

Delay in Recognition and Treatment of Sepsis in Emergency Departments: A Prospective Observational Study

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Abstract

Background: Sepsis remains a leading cause of morbidity and mortality globally, with outcomes heavily dependent on the promptness of recognition and antimicrobial administration in the emergency department (ED).

Objectives: To evaluate the frequency, causes, and clinical consequences of delays in the recognition and treatment of sepsis among adult emergency department patients.

Methods: A prospective observational study was conducted over a 12-month period across three tertiary care EDs, enrolling 1,248 adult patients presenting with sepsis or septic shock according to Sepsis-3 criteria. Data regarding triage vital signs, time to physician evaluation, time to lactate measurement, time to broad-spectrum antibiotic initiation, and in-hospital mortality were collected and analyzed using multivariable regression.

Results: The median time from ED arrival to physician evaluation was 42 minutes (IQR, 24–68), while the median time to intravenous antibiotic administration was 168 minutes (IQR, 112–235). Only 34.2% of patients received antibiotics within the benchmark 60-minute window. Each 60-minute delay in antibiotic administration was independently associated with a 1.18-fold increase in in-hospital mortality (adjusted odds ratio [aOR], 1.18; 95% confidence interval [CI], 1.09–1.28; $p < 0.001$) and prolonged intensive care unit (ICU) length of stay. Multivariable analysis identified triage by non-accredited nursing staff, atypical presentation (afebrile or normotensive), and ED overcrowding as primary independent predictors of treatment delay.

Conclusions: Significant delays in sepsis recognition and treatment persist in emergency departments, substantially worsening patient survival. Interventions must target early automated clinical decision support, rapid biomarker turnaround, and streamlined triage protocols.

1. Introduction

Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. It represents a critical medical emergency requiring immediate identification, hemodynamic resuscitation, and antimicrobial therapy. Worldwide, sepsis accounts for millions of deaths annually, imposing a staggering burden on healthcare systems [1, 2]. In acute care settings, the emergency department (ED) serves as the primary portal of entry for the vast majority of patients with community-acquired or healthcare-associated sepsis.

Decades of clinical research have established that time-to-treatment is a critical determinant of survival in sepsis and septic shock. Landmark studies by Kumar et al. demonstrated that each hour of delay in administering effective antimicrobial therapy over the first six hours following hypotension onset is associated with a measurable decrease in survival [3]. Consequently, international quality improvement initiatives, such as the Surviving Sepsis Campaign (SSC), have advocated for rigorous performance bundles requiring antibiotic delivery and initiation of protocolized fluid resuscitation within one hour of triage recognition [4, 5].

Despite widespread guideline dissemination and institutional quality campaigns, translating recommendations into rapid bedside execution remains profoundly challenging. Emergency departments frequently operate under severe operational strain characterized by overcrowding, boarding of admitted inpatients, high nurse-to-patient ratios, and diagnostic ambiguity [6, 7]. Patients presenting with sepsis often exhibit subtle or non-classic physiological presentations—such as normotension in younger cohorts or absence of fever in the elderly or immunocompromised—which frequently obscure prompt bedside recognition [8, 9].

While previous studies have highlighted global adherence rates to sepsis bundles, there remains a critical knowledge gap regarding the granular temporal bottlenecks occurring between ED arrival, physician assessment, diagnostic laboratory turnaround, and therapeutic delivery. Furthermore, the interplay between hospital crowding metrics and individual patient presentation factors contributing to delays has not been comprehensively evaluated in large prospective multi-center cohorts. Therefore, the primary objective of this prospective observational study was to quantify the extent of delays in sepsis recognition and treatment across diverse emergency care settings, identify the principal clinical and operational determinants of these delays, and evaluate their downstream impacts on in-hospital mortality and resource utilization.

2. Methods

2.1 Study Design and Setting

This investigation was designed as a prospective, multi-center observational study conducted over a 12-month period (January 1, 2025, through December 31, 2025). The study was executed across three urban tertiary care academic emergency departments with an aggregate annual census exceeding 240,000 patient visits. The institutional review boards at all participating medical centers approved the study protocol with a waiver of informed consent due to the observational, non-interventional nature of the quality improvement evaluation and adherence to strict data anonymization standards.

2.2 Selection of Participants

All adult patients (aged 18 years or older) presenting to the participating EDs during the study window who met Sepsis-3 operational definitions were eligible for inclusion. Sepsis was defined as suspected or documented infection coupled with an acute increase of 2 points or greater in the Sequential Organ Failure

Assessment (SOFA) score. Septic shock was further defined per Sepsis-3 criteria as sepsis with persisting hypotension requiring vasopressor therapy to maintain a mean arterial pressure ≥ 65 mmHg, together with a serum lactate level > 2 mmol/L, despite adequate volume resuscitation [14]. In the ED clinical workflow, screening was operationalized using a modified quick SOFA (qSOFA) score combined with systemic inflammatory response syndrome (SIRS) criteria and clinician gestalt. Patients were excluded if they were transferred from another acute care hospital with antimicrobial therapy already initiated, if they possessed limitations of care orders (e.g., Do Not Resuscitate / comfort care measures only) restricting aggressive resuscitation upon arrival, or if they left against medical advice prior to diagnostic completion.

2.3 Data Collection and Variables

Data were captured prospectively by trained clinical research coordinators embedded within the EDs 24 hours a day, 7 days a week, utilizing standardized electronic health record (EHR) abstraction tools. Recorded variables encompassed patient demographics, baseline comorbidities quantified via the Charlson Comorbidity Index, vital signs at triage (temperature, heart rate, respiratory rate, blood pressure, oxygen saturation), and physiological scoring parameters. Operational metrics included exact timestamps for ED arrival (electronic badge swipe / triage registration), initial physician medical evaluation, lactate blood draw and laboratory reporting, blood culture collection, and intravenous antimicrobial administration.

To evaluate operational confounders, ED crowding was assessed continuously using the National ED Overcrowding Scale (NEDOCS) recorded at hourly intervals. Clinical presentations were categorized into classic (fever, tachycardia, hypotension) versus atypical (normotensive presentation, afebrile, isolated altered mental status). The primary exposure variables were time-to-recognition (defined as the interval between ED arrival and physician documentation of suspected sepsis) and time-to-treatment (defined as the interval between ED arrival and administration of the first dose of intravenous broad-spectrum antibiotics).

2.4 Statistical Analysis

Continuous variables are presented as means with standard deviations or medians with interquartile ranges (IQRs), depending on data normality evaluated via Shapiro-Wilk tests. Categorical variables are reported as absolute counts and percentages. Bivariate comparisons were performed utilizing Student's t-tests or Mann-Whitney U tests for continuous data, and chi-square or Fisher's exact tests for categorical data. Multivariable logistic regression models were constructed to evaluate the independent association between time-to-treatment delays and in-hospital mortality, adjusting for potential confounders including age, initial SOFA score, lactate levels, Charlson Comorbidity Index, and septic shock status. Multivariable linear regression was utilized to examine predictors of extended length of stay. All statistical analyses were conducted using R statistical software (version 4.3.2), with two-sided p-values < 0.05 denoting statistical significance.

3. Results

3.1 Baseline Characteristics of the Cohort

During the 12-month study period, a total of 1,382 patients were screened for suspected sepsis. Following the application of exclusion criteria (104 transfers, 30 incomplete EHR records), the final analytical cohort comprised 1,248 patients. The median patient age was 67.4 years (IQR, 56–79), and 53.8% of the cohort were male. Pulmonary infections represented the most frequent suspected source of sepsis (43.2%), followed by genitourinary (24.6%), intra-abdominal (16.4%), skin and soft tissue (9.2%), and primary

bloodstream infections (6.6%). Septic shock upon arrival or developing within 6 hours of presentation was identified in 384 patients (30.8%). Detailed baseline demographic and clinical characteristics are summarized in Table 1.

Baseline Characteristic	Overall Cohort (N = 1,248)	Survivors (n = 1,024)	Non-Survivors (n = 224)
Age, years (median [IQR])	67.4 (56–79)	65.2 (54–77)	74.1 (63–84)
Male sex, n (%)	672 (53.8%)	548 (53.5%)	124 (55.4%)
Charlson Comorbidity Index (median [IQR])	3 (1–5)	2 (1–4)	5 (3–7)
Initial SOFA Score (mean $\pm$ SD)	6.4 $\pm$ 2.8	5.7 $\pm$ 2.4	9.2 $\pm$ 3.1
Initial Lactate, mmol/L (median [IQR])	2.8 (1.8–4.2)	2.5 (1.6–3.8)	4.6 (3.1–6.8)
Septic Shock, n (%)	384 (30.8%)	262 (25.6%)	122 (54.5%)
Source of Infection, n (%)			
- Pulmonary	539 (43.2%)	430 (42.0%)	109 (48.7%)
- Genitourinary	307 (24.6%)	264 (25.8%)	43 (19.2%)
- Intra-abdominal	205 (16.4%)	168 (16.4%)	37 (16.5%)
- Skin / Soft Tissue	115 (9.2%)	98 (9.6%)	17 (7.6%)
- Other / Unknown	82 (6.6%)	64 (6.2%)	18 (8.0%)

Table 1. Baseline demographic, clinical, and physiological characteristics of the study cohort.

3.2 Temporal Intervals and Treatment Delays

Analysis of time intervals from ED presentation to therapeutic interventions revealed substantial delays across the cohort. The median time from ED arrival to initial physician evaluation was 42 minutes (IQR, 24–68). The median time to blood culture collection was 58 minutes (IQR, 35–94), and serum lactate results were reported at a median of 74 minutes (IQR, 48–115). The median interval from arrival to the administration of the first dose of intravenous broad-spectrum antibiotics was 168 minutes (IQR, 112–235).

When evaluated against international quality benchmarks, only 427 patients (34.2%) received antimicrobial therapy within 60 minutes of arrival. Furthermore, in patients presenting with septic shock (n = 384), the median time to antibiotic administration was 124 minutes (IQR, 82–176), with only 41.1%

achieving the 60-minute benchmark. Detailed temporal intervals categorized by clinical presentation and shock status are presented in Table 2.

Clinical Metric	Interval	All Patients (N = 1,248)	Sepsis without Shock (n = 864)	Septic Shock (n = 384)
Time to Physician Evaluation, min (median [IQR])		42 (24–68)	45 (26–71)	34 (18–52)
Time to Blood Culture Collection, min (median [IQR])		58 (35–94)	62 (38–98)	48 (28–82)
Time to Lactate Result, min (median [IQR])		74 (48–115)	78 (52–120)	64 (40–96)
Time to Antibiotic Administration, min (median [IQR])		168 (112–235)	182 (124–248)	124 (82–176)
Antibiotics Administered within 60 min, n (%)		427 (34.2%)	269 (31.1%)	158 (41.1%)
Antibiotics Administered within 180 min, n (%)		782 (62.7%)	512 (59.3%)	270 (70.3%)
Time to Initial Fluid Bolus (>30 mL/kg), min		142 (94–204)	165 (110–228)	104 (68–152)

Table 2. Emergency department temporal intervals and treatment milestones for sepsis and septic shock.

3.3 Determinants of Treatment Delay

Multivariable linear and logistic regression models were executed to identify independent predictors of treatment delay (defined as antibiotic administration > 60 minutes). Several clinical and operational factors significantly predicted delayed care. Triage presentation with atypical physiological parameters (such as normal blood pressure in the presence of marked tachypnea or altered mental status) was associated with a 2.4-fold increased odds of treatment delay (aOR, 2.42; 95% CI, 1.84–3.18; $p < 0.001$). High ED crowding, represented by NEDOCS scores greater than 140 during the presentation hour, prolonged time to physician evaluation by a median of 38 minutes and increased overall time to antibiotics by 54 minutes ($p < 0.001$).

Patients presenting during evening and overnight shifts (16:00 to 08:00) experienced significantly longer intervals to antibiotic delivery compared to daytime arrivals (median 184 min vs. 142 min; $p = 0.002$). Furthermore, initial triage performed by non-accredited nursing staff without specific sepsis recognition training was independently associated with delayed physician notification.

3.4 Clinical Outcomes and Mortality Analysis

Overall in-hospital mortality for the cohort was 17.9% (224 of 1,248 patients). Unadjusted mortality was significantly higher among patients who experienced treatment delays beyond 180 minutes (21.9%) compared to those treated within 60 minutes (11.2%; $p < 0.001$). Multivariable logistic regression adjusting for age, Charlson Comorbidity Index, baseline SOFA score, and lactate revealed that each 60-minute delay in antibiotic administration was independently associated with an 18% increase in in-hospital mortality (adjusted odds ratio [aOR], 1.18 per hour delay; 95% CI, 1.09–1.28; $p < 0.001$).

In addition to mortality, treatment delays were strongly correlated with increased intensive care unit (ICU) admission rates among ward-admitted patients, prolonged mechanical ventilation duration, and extended hospital length of stay. Table 3 outlines the multi-variable regression outcomes assessing the impact of treatment delays on clinical endpoints.

Clinical Endpoint / Outcome	Reference (≤ 60 min)	Delayed (> 180 min)	Adjusted Effect Size (aOR / β [95% CI])
In-Hospital Mortality, n (%)	48 / 427 (11.2%)	102 / 466 (21.9%)	aOR 1.18 per hour (1.09–1.28)*
ICU Admission Rate, n (%)	142 / 427 (33.3%)	248 / 466 (53.2%)	aOR 1.54 (1.22–1.94)*
Ventilator Days (mean $\pm$ SD)	3.2 $\pm$ 2.1	5.8 $\pm$ 3.9	β +2.1 days (1.5–2.7)*
Hospital Length of Stay, days (median [IQR])	6.2 (4.1–9.8)	9.8 (6.4–15.2)	β +3.4 days (2.6–4.2)*
New-Onset Organ Failure Rate, n (%)	84 / 427 (19.7%)	176 / 466 (37.8%)	aOR 1.76 (1.38–2.25)*

Table 3. Multivariable regression analysis evaluating clinical outcomes associated with antimicrobial treatment delay (* $p < 0.001$).

4. Discussion

In this prospective multicenter study, substantial delays in the recognition and treatment of sepsis were observed across three tertiary care emergency departments. Despite widespread international guidelines advocating for antimicrobial administration within 60 minutes of presentation [4, 5, 15], Only 34.2% of patients received intravenous antibiotics within 60 minutes of presentation, with a median time to antibiotic administration of 168 minutes. Treatment delay was independently associated with increased

in-hospital mortality, with each additional hour of delay associated with an 18% increase in the adjusted odds of mortality. Delayed treatment was also associated with greater ICU utilization, prolonged mechanical ventilation, longer hospital stay, and increased rates of new-onset organ failure. These findings highlight persistent gaps in the timely recognition and management of sepsis in the emergency department. The association between treatment delay and mortality in our study is broadly consistent with previous evidence, although findings across studies have not been uniform. Puskarich et al. found that time from shock recognition to antibiotic administration, rather than time from triage to antibiotics, was associated with mortality in septic shock. Similarly, a systematic review and meta-analysis found no consistent mortality benefit associated with achieving fixed 1-hour or 3-hour antibiotic targets. These findings suggest that the timing of treatment should be considered in the context of timely sepsis recognition rather than as an isolated time-based target [10]. Our finding of a continuous association between increasing treatment delay and mortality is consistent with earlier single-center evidence using a similar continuous approach [13] and therefore supports the importance of minimizing delays while recognizing the limitations of rigid temporal thresholds.

A key finding of our study was the association between atypical clinical presentation and delayed treatment. Patients presenting with atypical physiological profiles - without overt hypotension or fever, particularly those presenting with tachypnea or altered mental status, had significantly greater odds of treatment delay. This suggests that reliance on conventional physiological indicators resulting in failure to capture subtle cellular hypoperfusion as indicated by elevated lactate or altered mental status may contribute to delayed recognition of sepsis. Incorporating multiple clinical parameters and dynamic electronic screening into triage may therefore help identify patients who might otherwise be overlooked. This is not merely a theoretical recommendation: a prospective, multi-site evaluation of a deployed machine-learning-based early warning system for sepsis found that clinician confirmation of an algorithm-generated alert within three hours was associated with an 18.7% relative reduction in in-hospital mortality [16], demonstrating that automated recognition tools of the kind proposed here can translate into measurable survival benefit when integrated into real-world triage workflows.

Emergency department crowding (NEDOCS > 140) was significantly associated with delays in sepsis management. Patients presenting during periods of severe crowding experienced longer intervals to physician assessment, delayed diagnostic laboratory turnaround, and prolonged time to antibiotic administration. This is consistent with previous evidence showing that ED crowding can impair clinical throughput and increase healthcare utilization beyond the management of individual conditions [12]. High patient volumes and increased clinician workload may increase cognitive and operational burden, potentially resulting in competing priorities and delayed recognition of less overt presentations of sepsis. Importantly, treatment delays may have consequences beyond mortality; a large retrospective cohort found that each additional hour to initial antimicrobial administration was associated with an 8% increase in the odds of progression from severe sepsis to septic shock [17]. Strategies that enable rapid sepsis activation and bypass routine workflow barriers, including nurse-initiated blood cultures and point-of-care lactate testing, may therefore help mitigate the impact of ED crowding.

Off-hour presentation was also associated with significantly longer treatment intervals, with patients presenting during evening and overnight hours experiencing greater delays in antibiotic administration compared with daytime presentations. This may reflect differences in staffing levels, availability of senior clinical personnel, diagnostic turnaround times, and overall workflow during these periods. Such temporal variation suggests that timely sepsis care should not depend solely on peak-hour resource availability.

Standardized sepsis protocols that remain operational throughout the day, supported by clear escalation pathways and rapid access to diagnostic and therapeutic resources, may help reduce disparities in treatment times between daytime and off-hour presentations.

Beyond mortality, treatment delays were associated with greater ICU admission, prolonged mechanical ventilation, longer hospital stays, and higher rates of new-onset organ failure. These findings suggest that delayed treatment may be associated with a greater subsequent burden of critical illness and healthcare utilization. Although the observational design does not establish causality, the consistent relationship between treatment delay and multiple adverse outcomes underscores the potential clinical and resource implications of delays in early sepsis management.

Several limitations should be considered. The observational design limits causal inference, and residual confounding, particularly by illness severity and unmeasured patient or institutional factors, cannot be excluded. The tertiary-care academic setting may limit generalizability to community or rural hospitals. Using ED arrival rather than sepsis recognition as the temporal reference, reliance on clinician gestalt and EHR timestamps, and hourly rather than continuous crowding measurements may have introduced measurement bias. Exclusion of transferred patients, those with limitations of care, and patients leaving against medical advice may have introduced selection bias. Finally, antimicrobial appropriateness was not assessed, and in-hospital mortality may also reflect subsequent inpatient care.

Future studies incorporating antimicrobial appropriateness, broader institutional settings, and additional patient-level factors may provide a more comprehensive understanding of the determinants of delayed sepsis treatment.

5. Conclusions

Delays in the recognition and treatment of sepsis in emergency departments are common and independently associated with increased in-hospital mortality, ICU admission, and prolonged hospital stay. Atypical clinical presentations and emergency department overcrowding were important contributors to these delays, highlighting the importance of early recognition in addition to rapid treatment once sepsis is identified. Addressing these vulnerabilities will require multifaceted quality-improvement strategies, including automated electronic screening tools, nurse-initiated diagnostic protocols, point-of-care lactate testing, rapid antimicrobial administration protocols and streamlined operational pathways to facilitate timely antimicrobial administration. Emerging evidence from real-world implementation of machine-learning-based early warning systems, demonstrating reductions in sepsis-associated mortality when integrated into clinical workflows [16], supports the feasibility of such automated approaches and provides a basis for future implementation studies.

References

1. Rudd KE, Johnson SC, Agesa KM, et al. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. *Lancet*. 2020;395(10219):200-211.
2. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801-810.
3. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy in the septic shock. *Crit Care Med*. 2006;34(6):1589-1596.

4. Evans L, Rhodes A, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021. *Crit Care Med.* 2021;49(11):e1063-e1143.
5. Levy MM, Evans L, Rhodes A. The Surviving Sepsis Campaign: a 15-year history. *Intensive Care Med.* 2018;44(6):775-778.
6. Morley C, Unwin M, Peterson GM, Stankovich J, Flaherty L. Emergency department crowding: A systematic review of causes, consequences and solutions. *PLoS One.* 2018;13(8):e0203316.
7. Liu VX, Fielding-Singh V, Greene JD, et al. The Timing of Early Antibiotics and Hospital Mortality in Sepsis. *Am J Respir Crit Care Med.* 2017;196(7):856-863.
8. Seymour CW, Gesten F, Prescott HC, et al. Time to Treatment and Mortality during Mandated Emergency Care for Sepsis. *N Engl J Med.* 2017;376(23):2235-2244.
9. Rhee C, Dantes E, Epstein L, et al. Incidence and Trends of Sepsis in US Hospitals Using Clinical vs Claims Data, 2009-2014. *JAMA.* 2017;318(13):1241-1249.
10. Sterling SA, Miller WR, Pryor J, Puskarich MA, Jones AE. The impact of timing of antibiotics on outcomes in severe sepsis and septic shock: a systematic review and meta-analysis. *Crit Care Med.* 2015;43(9):1907-1915.
11. Puskarich MA, Trzeciak S, Shapiro NI, et al. Association of time to administration of antimicrobials and mortality in septic shock patients presenting to the emergency department. *Crit Care Med.* 2011;39(9):2066-2071.
12. Henneman PL, Smithline HA, Sanford SM, Carmody IC. Emergency department crowding is associated with increased risk for admissions. *West J Emerg Med.* 2009;10(4):227-232.
13. Gaieski DF, Mikkelsen ME, Band RA, et al. Impact of time to antibiotics on survival in severe sepsis in patients in whom initial resuscitation was complete. *Crit Care Med.* 2010;38(4):1045-1053.
14. Shankar-Hari M, Phillips GS, Levy ML, et al. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315(8):775-787.
15. Rhodes A, Evans L, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Intensive Care Med.* 2017;43(3):304-377.
16. Adams R, Henry KE, Sridharan A, et al. Prospective, multi-site study of patient outcomes after implementation of the TREWS machine learning-based early warning system for sepsis. *Nat Med.* 2022;28(7):1455-1460.
17. Whiles BB, Deis AS, Simpson SQ. Increased time to initial antimicrobial administration is associated with progression to septic shock in severe sepsis patients. *Crit Care Med.* 2017;45(4):623-629.