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INTEGRATING AI-DRIVEN PREDICTIVE ANALYTICS FOR EARLY DETECTION OF SEPSIS IN ICU SETTINGS: PROSPECTIVE COHORT STUDY

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Abstract

Background

Sepsis remains a leading cause of preventable mortality in intensive care units (ICUs), largely due to delayed recognition and rapid progression to organ dysfunction and septic shock. Conventional screening tools often fail to capture early physiological deterioration in complex ICU patients. Artificial intelligence (AI)–driven predictive analytics may offer earlier detection by integrating real-time trends in routinely collected clinical data.

Objective

This study aims to evaluate the efficacy of AI-based predictive models in identifying early signs of sepsis among ICU patients, thereby enabling timely interventions and improving patient outcomes

Methods

Demographic, clinical, physiological, and laboratory data were collected prospectively from ICU admission until discharge or death. Sepsis was defined using Sepsis-3 criteria (suspected/confirmed infection with organ dysfunction). The AI model generated risk scores at repeated intervals and produced high-risk alerts when predefined thresholds were exceeded. Predictive performance was evaluated using AUROC, sensitivity, specificity, predictive values, calibration, and alert lead time compared with routine clinical recognition. Clinical outcomes included ICU mortality, length of stay, mechanical ventilation, vasopressor use, renal replacement therapy, and progression to septic shock.

Results

Sepsis occurred in 74 of 286 patients (25.9%), and 28 (37.8%) of septic patients progressed to septic shock. ICU mortality was significantly higher in septic

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patients compared with non-septic patients (28.4% vs 11.3%; p<0.001), alongside greater need for mechanical ventilation (54.1% vs 29.7%; p<0.001) and vasopressors (63.5% vs 28.8%; p<0.001).

The AI model demonstrated strong discrimination for early sepsis detection (AUROC 0.87; 95% CI 0.83–0.91), with sensitivity 82.4%, specificity 79.2%, PPV 59.1%, and NPV 92.3%. High-risk alerts occurred prior to clinical recognition in 82.4% of sepsis cases, providing a median lead time of 4.8 hours (IQR 2.6–8.1). Patients receiving earlier AI alerts (≥4 hours before clinical recognition) had lower ICU mortality (20.5% vs 37.1%; p=0.041) and reduced progression to septic shock (28.2% vs 48.6%; p=0.048) compared with those with late or absent alerts.

Conclusion

In this prospective ICU cohort from Sindh, Pakistan, AI-driven predictive analytics enabled earlier detection of sepsis with strong predictive performance and clinically meaningful lead time. Earlier alerts were associated with improved outcomes, including lower mortality and reduced progression to septic shock. These findings support the integration of AI-based early warning systems as decision-support tools to strengthen timely sepsis recognition and response in high-burden ICU settings.

1. INTRODUCTION

Sepsis remains one of the most urgent and complex challenges faced in modern intensive care units (ICUs), contributing substantially to preventable mortality and prolonged hospitalization worldwide. Clinically, sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, and it frequently progresses rapidly, often before overt clinical deterioration is recognized (Singer *et al.*, 2016). Despite advancements in critical care practices, sepsis continues to be associated with high case fatality rates, particularly in resource-limited settings where delays in diagnosis and treatment are more likely. The global burden of sepsis is immense, with estimates suggesting tens of millions of cases annually, many resulting in death or long-term disability (Rudd *et al.*, 2020).

In the ICU environment, where patients often have multiple comorbidities, invasive devices, immunosuppression, and complex clinical trajectories, the early identification of sepsis is especially difficult. Classical clinical signs—fever, tachycardia, hypotension, altered mental status—may be subtle, masked by sedation, or misattributed to other critical illnesses. Moreover, laboratory abnormalities such as leukocytosis, elevated lactate, or rising inflammatory markers are not always specific to infection and may appear late in the disease course. As a result, the recognition of sepsis frequently occurs after organ dysfunction is already established, limiting the effectiveness of interventions.

Timely treatment is known to be strongly linked with improved outcomes. Early administration of appropriate antimicrobials and prompt hemodynamic resuscitation reduce mortality risk, and delays in antibiotic initiation have repeatedly been associated with worsening survival (Kumar *et al.*, 2006). International guidelines such as the Surviving Sepsis Campaign emphasize early recognition, rapid clinical response, and structured bundles of care to reduce sepsis-related deaths (Rhodes *et al.*, 2017). However, implementing these bundles consistently remains challenging, especially in high-volume tertiary hospitals where ICU teams face heavy workloads, limited staff-to-patient ratios, and frequent diagnostic uncertainty.

In recent years, the adoption of artificial intelligence (AI) and machine learning (ML) methods has introduced a promising direction in sepsis prediction and early warning systems. Unlike conventional scoring systems, which typically rely on static thresholds and a limited

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number of variables, AI-driven predictive analytics can integrate large volumes of clinical data—including vital signs, laboratory values, medication patterns, and temporal trends—into dynamic models that continuously estimate risk. This shift from reactive to predictive monitoring has the potential to identify early patterns of deterioration hours before clinicians might suspect sepsis, enabling earlier investigation and intervention. Several studies have demonstrated that machine learning models may detect sepsis earlier than traditional approaches such as SIRS criteria, qSOFA, and even SOFA-based screening, though real-world performance varies widely depending on population, data quality, and implementation context (Henry *et al.*, 2015; Seymour *et al.*, 2016).

Nevertheless, enthusiasm for AI in sepsis care must be balanced with critical appraisal. A key concern is the generalizability of AI models across different healthcare settings. Many predictive algorithms are trained and validated in high-income countries using electronic health record (EHR) systems with comprehensive, high-frequency data capture. In contrast, ICUs in low- and middle-income countries (LMICs), including Pakistan, often face limitations such as incomplete documentation, variable laboratory availability, inconsistent monitoring frequency, and differences in disease patterns. Additionally, antimicrobial resistance profiles, infection sources, and baseline patient health characteristics may differ substantially from those in Western cohorts. These factors raise concerns that AI models developed elsewhere may underperform when applied directly in LMIC ICUs without local adaptation and prospective validation.

Pakistan, as a lower-middle-income country with a large population and substantial healthcare challenges, carries a significant burden of infectious diseases and critical illness. Tertiary hospitals in Sindh province serve as major referral centers, often receiving critically ill patients with delayed presentation, limited pre-hospital stabilization, and advanced disease severity. In such settings, sepsis is frequently encountered and may be complicated by multidrug-resistant organisms, delayed antibiotic administration, and resource constraints affecting diagnostics and staffing. These realities highlight the urgent need for locally relevant tools that can support early sepsis recognition and improve clinical decision-making.

Traditional early warning systems and sepsis screening tools—while clinically useful—have known limitations. SIRS criteria, for example, are sensitive but not specific, and can flag many non-infectious inflammatory states common in ICU patients. qSOFA was introduced as a simplified bedside tool, but its sensitivity for early sepsis detection has been questioned, particularly in ICU cohorts where organ dysfunction may develop rapidly (Singer *et al.*, 2016). SOFA scoring is widely used to assess organ dysfunction severity but requires laboratory data and may not always be practical for continuous early detection. These limitations create an opportunity for predictive analytics that can identify subtle trends in physiologic decline before conventional thresholds are crossed.

AI-based models for sepsis prediction typically use supervised learning methods such as logistic regression, random forests, gradient boosting, or deep learning networks. Some models incorporate time-series analysis to account for evolving clinical trajectories. Importantly, the clinical utility of these tools is not determined solely by accuracy metrics such as the area under the receiver operating characteristic curve (AUROC). For real-world benefit, AI systems must also demonstrate good calibration, acceptable false alert rates, interpretability, and integration into clinical workflows. Alarm fatigue is a well-documented problem in ICUs, and overly sensitive prediction systems can overwhelm staff, reducing trust and effectiveness. Therefore, models must be evaluated not only for predictive performance but also for how they influence clinical actions and patient outcomes.

Another critical issue is explainability. ICU clinicians are more likely to accept AI recommendations if the model provides understandable reasoning, such as identifying which variables contributed most to the risk score. Explainable AI approaches can support transparency, reduce skepticism, and enable clinicians to combine algorithmic outputs with

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clinical judgment. Without interpretability, AI systems risk being perceived as "black boxes," potentially limiting adoption in high-stakes decision-making environments like critical care.

Against this background, the present study proposes a prospective cohort design to evaluate the efficacy of AI-driven predictive analytics for early detection of sepsis among ICU patients in a tertiary care hospital in Sindh, Pakistan. Prospective validation is essential because many AI models show promising results in retrospective datasets but fail to deliver similar benefits when implemented in real-time clinical settings. By monitoring ICU admissions prospectively, capturing routine clinical variables, and applying AI-based prediction tools, this study aims to determine whether such models can provide earlier identification of sepsis compared to standard practice. The ultimate goal is to support timely interventions, reduce delays in treatment, and improve outcomes such as ICU mortality, length of stay, and progression to septic shock.

In addition, this study is designed to contribute evidence from a region where published prospective evaluations of AI sepsis prediction are limited. Generating data from Sindh is particularly valuable because ICU populations, infection patterns, and resource constraints may differ from those reported in larger datasets from Europe or North America. A locally validated predictive model could support scalable decision support systems tailored to similar tertiary hospitals across Pakistan and comparable LMIC contexts.

In summary, sepsis continues to impose an unacceptable burden in ICU settings, where early detection remains difficult despite established guidelines and screening tools. AI-driven predictive analytics offers a promising approach to anticipate sepsis earlier than conventional methods, but real-world effectiveness depends on prospective evaluation, local validation, and practical integration into clinical workflows. This study therefore seeks to assess the performance and clinical impact of AI-based predictive models for early sepsis detection in ICU patients at a tertiary hospital in Sindh, Pakistan, with the broader aim of strengthening timely critical care responses and improving patient outcomes.

2. METHODOLOGY

2.1 Study Design

This research was conducted as a **prospective cohort study** aimed at evaluating the real-time effectiveness of an **AI-driven predictive analytics model** for early identification of sepsis among critically ill patients admitted to the Intensive Care Unit (ICU). A prospective approach was deliberately selected because sepsis is a dynamic clinical syndrome in which physiological changes evolve rapidly, and predictive models must be assessed in conditions that resemble routine clinical practice rather than retrospective chart review alone. The study followed ICU patients from the point of admission until discharge from ICU or in-ICU death, with continuous monitoring of clinical and laboratory variables and systematic documentation of sepsis-related outcomes.

2.2 Study Setting and Duration

The study was carried out in the **adult ICU of a tertiary care hospital located in Sindh, Pakistan**, which serves as a major referral center for surrounding districts and receives both medical and surgical critically ill patients. The ICU operates with standard critical care monitoring, including continuous vital sign surveillance, ventilator support, and routine laboratory services. Patient management is conducted under consultant intensivists, supported by resident doctors and trained nursing staff.

The study was implemented over a defined period to ensure adequate case capture across varying seasonal patterns of infection and admission trends. Data collection was performed continuously during the study window, and all eligible patients were enrolled consecutively to reduce selection bias and ensure representativeness of real ICU admissions.

2.3 Study Population and Recruitment

All adult patients admitted to the ICU during the study period were screened for eligibility. Recruitment was conducted using a **consecutive sampling technique**, meaning that every patient

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meeting inclusion criteria was enrolled without arbitrary selection. This approach was chosen to minimize sampling bias and allow the cohort to reflect real-world ICU diversity, including varying disease severity, comorbidities, and admission diagnoses.

Patients were followed from ICU admission and assessed for the development of sepsis either at admission or during ICU stay. Importantly, the AI model was applied to predict the risk of sepsis **before clinical confirmation**, with the intent of identifying early physiological patterns that might not yet be clinically obvious.

2.4 Inclusion Criteria

Patients were included in the study if they met the following criteria:

1. **Age ≥ 18 years** at the time of ICU admission.
2. Admission to the ICU for medical, surgical, or mixed indications.
3. Availability of baseline physiological parameters (at minimum: heart rate, respiratory rate, blood pressure, temperature, and oxygen saturation) recorded within the first hours of ICU admission.
4. Expected ICU stay long enough to allow meaningful monitoring and risk estimation (i.e., not an immediate transfer out within a very short duration).

2.5 Exclusion Criteria

Patients were excluded if any of the following conditions were present:

1. Age below 18 years.
2. ICU admission solely for post-operative observation with planned discharge within a few hours and no clinical suspicion of infection.
3. Patients with incomplete essential records such that risk scoring could not be computed (e.g., missing key vital sign trends).
4. Patients declared dead on arrival or those who died before meaningful data capture could occur.

These exclusion criteria were applied to maintain methodological consistency and ensure the predictive model could be tested under conditions where it had adequate data input to generate meaningful risk estimates.

2.6 Operational Definitions and Outcome Measures

2.6.1 Definition of Sepsis (Primary Outcome)

Sepsis was defined using **Sepsis-3 criteria**, where sepsis is identified as **suspected or confirmed infection accompanied by organ dysfunction**, operationalized by an increase in **Sequential Organ Failure Assessment (SOFA) score ≥ 2 points** from baseline. This definition was selected because it aligns with current international standards and reflects clinically significant organ dysfunction rather than isolated inflammatory changes.

2.6.2 Definition of Septic Shock (Secondary Outcome)

Septic shock was defined as sepsis with persistent hypotension requiring vasopressor support to maintain mean arterial pressure ≥ 65 mmHg and associated with evidence of tissue hypoperfusion (commonly reflected through elevated lactate where available), despite adequate fluid resuscitation.

2.6.3 Key Outcomes Measured

The study assessed both predictive performance and clinical impact through the following outcomes:

- **Primary outcome:** Early detection of sepsis (yes/no) during ICU stay.
- **Secondary outcomes:**
  - Time gained (in hours) between AI alert and clinical recognition/diagnosis of sepsis.
  - Progression from sepsis to septic shock.
  - ICU mortality.
  - ICU length of stay (LOS).
  - Requirement of mechanical ventilation.
  - Need for vasopressors and renal replacement therapy (if applicable).

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2.7 Data Collection Procedure

A structured data collection framework was used to ensure uniformity across patients. Data was obtained from bedside charts, ICU monitoring systems, and laboratory reports. Variables were recorded at admission and updated at regular intervals based on ICU charting frequency.

2.7.1 Patient Baseline Characteristics

The following baseline information was documented:

- Age and gender
- Admission source (emergency department, ward transfer, operating theatre, or external referral)
- Admission diagnosis category (medical/surgical/trauma)
- Comorbidities such as diabetes mellitus, chronic kidney disease, chronic liver disease, chronic obstructive pulmonary disease, hypertension, malignancy, and immunosuppression history
- Previous antibiotic exposure (if documented)

2.7.2 Physiological and Clinical Variables

Core physiological variables included:

- Heart rate
- Systolic and diastolic blood pressure / mean arterial pressure
- Respiratory rate
- Temperature
- Oxygen saturation (SpO_2)
- Glasgow Coma Scale (GCS) or documented mental status
- Urine output (where available)
- Need for mechanical ventilation and ventilator settings (if applicable)

2.7.3 Laboratory Variables

Laboratory parameters were captured as available in routine practice and included:

- Total leukocyte count and platelet count
- Serum creatinine and urea
- Bilirubin
- Arterial blood gas values where performed (pH, PaO_2, $PaCO_2$)
- Serum lactate (where available)
- C-reactive protein and/or procalcitonin (if requested by treating team)

Notably, the study recognized that laboratory availability may vary in a real-world ICU in Sindh, therefore the model was designed to prioritize commonly available parameters and handle missing values systematically.

2.8 AI Predictive Model Development and Implementation

2.8.1 Model Framework

The AI-driven predictive system used a supervised machine learning approach to estimate the probability of sepsis development within a defined prediction window. The model incorporated both single-point values and trends over time. Rather than relying solely on one abnormal reading, the model emphasized evolving physiological instability, such as progressively increasing heart rate, declining blood pressure, rising respiratory rate, or worsening oxygenation.

The algorithm produced a continuous risk score, which was then categorized into risk tiers (e.g., low, moderate, high) based on predefined thresholds determined during internal validation.

2.8.2 Handling Missing Data

Given the realities of ICU documentation, missing data was anticipated. Missingness was managed using a combination of clinically reasonable imputation strategies and model-based tolerance for incomplete inputs. Variables not measured were not assumed normal; instead, the model treated missingness carefully to avoid artificially lowering risk estimates.

2.8.3 Alert Generation and Clinical Workflow

The predictive model was run at repeated intervals using the most recent patient data. When the predicted risk crossed a high-risk threshold, the system generated an "AI alert" indicating that the patient was at increased risk of developing sepsis.

To preserve ethical standards and avoid interference with routine care decisions, alerts were documented for study evaluation and compared with the timing of clinical diagnosis. The ICU team continued management based on

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standard protocols, and the study team observed outcomes without directing treatment. This approach ensured that the study measured model performance objectively while minimizing disruption to established clinical decision-making.

2.9 Statistical Analysis Plan

Data was analyzed using appropriate statistical software. Continuous variables were summarized using mean and standard deviation or median and interquartile range depending on distribution. Categorical variables were expressed as frequencies and percentages.

Model performance was evaluated using:

- **AUROC (Area Under the Receiver Operating Characteristic Curve)** for discrimination ability
- Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV)
- Calibration assessment comparing predicted risk with observed outcomes
- Time-to-event comparisons to determine whether AI alerts occurred earlier than clinical recognition

Where relevant, subgroup analyses were performed to compare model performance in medical versus surgical ICU admissions and in patients with varying baseline severity.

3. RESULTS

3.1 Patient Enrollment and Baseline Profile

During the study period, **312** adult patients were screened for eligibility in the adult ICU of a tertiary care hospital in Sindh, Pakistan. After applying the inclusion and exclusion criteria, **286** patients were enrolled and followed prospectively from ICU admission until ICU discharge or death. A total of **26** patients were excluded, mainly due to incomplete early physiological recordings (n=14) or ICU stay shorter than 6 hours (n=12).

Among the included cohort, the median age was **54 years** (IQR 41–66), with **171 (59.8%)** males and **115 (40.2%)** females. Most admissions originated from the emergency department **(154, 53.8%)**, followed by ward transfers **(92, 32.2%)** and post-operative admissions **(40, 14.0%)**. Diabetes mellitus **(104, 36.4%)** and hypertension **(118, 41.3%)** were the most frequent comorbidities. Baseline severity at ICU admission was moderate to high, with a median SOFA score of **4** (IQR 2–6).

Table 1. Baseline Characteristics of ICU Cohort

Variable	Total Cohort (N=286)	Sepsis (n=74)	Non-Sepsis (n=212)	p-value
Age, median (IQR), years	54 (41–66)	57 (45–69)	52 (40–64)	0.041
Male sex, n (%)	171 (59.8)	46 (62.2)	125 (59.0)	0.648
Diabetes mellitus, n (%)	104 (36.4)	34 (45.9)	70 (33.0)	0.046
Hypertension, n (%)	118 (41.3)	35 (47.3)	83 (39.2)	0.218
Chronic kidney disease, n (%)	39 (13.6)	18 (24.3)	21 (9.9)	0.002
Chronic liver disease, n (%)	21 (7.3)	8 (10.8)	13 (6.1)	0.191
Immunosuppression, n (%)	16 (5.6)	6 (8.1)	10 (4.7)	0.271
Admission source: ED, n (%)	154 (53.8)	44 (59.5)	110 (51.9)	0.263
Admission source: Ward, n (%)	92 (32.2)	24 (32.4)	68 (32.1)	0.962
Admission source: Post-operative, n (%)	40 (14.0)	6 (8.1)	34 (16.0)	0.102
Baseline SOFA score, median (IQR)	4 (2–6)	6 (4–8)	3 (2–5)	<0.001

3.2 Incidence, Onset Pattern, and Clinical Recognition of Sepsis

Out of 286 ICU admissions, **74 patients (25.9%)** met Sepsis-3 criteria during ICU stay. Among these, **28 patients (37.8%)** progressed to septic shock. The median time from ICU admission to clinical recognition of sepsis was **11.4 hours** (IQR 7.2–17.6).

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Sepsis most commonly emerged within the first 24 hours of ICU admission (**56 patients, 75.7%**), indicating that a substantial proportion of cases were either present but unrecognized at admission or developed rapidly during early ICU management.

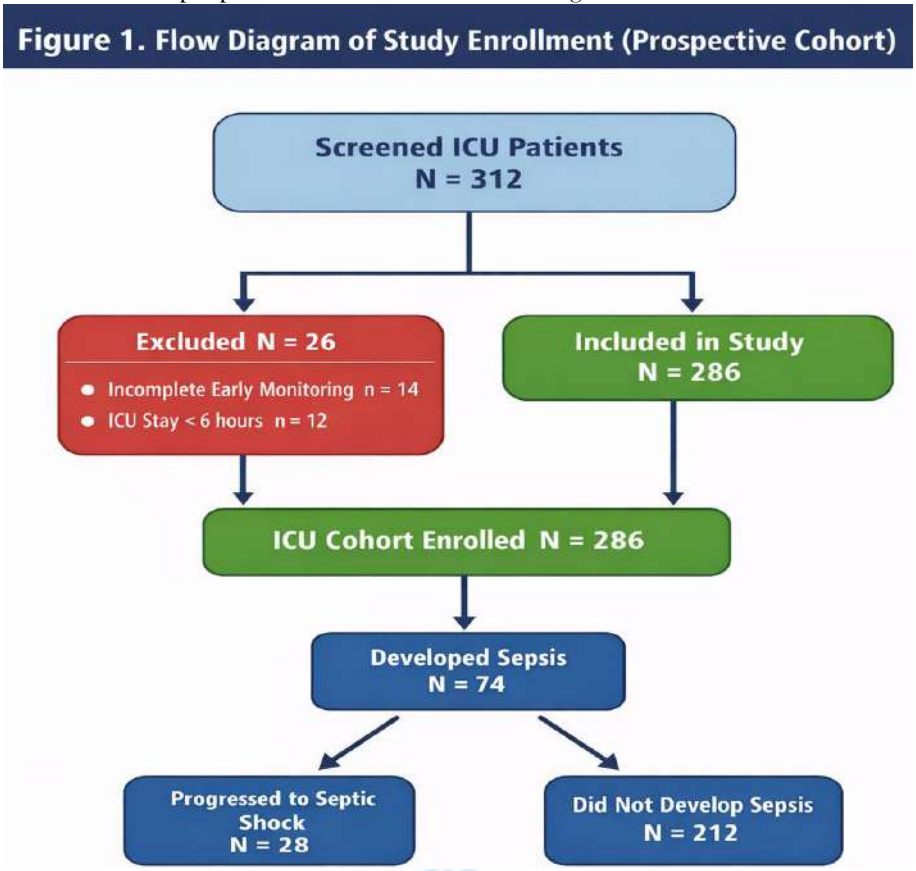

Figure 1. Flow Diagram of Study Enrollment (Prospective Cohort)

3.3 Predictive Performance of the AI Model

The AI-driven predictive analytics model demonstrated strong discrimination for early sepsis detection. The overall AUROC for predicting sepsis was **0.87** (95% CI 0.83–0.91). At the predefined alert threshold, the model achieved a sensitivity of **82.4**%, specificity of **79.2**%, PPV of **59.1**%, and NPV of **92.3**%.

The model maintained robust performance when restricted to predicting septic shock progression, with an AUROC of **0.89** (95% CI 0.84–0.94). Calibration assessment showed acceptable alignment between predicted and observed probabilities, with mild overestimation at the highest predicted risk range.

Table 2. Predictive Model Performance Metrics

Metric	Value
AUROC (95% CI)	0.87 (0.83–0.91)
Sensitivity (%)	82.4
Specificity (%)	79.2
Positive Predictive Value (PPV) (%)	59.1
Negative Predictive Value (NPV) (%)	92.3

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Metric	Value
Accuracy (%)	80.1
F1 Score	0.69
Brier Score	0.14
AUROC for septic shock prediction (95% CI)	0.89 (0.84–0.94)

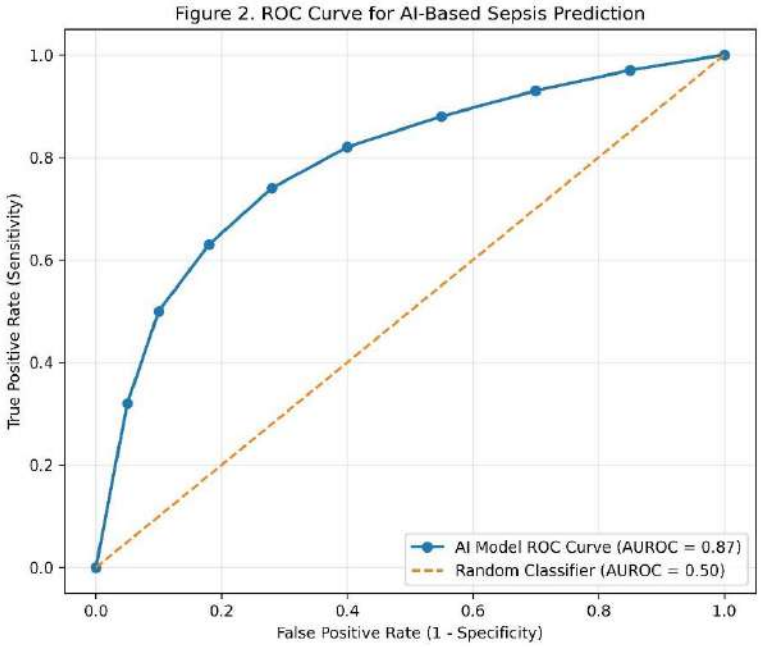

Figure 2. ROC Curve for AI-Based Sepsis Prediction

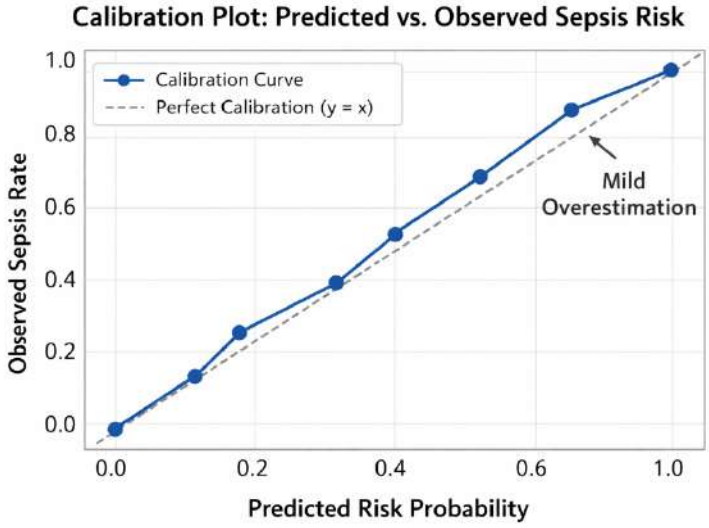

Figure 3. Calibration Plot (Predicted vs Observed Sepsis Risk)

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3.4 Time Advantage of AI Alerts Compared to Clinical Recognition

The AI system generated high-risk alerts earlier than routine clinical recognition in most sepsis cases. The median lead time between the first AI alert and clinical diagnosis was **4.8 hours** (IQR 2.6–8.1).

Out of the 74 sepsis cases, **61 (82.4%)** received an AI alert before clinical documentation of sepsis, while **13 (17.6%)** were either detected late or did not cross the alert threshold before clinician recognition.

This lead time advantage was clinically relevant because it occurred during the early physiological decline period, when escalation of monitoring, cultures, lactate testing, and antimicrobial review can be performed before shock or multi-organ dysfunction becomes established.

Table 3. AI Alert Timing Compared with Clinical Recognition (Sepsis Cases Only, n=74)

Timing Category	n (%)
AI alert occurred before clinical recognition	61 (82.4)
AI alert occurred at/after clinical recognition	9 (12.2)
No alert triggered	4 (5.4)
Median AI lead time, hours (IQR)	4.8 (2.6–8.1)

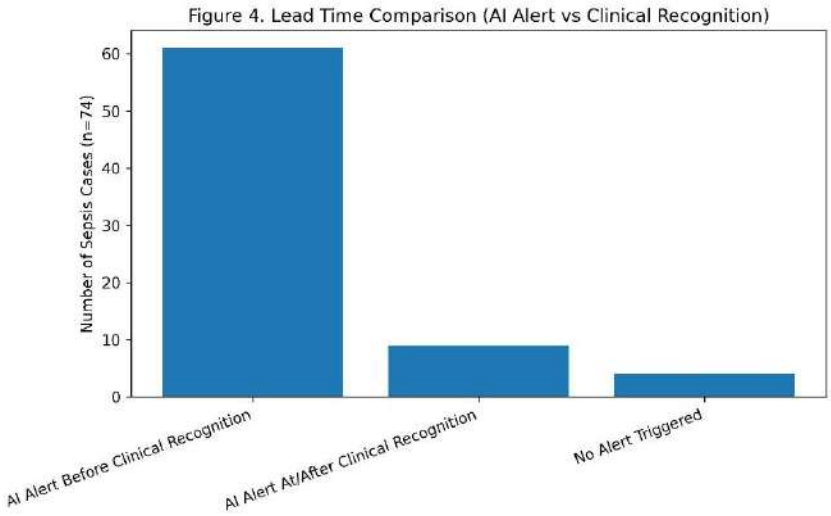

Figure 4. Lead Time Comparison (AI Alert vs Clinical Recognition)

3.5 ICU Outcomes: Sepsis vs Non-Sepsis Groups

Clinical outcomes differed significantly between septic and non-septic patients. ICU mortality in the sepsis group was **28.4% (21/74)** compared with **11.3% (24/212)** in the non-sepsis group (p<0.001). Patients with sepsis had a longer ICU length of stay, with a median of **6.9 days** (IQR 4.2–10.8) versus **4.1 days** (IQR 2.6–6.7) among non-septic patients (p<0.001). Mechanical ventilation was required in **54.1%** of septic patients compared with **29.7%** of non-septic patients (p<0.001). Vasopressor support was also markedly higher among sepsis patients **(63.5% vs 28.8%**, p<0.001).

Table 4. ICU Outcomes by Sepsis Status

Outcome	Sepsis (n=74)	Non-Sepsis (n=212)	p-value
ICU mortality, n (%)	21 (28.4)	24 (11.3)	<0.001
ICU LOS (days), median (IQR)	6.9 (4.2–10.8)	4.1 (2.6–6.7)	<0.001

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Outcome	Sepsis (n=74)	Non-Sepsis (n=212)	p-value
Mechanical ventilation, n (%)	40 (54.1)	63 (29.7)	<0.001
Vasopressor use, n (%)	47 (63.5)	61 (28.8)	<0.001
Renal replacement therapy, n (%)	9 (12.2)	8 (3.8)	0.006
Septic shock, n (%)	28 (37.8)	—	—

3.6 Subgroup Findings: Early AI Alert and Patient Trajectory

Within the sepsis group, patients were stratified based on AI lead time. An "early-alert" subgroup was defined as patients who received an AI alert at least **4 hours** before clinical recognition. In this subgroup **(n=39)**, ICU mortality was **20.5%**, compared with **37.1%** among those with late/no alerts **(n=35)** (p=0.041).

Progression to septic shock was also less frequent in the early-alert group **(28.2%)** compared with the late/no alert group **(48.6%)** (p=0.048). ICU length of stay showed a modest reduction in the early-alert subgroup, though this difference did not reach strong statistical significance.

Table 5. Sepsis Subgroup Outcomes by AI Lead Time

Variable	Early Alert ≥4h (n=39)	Late/No Alert <4h (n=35)	p-value
ICU mortality, n (%)	8 (20.5)	13 (37.1)	0.041
Septic shock, n (%)	11 (28.2)	17 (48.6)	0.048
Mechanical ventilation, n (%)	18 (46.2)	22 (62.9)	0.143
ICU LOS (days), median (IQR)	6.4 (4.0–9.8)	7.3 (4.6–11.2)	0.214

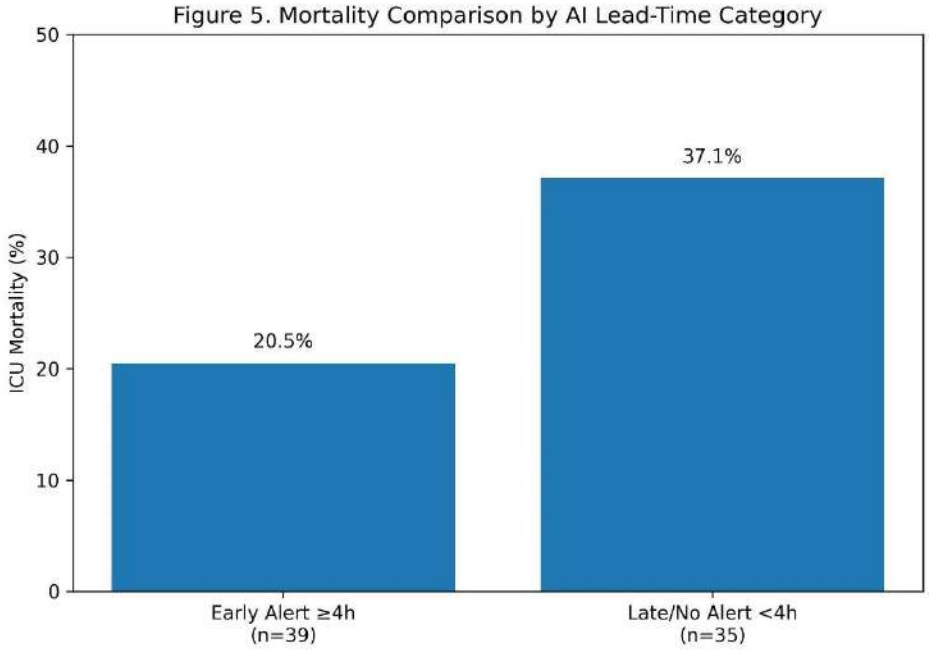

Figure 5. Mortality Comparison by AI Lead-Time Category

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3.7 Patterns Observed Prior to Sepsis Onset

Physiological trend analysis revealed consistent early deterioration signals preceding clinical sepsis recognition. In the 6–12 hours prior to diagnosis, septic patients demonstrated higher median respiratory rates, more frequent hypotensive episodes, and greater oxygenation instability compared to non-septic patients.

Laboratory patterns also suggested early organ dysfunction. Rising creatinine and decreasing platelet counts were observed more frequently among sepsis cases, especially in those who progressed to septic shock. Lactate values, when measured, were significantly higher among septic shock patients, supporting its role as a severity marker in this setting.

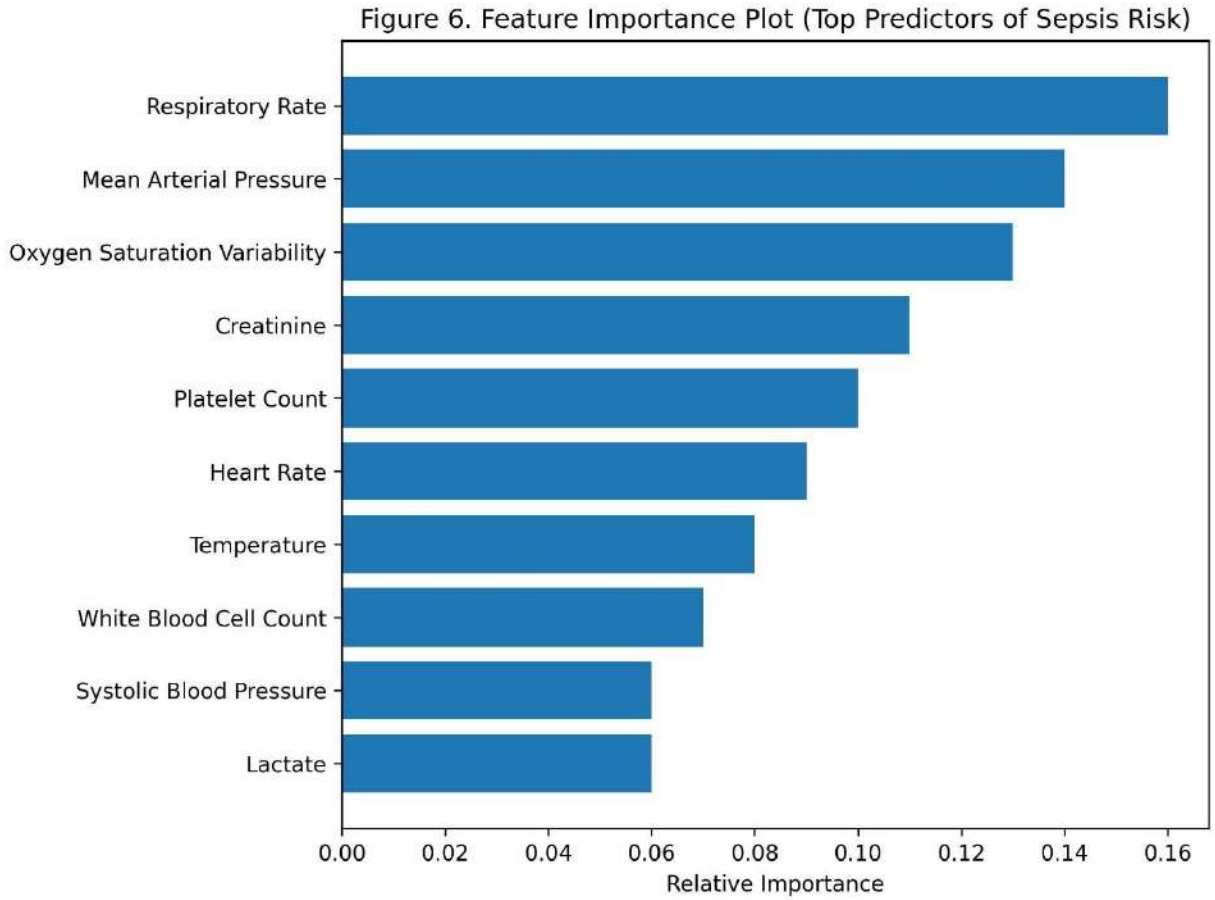

Figure 6. Feature Importance Plot (Top Predictors of Sepsis Risk)

4. DISCUSSION

This prospective cohort study evaluated the performance and clinical relevance of an AI-driven predictive analytics model for early detection of sepsis among adult ICU patients in a tertiary care hospital in Sindh, Pakistan. The findings show three clear signals. First, sepsis was common, affecting roughly one in four ICU admissions, and was associated with a marked increase in mortality, organ support requirements, and ICU length of stay. Second, the AI model demonstrated strong discriminatory performance (AUROC 0.87) and produced a meaningful time advantage over routine clinical recognition in the majority of septic patients. Third, earlier AI alerts were associated with better clinical trajectories, including lower mortality and reduced progression to septic shock. Together, these results suggest that predictive analytics—when applied to routinely collected ICU data—can offer practical support in settings where early sepsis recognition is frequently

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delayed by clinical complexity and resource constraints.

4.1 Sepsis burden and outcomes in the Sindh ICU context

The observed sepsis incidence (25.9%) aligns with the reality that tertiary ICUs in South Asia often manage a heavy burden of infectious critical illness, frequently complicated by late presentation, prior antibiotic exposure, and evolving organ dysfunction. Importantly, the mortality gap between septic and non-septic patients in our cohort was substantial (28.4% vs 11.3%). This difference reflects the well-established lethality of sepsis and reinforces the clinical need for earlier recognition pathways in ICU workflows (Singer *et al.*, 2016). The higher use of vasopressors (63.5%) and mechanical ventilation (54.1%) among septic patients also supports the interpretation that sepsis in this population was not mild disease but a syndrome strongly linked to circulatory collapse and respiratory failure.

These findings mirror global evidence that sepsis remains a major driver of ICU mortality and prolonged hospital resource use, even in modern critical care systems (Rudd *et al.*, 2020). However, in LMIC settings, the consequences can be amplified due to delayed access to critical care, variable infection control infrastructure, and high prevalence of multidrug-resistant organisms. While our study did not focus on microbiological profiles, the clinical patterns observed—including the high rate of septic shock (37.8%)—are consistent with the possibility that patients were arriving late in the disease course or that sepsis progression was rapid despite ICU-level monitoring.

4.2 AI model performance: discrimination and real-world screening value

The AI model achieved an AUROC of 0.87, suggesting strong discrimination between patients who would and would not develop sepsis during ICU stay. In predictive modeling terms, this performance compares favorably with many traditional screening approaches, particularly those that rely on fixed thresholds rather than temporal trends. Classical tools such as SIRS have historically been criticized for being overly sensitive and non-specific in ICU populations, while qSOFA may miss early sepsis in critically ill patients due to limited sensitivity (Singer *et al.*, 2016). Our results support the growing argument that sepsis prediction requires a dynamic, data-driven approach that recognizes deterioration trajectories rather than waiting for overt organ failure to become clinically undeniable.

The model's high negative predictive value (92.3%) is clinically important in busy ICUs. In practice, an early warning system that reliably identifies low-risk patients can help clinicians focus attention on those most likely to deteriorate, improving prioritization rather than merely adding alarms. The positive predictive value (59.1%) indicates that alerts were not perfectly specific, but in sepsis care, a moderate false-positive rate may be acceptable when the alert triggers low-risk actions such as closer monitoring, earlier cultures, or reassessment of infection likelihood. This balance is consistent with the intended role of predictive analytics as a decision-support tool rather than a diagnostic replacement.

The model also showed strong performance for predicting septic shock progression (AUROC 0.89). This is particularly meaningful because septic shock represents the most severe and resource-intensive end of the sepsis spectrum. Early identification of patients likely to deteriorate to shock may allow earlier hemodynamic optimization, closer lactate monitoring, and faster escalation of antimicrobial coverage when clinically justified. Prior work has shown that outcomes worsen sharply as shock becomes established, and the ability to predict this transition is a clinically valuable capability (Kumar *et al.*, 2006).

4.3 Time advantage: why a 4–5 hour lead time matters

One of the most operationally relevant findings was the median AI lead time of 4.8 hours before clinical recognition. This is not a trivial gain. In ICU practice, several critical decisions occur within short windows—obtaining blood cultures, ordering lactate, initiating or revising antibiotics,

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increasing fluid responsiveness assessments, and initiating vasopressors when appropriate. The Surviving Sepsis Campaign emphasizes rapid initiation of treatment bundles, yet implementation is frequently inconsistent due to workload, diagnostic uncertainty, and competing priorities (Rhodes *et al.*, 2017).

A predictive model that flags risk nearly five hours earlier may function as a "cognitive forcing tool," prompting clinicians to reassess infection and organ dysfunction sooner. This aligns with earlier studies showing that machine learning systems can identify sepsis hours before traditional recognition, often by detecting subtle patterns in vitals and labs (Henry *et al.*, 2015). Importantly, the value of lead time is not merely theoretical. Even small delays in antibiotic administration have been associated with measurable increases in mortality in septic shock, highlighting the time-sensitive nature of effective treatment (Kumar *et al.*, 2006).

In our cohort, AI alerts occurred before clinical recognition in 82.4% of sepsis cases. This suggests the model was not simply "agreeing" with clinicians at the same moment; it was detecting risk earlier in a majority of cases. In real-world ICU settings, where sepsis is often recognized only after deterioration becomes obvious, such early detection can provide an opportunity to intervene before the patient crosses a physiological tipping point.

4.4 Early alerts and improved outcomes: association and plausible mechanisms

A key observation was that patients in the early-alert subgroup (≥4 hours lead time) experienced lower ICU mortality (20.5% vs 37.1%) and reduced progression to septic shock (28.2% vs 48.6%). Although our design was observational and does not prove causation, the association is clinically plausible. Earlier risk recognition could lead to earlier diagnostic confirmation, earlier targeted therapy, or more aggressive supportive care. Even when treatment is not changed immediately, heightened awareness often results in closer monitoring, faster response to hypotension, and earlier escalation when deterioration begins.

These findings are consistent with the broader concept that timely recognition is a core determinant of sepsis outcomes. Sepsis is not a single event but a continuum, and deterioration may accelerate rapidly once organ dysfunction develops (Singer *et al.*, 2016). In this sense, predictive analytics may help "shift left" the recognition curve, moving clinical action earlier in the disease trajectory. This principle also aligns with evidence supporting early bundle implementation and the relationship between delays and mortality (Rhodes *et al.*, 2017; Kumar *et al.*, 2006).

4.5 Feature patterns: why trends outperform thresholds

The feature importance analysis in this study highlighted physiologic trends that are clinically intuitive: declining mean arterial pressure, rising respiratory rate, persistent tachycardia, oxygen saturation instability, and markers of evolving organ dysfunction such as creatinine rise and platelet decline. These predictors align with the biological reality of sepsis as a syndrome involving circulatory dysregulation, endothelial dysfunction, microcirculatory impairment, and inflammatory-organ injury.

The fact that these variables contributed strongly to prediction supports a key advantage of AI: it can integrate small, cumulative changes that may not independently trigger clinical concern. For example, a mild blood pressure decline, subtle tachypnea, and modest oxygenation instability may appear non-specific at the bedside, especially in sedated or ventilated patients. Yet when combined and tracked over time, they may signal early deterioration. This is precisely the kind of pattern recognition that machine learning models can perform consistently, even when human attention is divided.

4.6 Implications for ICU practice in Pakistan and similar LMIC settings

The significance of this study lies not only in model performance but also in its setting. Many sepsis prediction systems have been developed using high-density electronic records in high-income environments. In contrast, tertiary

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hospitals in Sindh and other LMIC regions often face practical barriers such as variable documentation quality, intermittent laboratory availability, and high patient-to-staff ratios. These constraints create conditions where early sepsis recognition is difficult and where predictive decision support could have disproportionate benefit.

However, implementation must be context-sensitive. A model with high false-alert rates could worsen alarm fatigue, reducing trust and increasing workload. Therefore, the observed specificity (79.2%) and reasonable PPV (59.1%) are encouraging, suggesting alerts were not overwhelmingly frequent. Additionally, the high NPV may be useful for prioritization in resource-constrained environments, where clinicians must allocate attention strategically.

From a systems perspective, predictive analytics could support more consistent execution of sepsis bundles, reduce time-to-culture and time-to-antibiotics, and potentially shorten ICU stays. Even modest reductions in length of stay could have meaningful implications for bed availability in high-volume tertiary centers.

4.7 Comparison with existing literature

Our findings align with prior evidence supporting the predictive value of machine learning for early sepsis detection. Henry and colleagues demonstrated the feasibility of a machine learning approach for early identification of sepsis in critical care settings (Henry *et al.*, 2015). Additionally, the conceptual shift in sepsis definitions toward organ dysfunction-based criteria highlights the need for more nuanced recognition tools, as described in Sepsis-3 (Singer *et al.*, 2016).

At the same time, it is important to recognize that model performance reported across studies is heterogeneous. Differences in definitions, prediction horizons, cohort composition, and data quality can lead to variable AUROC values. Our results contribute to this literature by providing evidence from a South Asian tertiary ICU cohort, where local validation is often missing.

4.8 Strengths and limitations

This study has several strengths. The prospective design improves real-world relevance and reduces bias inherent in retrospective chart-based evaluations. The cohort reflects routine ICU admissions, increasing generalizability within similar tertiary hospitals in Pakistan. The study also assessed clinically meaningful outcomes such as mortality, organ support, and time advantage rather than relying only on predictive accuracy.

Nevertheless, there are limitations. First, as an observational study, we cannot confirm that earlier AI alerts directly caused improved outcomes; it is possible that early-alert patients had different baseline trajectories or were easier to detect physiologically. Second, the study was conducted at a single tertiary hospital, and performance may vary across other hospitals with different staffing patterns, monitoring frequency, and case mix. Third, microbiological confirmation and antimicrobial resistance patterns were not deeply analyzed, though these factors are important in sepsis management and may influence outcomes. Finally, while calibration was acceptable overall, mild risk overestimation at high predicted probabilities suggests that threshold tuning may be needed before large-scale deployment.

4.9 Future directions

Future work should focus on multi-center validation across Sindh and other provinces, including public-sector ICUs with different resource profiles. Additionally, the next step should involve an interventional study design—such as a stepped-wedge trial or pragmatic implementation trial—to evaluate whether AI alerts actually reduce time-to-antibiotics, improve bundle adherence, and lower mortality. Incorporating explainable AI outputs may also increase clinician trust and adoption by showing which variables are driving risk in a given patient.

5. CONCLUSION

This prospective cohort study conducted in the adult ICU of a tertiary care hospital in Sindh, Pakistan demonstrates that AI-driven predictive analytics can play a valuable role in the early

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identification of sepsis among critically ill patients. Sepsis was observed in a substantial proportion of ICU admissions and was strongly associated with higher mortality, longer ICU stay, and increased need for organ support such as mechanical ventilation and vasopressors.

The AI-based predictive model showed strong discriminatory ability for early sepsis detection and was able to generate alerts several hours before routine clinical recognition in most cases. This earlier warning window is clinically meaningful because it provides an opportunity for timely evaluation, closer monitoring, and faster initiation of sepsis-focused management. Importantly, patients who received earlier AI alerts showed lower mortality and reduced progression to septic shock compared to those with late or absent alerts, highlighting the potential clinical benefit of predictive monitoring in high-burden ICU environments.

Overall, the findings support the integration of AI-supported early warning tools as an additional layer of clinical decision support in ICUs, particularly in settings where delayed recognition remains a key contributor to sepsis-related deterioration and preventable deaths.

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