Comparison of PIRO, APACHE IV, and SOFA Scores in Predicting Outcome in Patients with Sepsis Admitted to Intensive Care Unit: A Two-year Cross-sectional Study at Rural Teaching Hospital

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ABSTRACT

Introduction: Though many scoring systems for prognostication of sepsis are available in the intensive care set-up, predisposition, insult, response, and organ dysfunction (PIRO) score helps to assess each patient and evaluate response to therapy. There are few studies comparing the efficacy of PIRO score with other sepsis scores. Hence, our study was planned to compare PIRO score with acute physiology and chronic health evaluation IV (APACHE IV) score and sequential (sepsis-related) organ failure assessment (SOFA) score in predicting the mortality of intensive care patients with sepsis.

Materials and methods: This prospective cross-sectional study was done in the medical intensive care unit (MICU) from August 2019 to September 2021 among patients above 18 years of age with the diagnosis of sepsis. Predisposition, insult, response, and organ dysfunction score, SOFA score, and APACHE IV score on admission and at day 3 were calculated and statistically analyzed in the terms of outcome.

Results: A total of 280 patients fulfilling the inclusion criteria were included in the study, the mean age was 59.38 ± 15.9 years. There was a significant association of PIRO score, SOFA score, and APACHE IV score on admission and at day 3 with mortality (p-value <0.05). Among all three parameters, the PIRO score on admission and at day 3 was the best predictor of mortality at cut-off points of >14 and >16 with 92.50% and 96.50% chances of correctly predicting mortality, respectively.

Conclusion: Predisposition, insult, response, and organ dysfunction score can be considered as a strong predictor of prognostication of patients with sepsis admitted to the intensive care unit (ICU) and predict mortality. It should be routinely used as it is a simple and comprehensive score.

Keywords: Acute physiology and chronic health evaluation IV, Intensive care unit, Organ failure, Outcome, Sepsis, Sequential (sepsis-related) organ failure assessment.

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HIGHLIGHTS

In spite of the availability of many scoring systems for prognostication of sepsis, simple, and comprehensive score are lacking. This research article highlights about PIRO score (easy to interpret) which may be a strong predictor of morbidity and mortality in patients with sepsis admitted to the ICU.

INTRODUCTION

Sepsis is a common global health issue and a medical emergency in the ICUs. It is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. It is due to host's immune response to any infection. Despite significant recent advancements in the knowledge about its management, it remains one of the major causes of illness and mortality among patients admitted to the ICUs in a critically ill state.[1]

In an Indian intensive care case mix and practice patterns study, a multicenter study done in India reported the prevalence of sepsis to be 28.3%, of which positive cultures and microbial identification could be done in only nearly half the patients.[2] A point prevalence study conducted at a single center at a tertiary care hospital reported that the incidence of severe sepsis was 6% in their ICUs out of which 16% were hospital-acquired.[3]

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The phases of sepsis include sepsis, severe sepsis, septic shock, and multiorgan dysfunction syndrome (MODS).[4] According to the European Prevalence of Infection in Intensive Care II (EPIC II) study, the ICU mortality related to sepsis was underestimated because all sepsis-related deaths did not happen in an ICU setting.[5]

Infections anywhere in the body as in genitourinary tract infection, pneumonia, intra-abdominal, invasive devices infection, and post-surgical infections can lead to sepsis and it is sequelae. There are many well-known risk factors, including chronic diseases (e.g., acquired immunodeficiency syndrome, liver cirrhosis, cancers, and chronic obstructive pulmonary disease) and the use of immunosuppressive agents.[4,5]

Patients with sepsis are triaged using severity evaluation score methods to help physicians determine if intensive treatment is required. This can save the time and money of the patient while also ensuring that he receives adequate treatment. To evaluate the severity of the disease as well as the prognosis of patients admitted to the ICU, many scoring systems have been established. Multiple scoring systems such as SOFA and APACHE in predicting mortality in ICU patients with sepsis have shown good discriminative power.[6,7] Predisposition, insult, response, and organ dysfunction scoring has also been identified as one of the important predictors of mortality in ICU admissions with sepsis. The abbreviated form of PIRO is based on the assessing components of PIRO.[8] The field of predisposition encompasses all variables that exist prior to the onset of acute disease and can influence the clinical outcomes in patients with sepsis. Insult encompasses infection that triggers a harmful endogenous host response (also known as sepsis in case of infection being the cause). The response includes the magnitude of host response in the form of respiratory rate, heart rate, and band forms. Organ dysfunction is measured by blood urea nitrogen (BUN), hypoxia, serum lactate levels, systolic blood pressure, and total platelet count.

Till date, only few studies are available comparing the PIRO scores with other scores in severe sepsis and septic shock for predicting mortality and among them, it is not yet feasible to decide the better score. Thus, the present study was conducted to evaluate the PIRO score in comparison with SOFA and APACHE IV scores for predicting mortality in ICU patients with severe sepsis and septic shock.

MATERIALS AND METHODS

This prospective cross-sectional study was conducted in the MICU under the Department of Medicine at a tertiary care rural hospital in Central India from August 2019 to September 2021 after obtaining institutional ethics committee approval in a letter with the number DMIMS (DU)/IEC/Aug-2019/8211. A total of 340 patients were considered for the study, 280 patients fulfilling the inclusion criteria were included in the study. All the patients, regardless of gender, above 18 years of age, who were admitted under MICU with a clear diagnosis of systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis, and septic shock, were included in the study. Patients transferred to MICU from outside the hospital, patients with clear no sepsis diagnoses (e.g., trauma, myocardial infarction, and pulmonary embolism), post-surgical patients, and patients not willing to give informed consent were excluded from the study.

Study Definitions[9]

SIRS – At least 2 of the following should be present for diagnosis of SIRS, temperature more than 38°C or less than 36°C, heart rate more than 90/min, hyperventilation evidenced by respiratory rate more than 20/min, or arterial CO_2 lower than 32 mm Hg, and white blood cell counts more than 12000 cells/µL or lower than 4000 cells/µL or more than 10% immature band forms.

Sepsis – Defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection (severe sepsis).

Septic shock – Defined as sepsis with persisting hypotension requiring vasopressors to maintain mean arterial pressure ≥65 mm Hg and having a serum lactate level >2 mmol/L (18 mg/dL) despite adequate volume resuscitation.

A thorough history, including assessment for pre-existing comorbidities like hypertension, diabetes mellitus, chronic kidney disease, cirrhosis of the liver, chronic obstructive pulmonary disease, and malignancy was done. A detailed clinical examination was also done. Complete blood count was done after withdrawing samples aseptically. The sample was collected in a dipotassium ethylenediaminetetraacetic acid (EDTA) bulb and tested within 1 hour when maintained at room temperature. In case of a delay, the samples were cooled in a refrigerator until they were processed. An automated cell counter, Beckman Coulter-Unicel DxH 800 hematology analyzer, was used, which provided the values of hemoglobin, total platelet count, and total leukocyte count. Blood was drawn aseptically in vacuumed plain bulbs which contained clot activators. The serum bilirubin, SGOT, and SGPT values were assessed with the help of VITROS 5600 biochemistry and immunoassay analyzer. Serum sodium, serum potassium, blood urea, and creatinine were also analyzed by VITROS 5600 biochemistry analyzer. A pre-heparinized syringe was used to perform an arterial blood gas analysis (ABG) under all aseptic precautions. Radial/Femoral artery was the preferred sites. The sample was then transported to the central clinical laboratory on an ice pack immediately, and the sample was processed in ABL 800 Arterial Blood Gas Analyzer.

Predisposition, insult, response, and organ dysfunction, SOFA, and APACHE IV scores were calculated for each patient on arrival within 24 hours of ICU admission. All the 3 scores were reassessed on 3rd day of enrolment. All the patients were followed up until mortality or cure. The sum of all 3 scores was compared within 24 hours of admission and day 3. The primary outcome, the efficacy of PIRO score in comparison with APACHE IV and SOFA score in predicting mortality in ICU patients with sepsis was assessed.

The outcome was to assess the efficacy of PIRO score in comparison with APACHE IV and SOFA score in predicting mortality in patients admitted to the ICU with sepsis. Flowchart of the study is shown (Flowchart 1).

Statistical Analysis

The presentation of the categorical variables was done in the form of numbers and percentages (%). On the other hand, the quantitative data were presented as the means ± standard deviation (SD). The association of the variables, which were quantitative and not normally distributed in nature, was analyzed using Mann–Whitney test (for two groups). The association of the variables, which were qualitative in nature, was analyzed using Chi-square test. Receiver operating characteristic curve was used for predicting mortality and prolonged ICU stay. DeLong et al. test was used for comparison of area under the curve. Multivariate logistic regression was used to find out independent significant risk factors of mortality and prolonged ICU stay. The data entry was done in the Microsoft EXCEL spreadsheet, and the final analysis was done with the use of Statistical Package for Social Sciences

Flowchart 1: Flowchart showing scheme of study
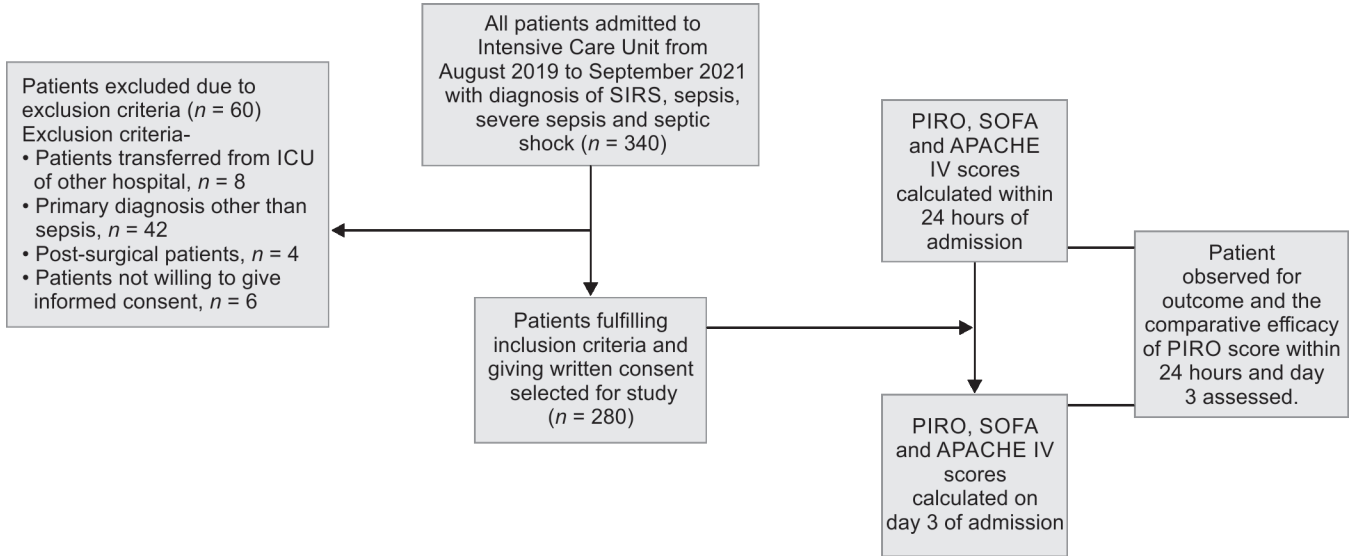
(SPSS) software, IBM manufacturer, Chicago, USA, version 21.0. For statistical significance, *p*-value of less than 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS

In total, 280 patients with sepsis aged between >18 years of either gender were included in the study. PIRO, SOFA, and APACHE IV scores were calculated for each patient on arrival to within 24 hours of ICU admission and again on day 3. In total, 194 (69.29%) patients were males, and 86 (30.71%) patients were females. Mean age (years) of the patients was 59.38 ± 15.9, out of 280 patients, 159 (56.79%) patients survived, and 121 (43.21%) patients died. Mean value of PIRO score on admission and at day 3 of study patients was 14.99 ± 4.17 and 14.99 ± 5.57, respectively, mean value of SOFA score on admission and at day 3 of patients was 9.65 ± 3.2 and 9.55 ± 3.8, respectively, and mean value of APACHE IV on admission and at day 3 of patients was 126.25 ± 30.33 and 124.65 ± 40.28, respectively. Other baseline characteristics of the patients are shown in Table 1.

Area under the ROC curve showed PIRO score on admission having a sensitivity of 98.3% (AUC 0.925; 95% CI: 0.888–0.953). Discriminatory power of SOFA score on admission having a sensitivity of 84.3% (AUC 0.879; 95% CI: 0.834–0.914) and APACHE IV score on admission having a sensitivity of 82.6% (AUC 0.868; 95% CI: 0.822–0.905). Among all the parameters, PIRO score (on admission) was the best predictor of mortality at cut-off point of >14, with 92.50% chance of correctly predicting mortality. SOFA score and APACHE IV on admission had a cut-off of 9 and 126, respectively, in prediction of mortality. APACHE IV score on admission had lowest sensitivity of 82.64%. On the other hand, SOFA score on admission had a specificity of 81.76%, followed by APACHE IV score on admission (77.36%) and PIRO score (on admission) (74.21%). The highest positive predictive value was found in SOFA score on admission (77.90%) and the highest negative predictive value was found in PIRO score (on admission) (98.30%). Overall, PIRO score (on admission) was the best predictor of mortality as shown in Figure 1.

Area under the ROC curve showed that the performance of PIRO score on day 3 had sensitivity of 94.4% (AUC 0.965; 95% CI: 0.934–0.984), SOFA score on day 3 had sensitivity of 84.3% (AUC 0.936; 95% CI: 0.898–0.963), and APACHE IV score on day 3 had

sensitivity of 91% (AUC 0.931; 95% CI: 0.893–0.960). Among all the parameters, PIRO score on day 3 was the best predictor of mortality at cut-off point of >16, with 96.50% chance of correctly predicting mortality. Sequential [sepsis-related] organ failure assessment score and APACHE IV on day 3 had a cut-off of 10 and 132, respectively, as shown in Figure 2.

On performing multivariate regression, systolic blood pressure (mm Hg) and serum lactate (mmol/L) were significant independent risk factors of mortality after adjusting for confounding factors. With the increase in serum lactate (mmol/L), risk of mortality significantly increases with an adjusted odds ratio of 1.672 (1.060–2.638), respectively, as shown in Table 2.

DISCUSSION

Sepsis is one of the costliest healthcare problems and is considered to be among the most prevalent causes of mortality in patients admitted to ICU with increased incidence in males and the elderly.[10,11]

The present study showed that the PIRO scoring system has better discrimination and performance compared with the other two scoring systems, like APACHE IV and SOFA, in predicting overall mortality in patients admitted with sepsis.

In our study, patients with sepsis admitted in the ICU had mortality rate 43.21%. There was significantly higher PIRO score, SOFA score, and APACHE IV score in nonsurvivors than survivors. For predicting mortality, area under the curve of PIRO score on admission and day 3 was significantly higher as compared to SOFA score and APACHE IV score at respective time points. Sequential (sepsis-related) organ failure assessment score >14 on admission and of >16 on day 3 showed 92.50% and 96.50% chances of correctly predicting mortality when compared to SOFA score on admission having a sensitivity of 84.3% and APACHE IV on admission 82.6%. SOFA score on day 3 having sensitivity of 84.3%, and APACHE IV, on day 3, was 91%.

A study by Posadas-Calleja et al.[12] found that the mean PIRO score was higher in nonsurvivors, and PIRO score is helpful in predicting mortality (having sensitivity of 80%) and performed better than the APACHE II score (having sensitivity of 72%) and the SOFA score (having sensitivity of 72%). But this study was conducted in surgical ICU and included APACHE II for comparison.

Table 1: Baseline characteristics of study patients

Demographic characteristics	Nonsurvivors (n = 121)	Survivors (n = 159)	Total
Gender			
Female	34 (28.10%)	52 (32.70%)	86 (30.71%)
Male	87 (71.90%)	107 (67.30%)	194 (69.29%)
Age (years)			
Mean ± SD	60.1 ± 15.54	58.83 ± 16.16	59.38 ± 15.88
Range	27–89	21–88	21–89
Heart rate (per minute)			
Mean ± SD	111.27 ± 15.76	89.04 ± 12.8	98.65 ± 17.93
Range	34–140	46–128	34–140
Respiratory rate (per minute)			
Mean ± SD	23.57 ± 4.31	16.97 ± 3.59	19.82 ± 5.1
Range	12–36	12–28	12–36
Systolic blood pressure (mm Hg)			
Mean ± SD	97.5 ± 22.93	122.83 ± 22.3	111.89 ± 25.8
Range	50–170	70–190	50–190
Hemoglobin (gm/dL)			
Mean ± SD	11.8 ± 2.65	11.83 ± 2.54	11.82 ± 2.58
Range	2.1–18.3	3.6–17.2	2.1–18.3
Platelets count (per µL)			
Mean ± SD	2.01 ± 1.24	2.13 ± 1.06	2.08 ± 1.14
Range	0.11–6.69	0.35–6.64	0.11–6.69
White blood cells (per µL)			
Mean ± SD	15339.67 ± 7951.95	13816.35 ± 7453.14	14474.64 ± 7695.89
Range	700–44800	2200–59800	700–59800
Serum urea (mg/dL)			
Mean ± SD	75.48 ± 65.03	49.93 ± 44.24	60.97 ± 55.57
Range	15–500	11–374	11–500
BUN (mg/dL)			
Mean ± SD	35.24 ± 30.36	23.31 ± 20.65	28.46 ± 25.94
Range	7–233.43	5.14–174.6	5.14–233.43
Serum creatinine (mg/dL)			
Mean ± SD	2.26 ± 3.57	1.49 ± 1.91	1.82 ± 2.77
Range	0.5–35	0.4–14	0.4–35
Serum bilirubin (mg/dL)			
Mean ± SD	1.16 ± 1.16	1.39 ± 2.73	1.29 ± 2.19
Range	0.2–9.1	0.1–26	0.1–26
Serum albumin (gm/dL)			
Mean ± SD	3.31 ± 0.74	3.42 ± 0.71	3.37 ± 0.73
Range	1.8–6.4	1.8–6.4	1.8–6.4
SGOT (U/L)			
Mean ± SD	115.77 ± 205.16	90.21 ± 285.44	101.25 ± 253.78
Range	8–2012	12–3586	8–3586
SGPT (U/L)			
Mean ± SD	80.22 ± 190.47	64.61 ± 197.96	71.36 ± 194.57
Range	8–1924	7–2364	7–2364
Serum lactate (mmol/L)			
Mean ± SD	3.37 ± 1.45	2.26 ± 0.96	2.74 ± 1.31
Range	1–6.7	1–6.3	1–6.7

Table 1: *(Contd...)*

| Comorbidities	Frequency (%)	Frequency (%)	Total (%)
Hypertension	9 (7.44)	41 (25.79)	50 (17.86)
Diabetes mellitus	13 (10.74)	25 (15.72)	38 (13.57)
Cirrhosis	0 (0)	4 (2.52)	4 (1.43)
CKD	9 (7.44)	9 (5.66)	18 (6.43)
COPD	3 (2.48)	2 (1.26)	5 (1.79)
Malignancy	3 (2.48)	0 (0)	3 (1.07)
PIRO score (on admission)			
Median (25th–75th percentile)	18 (16–19)	12 (11–15)	15 (12–18)
Range	11–28	2–20	2–28
PIRO score (on day 3)			
Median (25th–75th percentile)	20 (18–23)	11 (10–14)	15 (10–19)
Range	11–28	2–23	2–28
SOFA score (on admission)			
Median (25th–75th percentile)	12 (11–14)	8 (6–9)	9 (7–12)
Range	6–20	2–20	2–20
SOFA score (on day 3)			
Median (25th–75th percentile)	14 (12–15)	7 (6–9)	9 (6–13)
Range	7–19	2–16	2–19
APACHE IV score (on admission)			
Median (25th–75th percentile)	146 (128–166)	112 (96–126)	126 (107.5–146)
Range	90–212	48–178	48–212
APACHE IV score (on day 3)			
Median (25th–75th percentile)	158 (144–178)	102 (83–124)	124 (94–148)
Range	82–256	42–178	42–256
Outcome	121 (43.21)	159 (56.79)	280 (100)
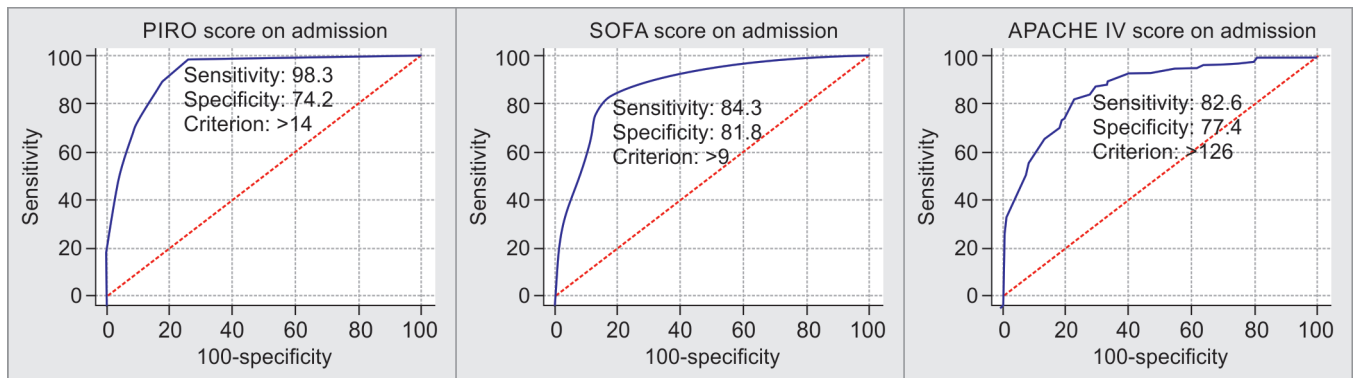
Fig. 1: Receiver operating characteristic curve of PIRO, SOFA, and APACHE IV score on admission for predicting mortality
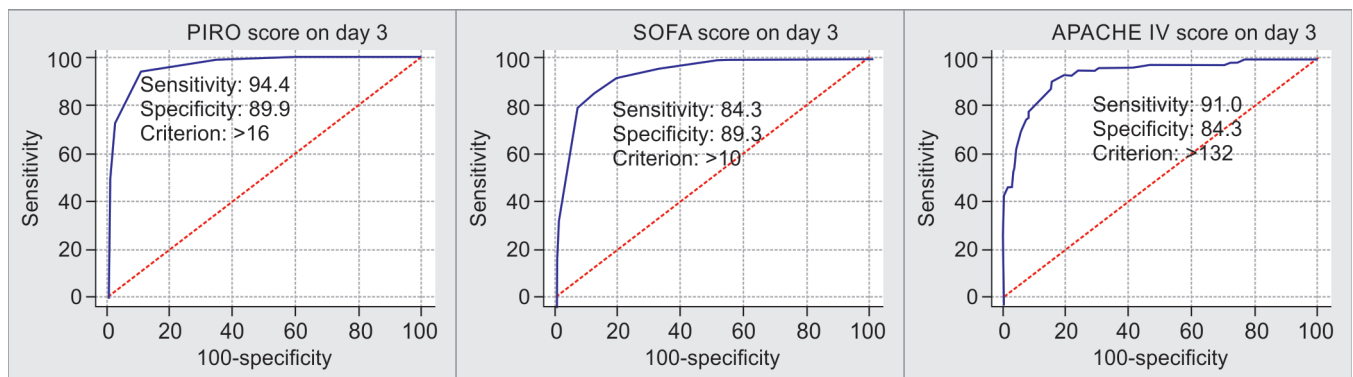

Fig. 2: Receiver operating characteristic curve of PIRO, SOFA, and APACHE IV score on day 3 for predicting mortality

Table 2: Multivariate logistic regression to find out independent significant risk factors of mortality

Mortality	Beta coefficient	Standard error	p-value	Odds ratio	Odds ratio lower bound (95%)	Odds ratio upper bound (95%)
PIRO score on admission	0.354	0.269	0.189	1.424	0.840	2.415
PIRO score at day 3	−0.056	0.210	0.790	0.946	0.627	1.426
SOFA score on admission	−0.189	0.392	0.631	0.828	0.384	1.786
SOFA score at day 3	0.463	0.376	0.218	1.589	0.760	3.320
APACHE IV score on admission	−0.061	0.036	0.089	0.941	0.878	1.009
APACHE IV score at day 3	0.060	0.035	0.088	1.062	0.991	1.138
Heart rate (per minute)	0.000	0.031	0.988	1.000	0.941	1.062
Respiratory rate (per minute)	0.185	0.096	0.055	1.203	0.996	1.453
Systolic blood pressure (mm Hg)	−0.039	0.014	0.006	0.962	0.935	0.989
Serum urea (mg/dL)	−0.008	0.008	0.333	0.992	0.976	1.008
Serum creatinine (mg/dL)	0.132	0.173	0.444	1.141	0.814	1.601
SGOT (U/L)	0.002	0.003	0.365	1.002	0.997	1.008
SGPT (U/L)	−0.003	0.004	0.453	0.997	0.989	1.005
Serum lactate (mmol/L)	0.514	0.233	0.027	1.672	1.060	2.638
Hypertension	−2.154	0.959	0.025	0.116	0.018	0.760

In a study by Macdonald et al.,[13] mortality rate of 20% was observed. When compared, PIRO scoring had sensitivity of 86%, while Mortality in Emergency Department Sepsis (MEDS) score 81% and SOFA 78%. The comparative evaluation of the scoring systems showed that PIRO was a better score than SOFA ($p = 0.01$) and similar to MEDS ($p = 0.064$).

In a study by Rathour et al.,[14] mortality rate was 58% in which only the PIRO scoring system was used. Higher values of the PIRO score were found to be associated with increased in-hospital mortality. The PIRO score was predictor of in-hospital mortality with sensitivity of 94%.

In a study by Badrinath et al.,[15] overall mortality was 55.9%. The calculated area under the receiver operating characteristic curve was 0.86 [95% confidence interval (CI): 0.80–0.90] for APACHE II, 0.80 (95% CI: 0.74–0.86) for SOFA, and 0.78 (95% CI: 0.71–0.84) for PIRO. Sensitivity and specificity for APACHE II were 81.5 and 75.3, respectively. The comparative evaluation of the scoring systems showed that PIRO was a better score than SOFA with an AUC curve of 0.78. But APACHE II score was found to be more sensitive and specific for predicting the severity of sepsis.

In a study by Vafaei et al.,[16] mortality rate of 33% was observed. The area under the ROC curve of PIRO, MEDS, and SOFA scores were 0.83 (95% CI = 0.78–0.89), 0.94 (95% CI = 0.91–0.97) and 0.87 (95% CI = 0.81–0.92). The comparative evaluation of the scoring systems showed that MEDS was a better score than PIRO.

Thus, PIRO score can be considered as one of the strong predictors of ICU mortality. Thus, from the available studies and from our study, it is clear that PIRO scoring system can be valuable in predicting mortality and has good discriminative power as compared to SOFA and APACHE scores. Routine use of PIRO scoring can be considered in sepsis patients as it is more comprehensive than SOFA scoring and simpler to calculate than APACHE IV score.

Strength and Limitations

The strength of our study is serial measurement of scores. Sepsis is a dynamic process so serial measurement of scores rather than single-point measurement gives a better insight into the outcome of patients with sepsis.

The main limitation of our study was that though we measured serum lactate levels and found a significant association with mortality, we did not compare lactate levels with different scores for mortality prediction. This would have provided further insight in understanding the role of different parameters in predicting ICU mortality with sepsis. The second limitation was the small sample size.

Conclusion

Predisposition, insult, response, and organ dysfunction score can be considered as one of the strong predictors of ICU mortality. It should be routinely used and assessed in the risk stratification of patients with sepsis. Predisposition, insult, response, and organ dysfunction scores help to assess the individual patient's pathophysiology of sepsis, aid in better prognostication, and sequential scoring may throw light upon response to interventions. Further studies are required with a large sample size to generalize the results in ICU setup.

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