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Research Article

Clinical Scores Can Predict Mortality in Septic Patients in the Intensive Care Unit

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Abstract

Background: Sepsis was a major factor in mortality inside intensive care units (ICU) worldwide. There was a paucity of knowledge about early markers that may forecast mortality and morbidity. This research aimed to assess the efficacy of Clinical Scores in predicting death among septic patients in the ICU. **Methodology:** This prospective clinical research included 91 patients of both genders, aged over 20, who presented to the ICU with serious infections or developed sepsis while in the ICU. The primary result was mortality among the examined patients; scores assessed upon admission constituted the secondary outcome. Demographic and clinical data were gathered at the trial's commencement. **Results:** Among 91 ICU patients diagnosed with severe sepsis, the overall death rate was 63%. Non-survivors had markedly elevated clinical scores, including APACHE II (median 29 vs. 17), SOFA (median 12 vs. 9), and NUTRIC (median 8 vs. 2), in comparison to survivors ($p < 0.001$). Optimal cutoff values for mortality prediction were >20 for APACHE II, with 100% sensitivity and 91% specificity; >9.5 for SOFA, exhibiting 98% sensitivity and 97% specificity; and >3.5 for NUTRIC, with 100% sensitivity and 94% specificity. **Conclusion:** The research indicated a mortality rate of 63% in individuals diagnosed with severe infection. Individuals with severe sepsis exhibiting an APACHE II score above 25, a SOFA score surpassing 8.5, and a NUTRIC score more than 5 at ICU admission had an elevated mortality risk.

Keywords: APACHE II score, Mortality, NUTRIC score, Prediction, Sepsis, SOFA score.

Introduction

Sepsis is now a critical concern due to its complex character from several viewpoints. Infection is a major contributor to hospitalization and a key determinant in death rates in ICUs worldwide[(1)]. Given the complex nature of infection, it is unlikely that a single study could fully depict the many host responses to infection.

The integration of many biomarkers into a cohesive classification system is anticipated to improve their accuracy and, therefore, their applicability [(2)]. Cases of severe infection often have elevated levels of lactate in the bloodstream. Both the first and subsequent lactate readings have been used to classify patients according to their risk and perhaps guide therapeutic measures [(3)].

Therapeutic scoring systems are used to classify risks, anticipate health outcomes, or enhance other therapeutic procedures. The Acute Physiology and Chronic Health Evaluation II (APACHE II score) is extensively validated; a prospective study in emergency department sepsis indicated an AUC of 0.801 for forecasting 30-day death [(4)].

The SOFA score has shown significant prognostic significance; one ICU observational

research indicated that rising SOFA scores over the first 96 hours were associated with increased death, whereas declining scores forecasted reduced mortality. Additionally, in cases with hospital-acquired pneumonia, the SOFA score had an AUC of 0.856 for 30-day mortality [5].

The NUTRIC score, however less prevalent in data, is emerging as a significant predictor of nutritional risk: critically ill patients exhibiting elevated NUTRIC scores regularly show worse outcomes, particularly when correlated with inflammatory biomarkers [6].

Despite aiding doctors in delivering patient care, their use in clinical practice is rare. The intricacy and need for expertise and training in using scoring systems add to this [7]. Therefore, This study aimed to assess the effectiveness of clinical scoring systems including; APACHE II, SOFA, and NUTRIC in predicting mortality among adult ICU patients with severe sepsis as the primary objective, while the secondary objective was to evaluate the association of mortality with laboratory markers including complete blood count (TLC, hemoglobin), inflammatory markers (CRP, serum lactate, NLR), and liver enzymes (AST, ALT).

Patients and methods

This prospective clinical research included 91 patients of both genders, aged over 20, who presented to the ICU with severe infections, as well as those who developed sepsis while in the ICU.

Following clearance from the institutional ethics committee of the Faculty of Medicine, Minia University (clearance No. 84:6/2021) and securing written consent from participants, the research was conducted at El-Minia University Hospital from May 2021 to December 2023.

The study excluded participants with mental disorders, those who declined to provide informed permission, and persons with noninfectious conditions.

Severe sepsis is defined as sepsis accompanied with organ dysfunction.

Management of patients in the ICU for sepsis includes the administration of broad-spectrum antibiotics upon admission, followed by adjustments based on blood and urinary cultures. Fluid management encompasses colloids, crystalloids, plasma, and blood transfusions as necessary. Additionally, antacids and analgesics may be provided if required, along with vasopressors, particularly norepinephrine. All patients were monitored until release or death.

At the conclusion of the investigation, cases were categorized into group A (survivors) and group B (non-survivors).

Parameters assessed (for survivors and non-survivor patients)

Upon admission to the ICU, all adult patients with severe sepsis were assessed for demographic and clinical parameters, including age, gender, body temperature, and BMI.

Upon admission, vital signs were assessed, including MBP, HR, respiratory rate, oxygen saturation (SpO_2), and the PaO_2/FiO_2 ratio.

Upon admission, laboratory tests were performed, including CBC (total leukocyte count, hemoglobin concentration), inflammatory markers (CRP, serum lactate, NLR), and liver enzymes (AST/ALT).

Imaging examinations (ultrasound, chest X-ray, and CT) were analyzed for indicators of organ failure and infection dissemination, including interstitial infiltrates, pleural effusions, or pneumothorax.

A complete array of clinical grading methods was implemented within the first 24 hours. The GCS evaluated neurological condition.

The APACHE II score, originally delineated by William et al., in 1981, was used to assess acute physiological disturbance and chronic health effects [8].

The SOFA score, established in 1994, encompasses assessments of the circulatory, respiratory, renal, hepatic, coagulation, and neurological systems, with each evaluated on a scale from 0 to 4 points. A score of ≥2 on the scale indicates a diagnosis of sepsis, with higher values reflecting more severe patient conditions [9].

Modified nutric score Heyland et al.,[10] assessed within 24 hours of admission. This score integrates five elements: age, quantity of comorbidities, duration since hospital admission, APACHE II score, and SOFA score. The mNUTRIC score was computed on a scale from 0 to 9. A total score of four or below indicates little nutritional risk, while a score over four signifies significant nutritional risk.

Statistical analysis:

The collected data was coded using SPSS software, version 20 (SPSS Inc., PASW Statistics for Windows version 20). Chicago: SPSS Inc. Quantitative variables were expressed as mean and SD or median and IQR. Qualitative factors were expressed as frequency (%). A Chi-square test was performed to assess the significance of the relationship between gender and mortality. Independent Samples examination for age and BMI. The Mann–Whitney test was used for intergroup comparisons of APACHE II, NUTRIC, SOFA, and GCS scores. $P < 0.05$ indicates a statistically significant change. ROC curves were generated to assess mortality and establish cutoff thresholds.

Results

Table (1) illustrated the demographic and clinical characteristics of the cases. The range of age between patients was (18:76), and the mean age was 45.5 ± 15.8. 59.3% were men and 37 (42.7%)) were women. The mean BMI was 25± 1.6 with a range of (18:41).

Table (1): Demographic data of the studied cases.

Demographic data (N=91)			**Descriptive statistics**
Age(years)	***Mean ± SD (Range)***		45.5 ± *15.8* *(18:76)*
Sex	**Male**	**Number**	54
		Percent %	(59.3%)
	Female	**Number**	37
		Percent %	(40.7%)
BMI ***(Kg/m^2)***	***Mean ± SD (Range)***		25± *1.6* *(18:41)*

Data are presented as *Mean ± SD or range*

There was no significant difference between groups regarding BMI, sex in addition to age in our study as illustrated in table (2)

Table (2): the two groups regarding demographics

Demographic data		**Survivors**	**Non-survivors**	**P value**
Age	**Mean ± SD (Range)**	46.7 ±15.9 (23:76)	44.9 ± 15.9 (18:76)	0.74
Sex	**Men** **Women**	22(60.6%) 14 (39.4%)	34(58.6%) 24(41.4%)	0.86
BMI	**Mean ± SD (Range)**	26± 4.5 (18:41)	24.5 ±4.5 (19:39)	0.20

Independent Samples Test for age, BMI, Chi square test for gender. BMI: body mass index

There was no statistically significant difference between the studied groups regarding co-morbidities and source of infection. Mechanically ventilated patients were significantly higher among the non-survivor group than the survivor group ($p< 0.001$). Length of ICU stay was significantly elevated in the non-survivor group (18±9 days), then the survivor group (12 ±5 days), respectively. **Table 3**

Table (3): comparison between survivors and non-survivors as regard to Co-morbidities, source of infection, MV and ICU stay

Co-morbidities, source of infection, and ICU stay and MV (N=91) No (%)		Survivors (N =33)	Non survivors (N =58)	P value
Co-morbidities	No	12(36.4%) #	15(26%) #	0.43
	Asthma	2(6.1%)	8(13.8%)	
	DM	3(9.1%)	9(15.5%)	
	HTN	4(12.1%)	6(10.3%)	
	DM&HTN	7(21.2%)	4(6.4%)	
	Liver failure	0	4(6.4%)	
	Renal failure	1(3%)	3(5.2%)	
	Ischemic heart	1(3%)	1(1.7%)	
	COPD	2(6.1%)	6(10.3%)	
	CKD	0	1(1.7%)	
	AF	1(3%)	1(1.7%)	
Source of infection	Respiratory	13(39.4%)#	22(37.9%)#	0.83
	intestinal fistula	1(3%)	6(10.3%)	
	Cellulitis	1(3%)	4(6.4%)	
	diabetic foot	5(15.2%)	7(12.1%)	
	hand infection	2(6.1%)	2(3.4%)	
	Burn	2(3%)	5(8.6%)	
	pelvic abscess	4(12.1%)	5(8.6%)	
	bed sores	3(9.1%)	2(3.4%)	
	infected shunt	2(3%)	2(3.4%)	
ICU stay (Days)	Mean ± SD (Range)	12 ±5 6-18	18±9 2-30	<0.001*
Mechanical ventilation	Yes	5(15.2%)	33(56.8%)	<0.001*
	No	28(84.8%)	25(43.2%)	

Chi square test for Co-morbidities, Source of infection, and MV, Independent sample t-test for ICU stays. *: Significant level at P value < 0.05

There was a statistically significant difference between both groups as regards mean hemodynamics (MBP and HR) on admission, while there was no statistical difference between groups regarding respiratory rate, O_2 saturation, and Po2\Fio2 ratio measured on admission. **Table (4)**

Table (4): comparison between survivors and non-survivors as Regard Hemodynamics and respiratory data on admission.

Vital sign		Survivors (N =33)	Non-survivors (N =58)	P value
Mean blood pressure (mmhg)	**Mean ± SD (Range)**	89.6± 3.3 (79:93)	74.4± 3.2 (67:82)	<0.001*
Heart rate (Beat/min)	**Mean ± SD (Range**	88.5± 4 82:94)	103.3± 2 (99:105)	<0.001*
Respiratory rate (Breath/min)	**Mean ± SD (Range**	23.2± 3 (20:31)	24.7± 3.3 (21:36)	0.83
O2 saturation %	**Mean ± SD (Range)**	96.7± 1 95:98)	96.7± 0.9 (95:98)	0.90
Po2\Fio2 ratio	**Mean ± SD (Range)**	216 ± 56 (137:325)	212.6 ± 54.5 (128:365)	0.78

Independent Samples Test.*: Significant level at P value < 0.05

There was no statistical difference between groups regarding all radiological findings. (Table 5)

Table (5): comparison between survivors and non-survivors as regard Radiology finding

Radiology finding (N=91) No & %		Survivors (N =33)	Non-survivors (N =58)	P value
US	**Normal**	18(51.5%)	15(25.9%)	0.12
	B line *(*interstitial disease*)*	10(24.2%)	17(27.6%)	
	pleural effusion	3(6.1%)	12(17.2%)	
	Pneumothorax	2(3%)	5(6.9%)	
X-ray	**Normal**	15(51.5%)	19(25.9%)	0.12
	interstitial disease	7(24.2%)	13(27.6%)	
	obscured RT angle	2(6.1%)	10(17.2%)	
	obscured LT angle	1(3%)	4(6.9%)	
CT	**Normal**	17(51.5%)	15(25.9%)	0.12
	interstitial disease	10(24.2%)	17(27.6%)	
	pleural effusion	3(6.1%)	12(17.2%)	
	Pneumothorax	1(3%)	5(6.9%)	

Chi-square test for Radiology finding

Patients with CNS, CVS, and renal dysfunction were significantly higher in the non-survivor group than survivor (p<0.001). As regard intergroup comparison CVS and Metabolic dysfunction were more than other systems dysfunction in the survivor group, while in non-survivors group CNS, CVS and renal dysfunction were more than another organs dysfunction. **Table (6)**

Table (6): comparison between survivors and non-survivors as regard to organ dysfunction

Organ dysfunction No (%)	Survivors (N =33)	Non-survivors (N =58)	P value
CNS	4(12.1%)	48(82.7%)#	<0.001*
CVS	14(42.5%) #	37(63.7%)#	<0.001*
Respiratory	6(18%)	12(20.6%)	0.90
Liver	*0*	1(1.7%)	0.97
Renal	0	31(53.4%)#	<0.001*
Metabolic	15(45.5%) #	18(31%)	0.16
Hematology	9(27.2%)	20(34.5%)	0.51

Chi-square test for organ dysfunction between the two groups. *: Significant level at P value < 0.05. # significant difference in the same group

There was significant elevation in TLC, CRP, Serum lactate, Mean NLR and fluid balance in non-survivor group than survivor group while platelet count was decreased significantly in non-survivor group than survivor group. Both groups were comparable regarding other laboratory investigations. **Table (7)**

Table (7): comparison between survivors and non-survivors as regard laboratory data

Laboratory data		**Survivors (N =33)**	**Non-survivors (N =58)**	**P value**
Hemoglobin (g/dl)	**Mean ± SD (Range)**	11.4 ±1.1 (8.5:15)	11.3 ±1.4 (8.5:15)	0.69
TLC (X10*3)	**Mean ± SD (Range)**	15.8 ± 2.8 (11.6:23)	20.7 ± 2.8 (14:32)	<0.001*
AST (U/L)	**Mean ± SD (Range)**	19.1 ± 7.6 (10:42)	20.4 ±9.3 (10:42)	0.97
ALT (U/L)	**Mean ± SD (Range)**	27.6 ± 8.5 (14:46)	28 ± 8.2 (9:42)	0.70
CRP (g/dl)	**Mean ± SD (Range)**	57.2± 37.7 (9:121)	174.8 ± 57 (54:290)	<0.001*
Serum lactate(mmmol/l)	**Mean ± SD (Range)**	2.4 ± 0.6 (1.8:3.2)	4.9 ± 1.3 (3.6:6.2)	<0.001*
NLR	**Mean ± SD (Range**	5.3 ± 1.7 (2.4:7.5)	8.7 ± 2.8 (4.38:12.6)	<0.001*
Fluid balance (L)	**Mean ± SD (Range**	0.9±0.6 (0.09:2.67)	2.8 ± 0.7 (4:1.03)	<0.001*

- Independent Samples Test for Lad data. *: Significant level at P value < 0.05

APACHE II was significantly lower in the improved patients compared to the dead cases. SOFA and NUTRIC scores were elevated significantly in the dead cases than improved cases. No statistical difference regarding GCS. Table (4)

Table (8): the two groups regarding APACHEII, NUTRIC, SOFA & GCS

(m)		**Survivors (N =33)**	**Non survivors (N =58)**	**P value**
APACHE11	**Median**	17 (13:21)	29 (21:34)	<0.001*
NUTRIC	**Median**	2(2:5)	8(5:9)	<0.001*
SOFA	**Median**	9(5:10)	12(10:15)	<0.001*
GCS	**Median**	14(13:15)	15(12:15)	0.21

Mann-Whitney Test for APACHEII, NUTRIC, SOFA & GCS. *: Significant level at P value < 0.05

The study identified optimal cutoff values for several biomarkers in predicting mortality. A TLC greater than 17.5 $\times 10^3/\mu L$ predicts mortality with 96% sensitivity, and 73% specificity. CRP levels above 88.5 g/dL predict mortality with 98% sensitivity, and 79% specificity. Serum lactate levels exceeding 2.8 mmol/L predict mortality with 77% sensitivity, and 65% specificity and NLR above 9.5 indicates mortality with 93% sensitivity, and 89% specificity. **(Figures1)**

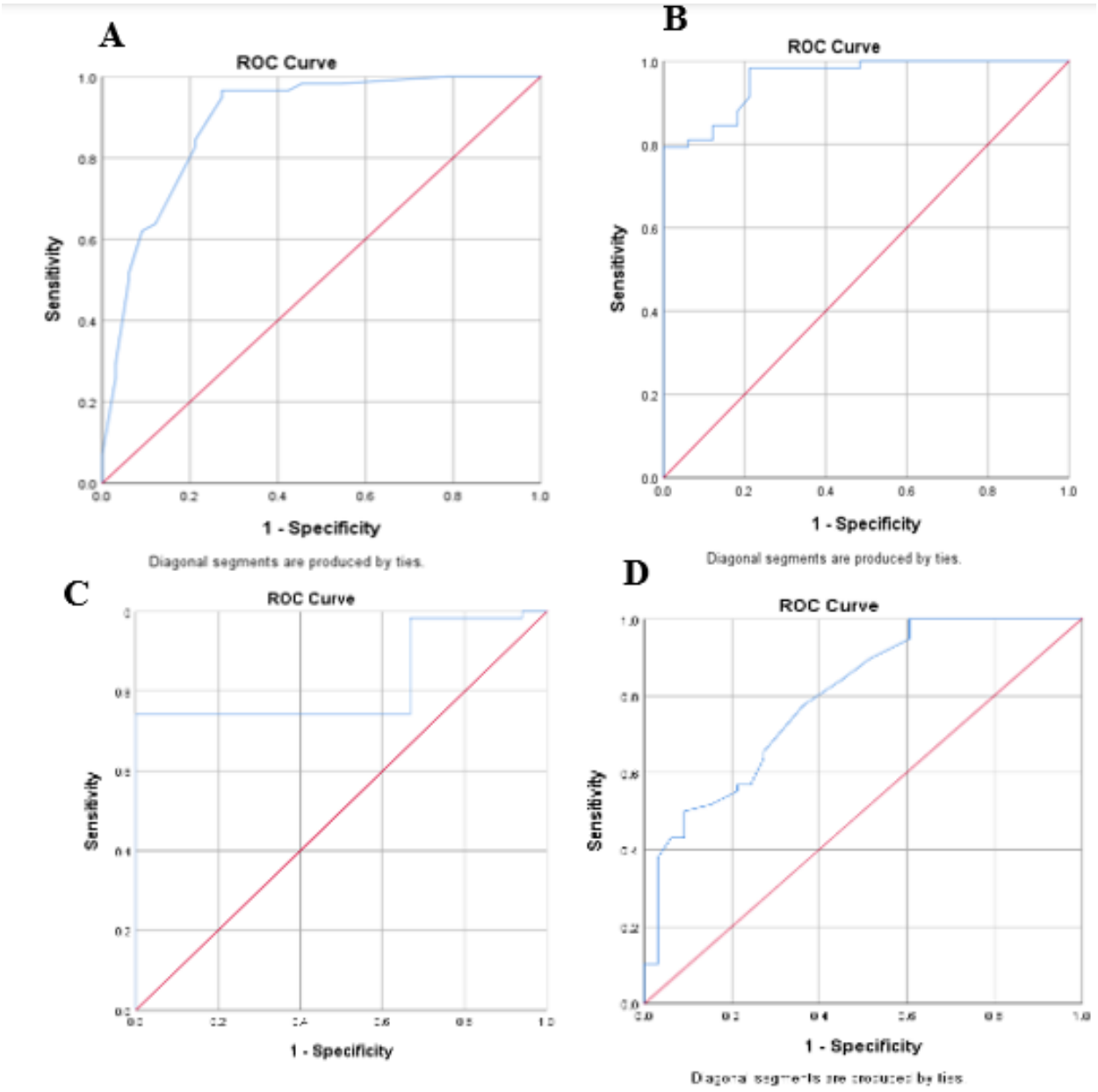

Figure 1: ROC curve for prediction of mortality by A) total leucocyte count (TLC), B) C-reactive protein (CRP), C) neutrophil-lymphocyte ratio (NLR), and D) Serum lactate

Also, the study determined optimal cutoff values for clinical scoring systems in predicting mortality. An APACHE II score greater than 20 predicted mortality with 100% sensitivity, while a score of 20 or below predicted improvement with 91% specificity. A SOFA score above 9.5 indicated mortality with 98% sensitivity, whereas scores at or below 9.5 predicted improvement with 97% specificity. Similarly, a NUTRIC score above 3.5 predicted mortality with 100% sensitivity, and scores of 3.5 or less predicted improvement with 94% specificity. **(Figure 2)**

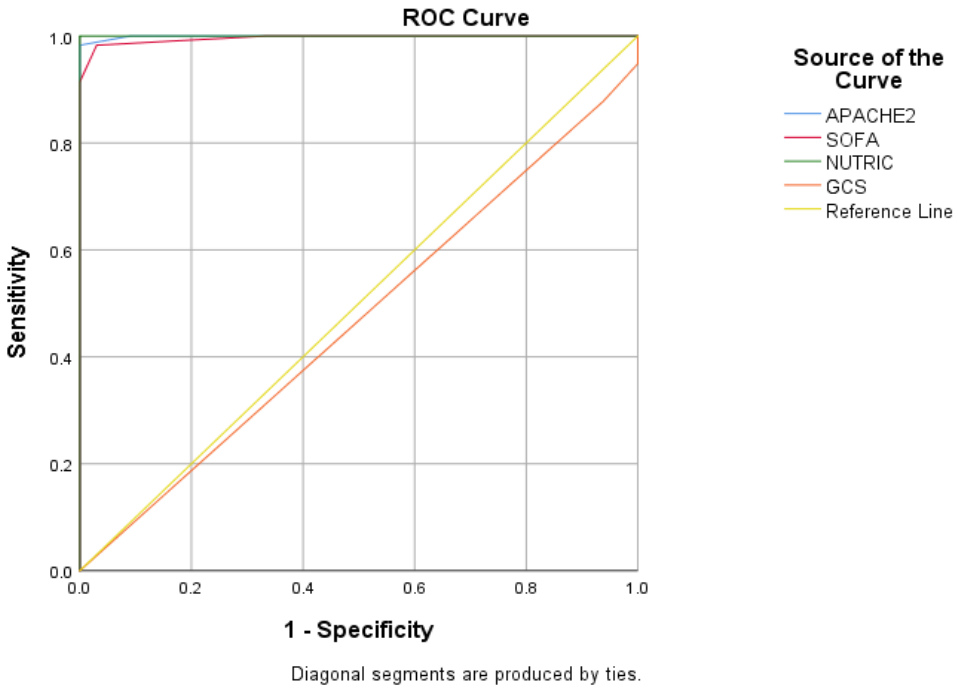

Figure (2): ROC curve for APACHE II, SOFA, NUTRIA & GCS score for prediction of mortality

Discussion

Infection is a significant medical concern whereby the immune system responds to pathogens, resulting in serious organ failure and perhaps culminating in death [11].

The high mortality rates linked to sepsis are due to the lack of a dependable mechanism for forecasting sepsis outcomes. Understanding the causes of sepsis-induced mortality is essential, as is the identification of enhanced predictive models to facilitate the development of personalized therapeutics for diverse sepsis patients [12].

A timely diagnosis is essential to swiftly start treatment and enhance the likelihood of a positive outcome, since any delay in therapy correlates with increased death rates [13].

Numerous diagnostic and prognostic methodologies have been developed and/or validated to facilitate the early prediction of adverse outcomes in sepsis patients upon their admission to the emergency department [14].

This research aimed to assess the efficacy of clinical scoring systems, namely APACHE II, SOFA, and NUTRIC scores, in forecasting death in adult patients admitted to the ICU with severe sepsis.

The present investigation demonstrated no statistically significant difference among the analyzed groups for comorbidities, infection etiology, or mechanical ventilation.

On the other hand, Thomas et al.,[15] performed a retrospective observational cohort study including ICU patients with sepsis. Research indicates that comorbidities significantly influence mortality rates, revealing that fatalities attributed to sepsis without associated comorbidities are few, including 6-12% of instances where sepsis is the only cause of death, 54-76% when sepsis coexists with comorbidities, and 18-40% where comorbidities are the exclusive cause of death.

However, Dhital et al.,[16] demonstrated that among 4827 septic patients, 769 required mechanical ventilation, which correlated with an extended length of stay (9.72 ± 0.17 days), prolonged hospitalization, and elevated in-hospital mortality (41.33% vs 8.91%) relative to patients who did not necessitate mechanical ventilation.

The current study demonstrated that ultrasound findings, including interstitial disease, pneumothorax, and pleural effusion, were somewhat elevated when employing ultrasound and CT in comparison to X-ray in both cohorts; however, no statistical differences were observed between the groups regarding any radiological findings related to lung imaging.

In a study conducted by Xirouchaki et al., [17], evaluated the diagnostic efficacy of bedside CXR and lung ultrasonography in a cohort of unselected critically unwell patients. Thoracic CT served as the definitive benchmark for this assessment. This research demonstrated that lung ultrasound outperformed CT in identifying common pathological conditions, indicating its potential to replace thoracic CT. The limited sample size (n=8) and suboptimal methodologies may account for the decreased sensitivity of lung ultrasonography in detecting pneumothorax.
Our data indicate that non-survivors had markedly elevated levels of TLC, CRP, serum lactate, and mean NLR in comparison to survivors.

Along with our findings, Devran et al., [18] performed an observational cohort study on patients who acquired severe sepsis due to respiratory illnesses. Among 45 individuals, 14.2% succumbed, and the findings indicated that CRP levels over 100 mg/L and elevated SOFA scores on the third day were prognostic indicators for ICU death. According to Filho et al., [19], conducted a retrospective cohort research on patients with severe sepsis or septic shock, using a ROC curve to determine the optimal initial blood lactate cutoff value correlated with 28-day death in septic individuals. Lactate levels above 2.5 mmol/L were associated with enhanced prediction of 28-day death.

In a recent meta-analysis Huang et al., [20] of 14 trials including 11,564 sepsis patients revealed that an elevated NLR correlated with prognosis, with this correlation being much larger in non-survivors compared to survivors.

A similar study by Sari et al., [21] aimed to assess the NLR in relation to forecasting mortality and treatment efficacy in ICU patients suffering from sepsis. It was observed that, in comparison to patients who exhibited partial or full responsiveness, those whose bodies did not react to the antibiotic had an increased NLR on the third day of the response.

In our study, we used several grading methods to predict death. The levels of APACHE II, SOFA, and modified nutritional scores substantially increased in nonsurvivors compared to survivors. An APACHE II score over 20 predicted death with 100% sensitivity and 91% specificity. A SOFA score over 9.5 signifies mortality with 98% sensitivity and 97% specificity. A NUTRIC score over 3.5 predicted death with 100% sensitivity and 94% specificity.

In concordance with our results Hai and Viet Hoa [22] performed a research including 194 ICU patients with sepsis to assess the predictive significance of the NUTRIC score. The research revealed that non-survivors had markedly elevated NUTRIC scores, with mortality much higher in individuals with a NUTRIC score of 5 or above relative to those with lower values. Furthermore, SOFA, APACHE II, and SAPS 2 scores were markedly elevated in non-survivors, underscoring their utility in mortality prediction. Thakur et al., [23] performed a research involving 72 sepsis patients to evaluate the efficacy of APACHE II and SOFA scores in forecasting death. ROC curve research revealed that both APACHE II and the average SOFA score were effective mortality predictors, with the average SOFA exhibiting notably high sensitivity.

In conclusion, elevated APACHE II, SOFA, and NUTRIC scores within the first 24 hours of ICU admission are significantly correlated with heightened mortality risk. Moreover,

biomarkers like increased TLC, CRP, serum lactate, and NLR were considerably greater in non-survivors and may aid in clinical decision-making.

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