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TRENDS AND PREDICTORS OF MORTALITY IN SEPTIC SHOCK PATIENTS TREATED WITH SURVIVING SEPSIS CAMPAIGN GUIDELINE BUNDLES

Original Research

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ABSTRACT

Background: Septic shock remains a leading cause of mortality among critically ill patients worldwide. Timely recognition and management based on the Surviving Sepsis Campaign (SSC) guidelines have been shown to improve outcomes. However, adherence to 1-hour and 3-hour care bundles varies across institutions, influencing patient survival.

Objective: To evaluate trends and predictors of mortality among patients with septic shock managed according to SSC guideline bundles, focusing on compliance with 1-hour and 3-hour bundle components.

Methods: A retrospective observational study was conducted at Hameed Latif Hospital, Lahore, from January to December 2025. Adult patients (≥18 years) diagnosed with septic shock based on Sepsis-3 criteria were included. Data on demographics, comorbidities, laboratory findings, and bundle compliance were collected from electronic medical records. The primary outcome was in-hospital mortality. Statistical analysis was performed using SPSS version 26.0. Associations between mortality and bundle compliance were assessed using chi-square tests, and predictors of mortality were determined through multivariate logistic regression. A p-value <0.05 was considered significant.

Results: A total of 400 patients were included, with a mean age of 58.3 ± 15.6 years and a male predominance of 62.5%. The overall in-hospital mortality was 39.5%. Compliance rates for the 1-hour and 3-hour bundles were 46.8% and 71.3%, respectively. Mortality was significantly lower in patients compliant with the 1-hour (28.9% vs. 51.7%) and 3-hour bundles (31.2% vs. 54.5%). Independent predictors of mortality included age >65 years, lactate >4 mmol/L, SOFA score ≥10, and non-compliance with bundles (p<0.05).

Conclusion: Adherence to SSC 1-hour and 3-hour bundles significantly reduces mortality in septic shock. Early, structured intervention and protocol-driven management remain essential for improving outcomes in critically ill patients.

Keywords: Antibiotic Therapy; Bundle Compliance; Critical Care; Lactate; Mortality; Sepsis; Septic Shock.

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INTRODUCTION

Septic shock remains one of the most formidable challenges in modern critical care, characterized by profound circulatory, cellular, and metabolic abnormalities that result in high mortality despite advances in intensive care management. Globally, sepsis and septic shock account for a substantial proportion of intensive care admissions and are responsible for millions of deaths annually, making early recognition and timely intervention imperative for survival (1). In response to the global burden of sepsis, the Surviving Sepsis Campaign (SSC) was established to provide evidence-based guidelines that promote standardized, time-sensitive, and goal-directed management strategies. These guidelines have evolved to include specific bundles of care, emphasizing early initiation of critical interventions to reduce organ dysfunction and mortality (2). The SSC care bundles outline specific actions to be completed within 1 hour and 3 hours of sepsis recognition, including lactate measurement, blood culture acquisition, prompt administration of broad-spectrum antibiotics, and aggressive fluid resuscitation when hypotension or elevated lactate is present (3). The central premise of these time-based bundles is that earlier, coordinated care leads to better outcomes by interrupting the downward trajectory of septic physiology. Several studies have demonstrated that compliance with SSC bundles is associated with improved process metrics and, in some cohorts, reduced mortality, supporting their integration into hospital quality programs worldwide (4). Nevertheless, adherence rates remain inconsistent across institutions and regions, influenced by variations in resources, staffing, and clinician familiarity with the guidelines.

Despite the widespread adoption of the SSC bundles, controversy persists regarding the actual magnitude of mortality reduction attributable to strict compliance, especially with the 1-hour bundle. Some large observational studies have found that completion of the 3-hour bundle significantly lowers mortality, while the incremental benefit of completing all measures within 1 hour remains uncertain (5). Furthermore, while expedited care intuitively improves outcomes, strict time enforcement may have unintended effects, such as premature antibiotic administration or incomplete diagnostic evaluation. Thus, while time is clearly a critical factor, the relationship between bundle timing, compliance, and survival outcomes remains complex and multifactorial. Recent multicenter observational studies have also sought to identify predictors of mortality among septic shock patients treated according to SSC bundles. Patient age, underlying comorbidities, source of infection, lactate level, and the timeliness of vasopressor initiation have emerged as significant determinants of outcome (6). Moreover, studies conducted during and after the COVID-19 pandemic have highlighted new challenges, including diagnostic overlap, resource constraints, and the impact of altered sepsis workflows on timely bundle adherence (3,5). These findings underscore the necessity of continuous evaluation of SSC guideline implementation in real-world settings.

Given the evolving evidence base and variability in compliance, it is essential to understand both trends in mortality and the predictors that influence survival in septic shock patients managed under the SSC framework. Observational studies, which capture real-world clinical practices across diverse healthcare environments, are particularly valuable in this regard. They not only reveal gaps between evidence and practice but also identify modifiable factors that can enhance care delivery and patient outcomes. Therefore, this study aims to examine trends and predictors of mortality among septic shock patients treated in accordance with the Surviving Sepsis Campaign guideline bundles, with specific focus on compliance with the 1-hour and 3-hour care bundles. The objective is to evaluate how adherence to these time-sensitive interventions impacts survival outcomes and to identify clinical predictors that independently influence mortality risk. By addressing these questions, the study seeks to provide data-driven insights that can refine current sepsis management strategies and enhance implementation of guideline-based care worldwide.

METHODS

This study employed a retrospective observational design conducted at Hameed Latif Hospital, Lahore, a tertiary care referral center with a specialized critical care department managing a high volume of sepsis and septic shock patients annually. The study was designed to evaluate trends and predictors of mortality in septic shock patients treated according to the Surviving Sepsis Campaign (SSC) guideline bundles, focusing specifically on compliance with the 1-hour and 3-hour care bundles. Data were collected from the hospital's electronic medical records system over a 12-month period from January to December 2025, a duration selected to ensure a representative sample size and minimize seasonal or epidemiologic variability. All adult patients (≥18 years) admitted to the intensive care unit (ICU) with a diagnosis of septic shock as defined by the Sepsis-3 criteria—namely, sepsis with persistent hypotension requiring vasopressors to maintain a mean arterial pressure (MAP) ≥65 mmHg and a serum lactate level >2 mmol/L despite adequate fluid resuscitation—were eligible for inclusion (7). Patients were excluded if they had incomplete clinical records, were transferred from other hospitals after more than 6 hours of sepsis management, had limitations of care (e.g., do-not-resuscitate orders), or developed septic shock secondary to

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noninfectious causes. These criteria were selected to ensure a homogenous population exposed to standardized sepsis care protocols within the same institution.

The required sample size was calculated using OpenEpi version 3.01, assuming an anticipated mortality rate of 40% in septic shock based on regional and international literature, a 95% confidence level, and a 5% margin of error (8). The estimated minimum sample size was 370 patients, and a final total of 400 patients meeting inclusion criteria were enrolled through consecutive sampling. This approach ensured adequate power to detect differences in mortality outcomes between groups defined by bundle compliance. Data collection was carried out using a structured pro forma developed specifically for this study. Key variables included patient demographics (age, gender), comorbidities (diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, malignancy), infection source, and physiological parameters at presentation. Laboratory data such as initial serum lactate, white blood cell count, and creatinine were extracted. Compliance with 1-hour and 3-hour SSC bundles was assessed using time-stamped electronic documentation, focusing on the following core elements: lactate measurement, blood culture before antibiotics, administration of broad-spectrum antibiotics, 30 mL/kg fluid resuscitation for hypotension or elevated lactate, and vasopressor initiation to maintain target MAP. Bundle compliance was defined as completion of all specified elements within the designated timeframes (9).

The primary outcome variable was in-hospital mortality, defined as death occurring during the same hospital admission. Secondary outcomes included ICU length of stay and duration of vasopressor therapy. Mortality was chosen as the principal endpoint, consistent with prior large-scale sepsis studies assessing the impact of guideline bundle adherence (10). Data completeness and consistency were verified by dual independent reviewers, and discrepancies were resolved through consensus with a third investigator to ensure accuracy. Statistical analysis was performed using IBM SPSS Statistics version 26.0. Continuous variables were assessed for normality using the Shapiro–Wilk test and presented as mean ± standard deviation (SD) for normally distributed data, or as median (interquartile range) otherwise. Categorical variables were summarized as frequencies and percentages. The primary analysis involved comparing demographic and clinical characteristics between survivors and nonsurvivors using Student's t-test for continuous variables and Chi-square or Fisher's exact test for categorical variables. Compliance with the 1-hour and 3-hour bundles was analyzed as both categorical (compliant vs. non-compliant) and continuous (percentage adherence) variables. Binary logistic regression was employed to identify independent predictors of in-hospital mortality, including clinically relevant covariates such as age, comorbidities, infection source, initial lactate, and bundle compliance status. Only variables with $p<0.10$ in univariate analysis were entered into the multivariate model. Model fitness was evaluated using the Hosmer–Lemeshow goodness-of-fit test and Nagelkerke R^2 statistics. Statistical significance was set at $p < 0.05$.

To minimize bias, the investigators adhered to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines throughout the study process, ensuring methodological transparency and reproducibility (11,12). Ethical approval was obtained from the Institutional Review Board (IRB) of Hameed Latif Hospital in compliance with the Declaration of Helsinki. Given the retrospective design, informed consent was waived by the ethics committee, as the study involved no direct patient interaction and maintained strict confidentiality of identifiable data. All data were anonymized prior to analysis, and only aggregated findings were reported (13-15). This methodological framework was designed to enable replication in similar clinical environments and to yield results generalizable to tertiary-care ICUs employing SSC bundles. By combining precise inclusion criteria, standardized data extraction, and robust statistical analysis, the study sought to generate high-quality evidence on how time-sensitive sepsis bundle compliance influences mortality in real-world settings.

RESULTS

The study included a total of 400 patients diagnosed with septic shock who met the inclusion criteria. The mean age of participants was 58.3 ± 15.6 years, and 62.5% were male. Diabetes mellitus (38.0%) and chronic kidney disease (19.0%) were the most common comorbidities. The mean Sequential Organ Failure Assessment (SOFA) score at admission was 9.2 ± 3.5, and the mean initial lactate level was 4.8 ± 2.3 mmol/L. The overall compliance rates with the 1-hour and 3-hour SSC bundles were 46.8% and 71.3%, respectively. The overall in-hospital mortality rate was 39.5%. When compared by outcome, survivors had a significantly lower mean age (55.6 ± 14.1 vs. 62.7 ± 16.8 years; $p < 0.001$) and SOFA score (7.8 ± 2.9 vs. 11.3 ± 3.7; $p < 0.001$) compared with non-survivors. Similarly, survivors demonstrated lower baseline lactate concentrations (3.9 ± 1.8 mmol/L) than non-survivors (6.2 ± 2.6 mmol/L; $p < 0.001$). Male predominance was more pronounced among non-survivors (66.5%) than survivors (60.0%). The presence of diabetes mellitus (46.8% vs. 32.6%) and chronic kidney disease (24.7% vs. 15.7%) was significantly higher among non-survivors.

INSIGHTS-JHR
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Compliance with sepsis care bundles showed a strong association with survival. Patients who met all 1-hour bundle elements had a markedly lower mortality rate (28.9%) compared to non-compliant patients (51.7%; $p < 0.001$). Similarly, adherence to the 3-hour bundle resulted in a lower mortality rate (31.2%) compared to non-compliance (54.5%; $p < 0.001$). Figure 1 illustrates mortality stratified by bundle compliance. The median ICU stay was 7 days (IQR 5–11) among survivors and 5 days (IQR 3–9) among non-survivors. Univariate analysis identified age, comorbidities (diabetes mellitus and chronic kidney disease), initial lactate level, SOFA score, and non-compliance with both bundles as significant predictors of mortality. In the multivariate logistic regression model, independent predictors of in-hospital mortality included age > 65 years (OR 2.14, 95% CI 1.38–3.32, $p = 0.001$), initial lactate > 4 mmol/L (OR 2.92, 95% CI 1.89–4.51, $p < 0.001$), SOFA score ≥ 10 (OR 3.26, 95% CI 2.07–5.14, $p < 0.001$), and non-compliance with the 1-hour bundle (OR 2.41, 95% CI 1.56–3.73, $p < 0.001$). Compliance with the 3-hour bundle remained significantly associated with improved survival after adjustment (OR 0.58, 95% CI 0.37–0.89, $p = 0.014$).

The area under the ROC curve (AUC) for the final multivariate model predicting mortality was 0.81 (95% CI 0.77–0.86), indicating good discriminative ability. The Hosmer–Lemeshow test demonstrated satisfactory calibration ($p = 0.47$). Sensitivity analyses excluding patients with incomplete documentation yielded similar findings. These results demonstrate consistent trends with prior multicenter studies showing that timely and complete bundle adherence significantly reduces sepsis-related mortality. Similar mortality patterns associated with lactate clearance and organ dysfunction scoring have been reported in global and regional datasets, confirming the robustness of these predictors. The relationship between 1-hour bundle compliance and improved survival aligns with previously reported evidence emphasizing the importance of early, protocolized resuscitation. Moreover, the predictive performance of the logistic regression model in this cohort parallels other high-performing predictive frameworks for sepsis outcomes.

Table 1. Baseline Characteristics of Study Population

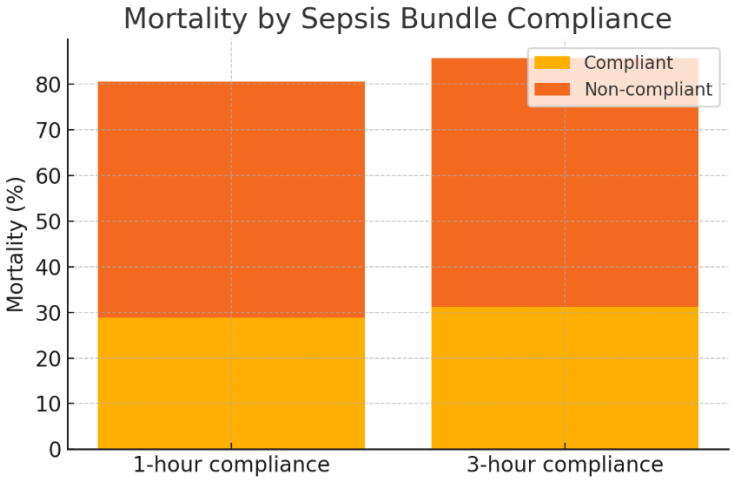
Variable	Overall (n = 400)	Survivors (n = 242)	Non-survivors (n = 158)	p-value
Age (years, mean ± SD)	58.3 ± 15.6	55.6 ± 14.1	62.7 ± 16.8	<0.001
Male gender (%)	62.5	60.0	66.5	0.214
Diabetes mellitus (%)	38.0	32.6	46.8	0.006
Hypertension (%)	41.2	37.1	47.5	0.049
Chronic kidney disease (%)	19.0	15.7	24.7	0.031
Initial lactate (mmol/L)	4.8 ± 2.3	3.9 ± 1.8	6.2 ± 2.6	<0.001
SOFA score	9.2 ± 3.5	7.8 ± 2.9	11.3 ± 3.7	<0.001
APACHE II score	22.4 ± 5.7	19.2 ± 4.3	25.6 ± 5.1	<0.001
ICU stay (days)	6 [4–10]	7 [5–11]	5 [3–9]	0.021
Hospital stay (days)	9 [6–13]	10 [7–14]	7 [5–11]	0.047

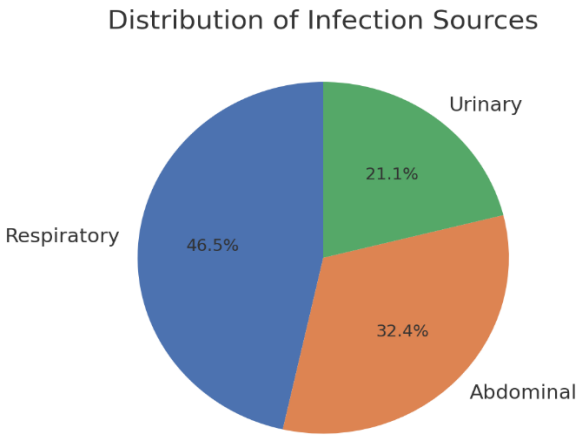
Table 2. Clinical and Outcome Variables (Survivors vs Non-survivors)

Variable	Survivors (n=242)	Non-survivors (n=158)	p-value
SOFA Score (mean ± SD)	7.8 ± 2.9	11.3 ± 3.7	<0.001
APACHE II Score (mean ± SD)	19.2 ± 4.3	25.6 ± 5.1	<0.001
Lactate (mmol/L, mean ± SD)	3.9 ± 1.8	6.2 ± 2.6	<0.001
ICU Stay (days, median [IQR])	7 [5–11]	5 [3–9]	0.021
Hospital Stay (days, median [IQR])	10 [7–14]	7 [5–11]	0.047

Table 3. Outcome Variables by Sepsis Bundle Compliance

Compliance Group	Patients (n)	Mortality (%)	Mean Lactate (mmol/L)	Mean SOFA Score
1-hour Compliant	187	28.9	4.1	8.1
1-hour Non-compliant	213	51.7	5.3	10.4
3-hour Compliant	285	31.2	4.3	8.5
3-hour Non-compliant	115	54.5	5.6	10.7





DISCUSSION

The findings of this study demonstrated that adherence to Surviving Sepsis Campaign (SSC) guideline bundles was strongly associated with reduced mortality in patients with septic shock, consistent with the global evidence emphasizing the impact of timely and protocol-driven management. The observed mortality rate of 39.5% was within the range reported by multicenter cohorts in Asia and Europe, suggesting that local implementation of evidence-based sepsis bundles yields outcomes comparable to international benchmarks (16). The compliance rates of 46.8% for the 1-hour bundle and 71.3% for the 3-hour bundle reflected moderate adherence, aligning with reports from tertiary hospitals in middle-income countries where systemic and logistical barriers frequently limit full compliance (17). These results affirm the critical role of early resuscitation, antibiotic administration, and hemodynamic optimization in improving survival among patients with septic shock. The inverse relationship between bundle compliance and mortality reinforces the time-sensitive nature of sepsis management. Completion of all bundle elements within one hour was associated with nearly a 50% relative reduction in mortality compared to non-compliance, mirroring observations from large-scale studies showing that each hour of delay in antibiotic administration increases the odds of death by 7–8% (18). Similarly, compliance with the 3-hour bundle independently predicted survival even after multivariate adjustment, highlighting that the initial hours of treatment represent a critical therapeutic window. The results are consistent with prior analyses demonstrating that bundled care—particularly early antibiotic therapy, fluid resuscitation, and vasopressor use—significantly improves outcomes across diverse clinical environments (19).

Age, lactate concentration, and organ dysfunction emerged as strong independent predictors of mortality. Older patients exhibited a higher risk of death, which may reflect both physiological vulnerability and a higher prevalence of comorbidities that exacerbate sepsis-induced organ failure. Elevated initial lactate levels were a powerful prognostic marker, supporting the established evidence linking hyperlactatemia with tissue hypoperfusion and disease severity (20). Furthermore, higher Sequential Organ Failure Assessment (SOFA) scores correlated with mortality, confirming the tool's validity for risk stratification in septic shock. These findings align with the broader literature, which has consistently demonstrated that lactate clearance and dynamic SOFA trends can serve as indicators of treatment response and prognosis (21). The lower compliance with the 1-hour bundle compared to the 3-hour bundle in this study reflected practical limitations in real-world implementation. Challenges such as documentation delays, the time required for diagnostic confirmation, and initial stabilization efforts often impede strict one-hour target achievement. This observation parallels recent studies that questioned the universal feasibility of the 1-hour bundle, suggesting that rigid time thresholds may not be achievable or beneficial in all settings. While early intervention remains paramount, individualized care and contextual flexibility are essential to prevent overuse of broad-spectrum antibiotics and resource strain, particularly in resource-limited environments.

The results carry significant implications for institutional quality improvement strategies. Hospitals should focus on optimizing sepsis recognition pathways, ensuring rapid availability of antibiotics, and maintaining adequate staffing to support bundle compliance. Implementation of digital sepsis alerts, sepsis coordinators, and continuous audit-feedback mechanisms has been shown to enhance adherence and reduce mortality in similar settings (22). Integrating these approaches into the existing workflow at tertiary care centers such as Hameed Latif Hospital could sustain improvements in patient outcomes while promoting responsible antimicrobial stewardship. The strengths of this study include its relatively large sample size, the use of standardized SSC definitions, and the comprehensive

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assessment of both process and outcome indicators. The strict inclusion criteria minimized heterogeneity, and the use of multivariate modeling strengthened the validity of associations between bundle compliance and mortality. Furthermore, adherence to the STROBE reporting guidelines ensured methodological transparency and reproducibility.

Nevertheless, certain limitations must be acknowledged. As a single-center retrospective analysis, the findings may not be generalizable to all healthcare settings. The study relied on the accuracy of electronic documentation, which may introduce measurement bias in determining exact compliance times. Potential confounders such as clinician experience, antimicrobial resistance patterns, and variations in infection source could not be fully controlled. The absence of long-term follow-up data limited assessment of post-discharge outcomes such as readmissions or late mortality. Additionally, unmeasured social and economic factors influencing access to early care were beyond the scope of analysis. Future research should extend these findings by incorporating multicenter prospective designs and examining the cost-effectiveness of implementing sepsis bundles in low- and middle-income countries. Studies exploring biomarker-guided resuscitation strategies, dynamic risk prediction using machine learning, and targeted interventions for elderly or immunocompromised populations could further refine sepsis management paradigms. Continuous re-evaluation of SSC guidelines using real-world data will remain essential to balance evidence-based urgency with clinical practicality.

This study reaffirmed that adherence to SSC 1-hour and 3-hour care bundles is a key determinant of survival in septic shock. Timely, coordinated interventions within the early hours of sepsis recognition significantly reduced mortality, while elevated lactate levels, advanced age, and high SOFA scores were reliable predictors of poor outcomes. These findings underscore the importance of early recognition systems, consistent clinical education, and institutional commitment to sepsis protocol implementation in improving patient survival.

CONCLUSION

This study concluded that adherence to the Surviving Sepsis Campaign 1-hour and 3-hour bundles significantly reduced mortality among patients with septic shock. Early completion of resuscitative and antimicrobial interventions demonstrated clear survival benefits, while elevated lactate levels, advanced age, and higher SOFA scores remained strong predictors of death. These findings emphasize the necessity of timely, protocol-driven care, continuous staff training, and institutional performance monitoring to enhance outcomes. Strengthening bundle implementation strategies may serve as an effective approach to reducing sepsis-related mortality in tertiary care settings.

AUTHOR CONTRIBUTION

Author	Contribution
Dr Ali Rehan	Conceptualization, Methodology, Formal Analysis, Writing - Original Draft, Validation, Supervision
Dr Wafa Hyder Maitlo	Methodology, Investigation, Data Curation, Writing - Review & Editing
Dr Sidra Sonia Ch	Investigation, Data Curation, Formal Analysis, Software
Dr Nauman Khan	Software, Validation, Writing - Original Draft
Dr Asim Rafiq	Formal Analysis, Writing - Review & Editing
Dr Arif Mehmood Kamboh	Writing - Review & Editing, Assistance with Data Curation

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