate the complex interplay between these factors and sepsis outcomes

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