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Original Research Article

Study of spectrum of sepsis and prediction of its outcome in patients admitted to ICU using different scoring systems

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ABSTRACT

Background: Although sepsis is one of the leading causes of mortality in hospitalized patients, information regarding early predictive factors for mortality and morbidity is limited. The aim was to identify reliable and early prognostic variables predicting mortality in patients admitted to ICU with sepsis.
Methods: Patients fulfilling the Surviving Sepsis Campaign 2012 guidelines criteria for sepsis within the ICU were included over two years. Apart from baseline haematological, biochemical and metabolic parameters, APACHE II, SAPS II and SOFA scores were calculated on day 1 of admission. Patients were followed till death or discharge from the ICU. Chi-square test, student t-test, receiver operating curve analyses were done.
Results: 100 patients were enrolled during the study period. The overall mortality was 35% (68.6% in males and 31.4% in females). Mortality was 88.6% and 11.4% in patients with septic shock and severe sepsis and none in the sepsis group, respectively. On multivariate analysis, significant predictors of mortality were APACHE II score greater than 27, SAPS II score greater than 43 and SOFA score greater than 11 on day the of admission. On ROC analysis APACHE II had the highest sensitivity (92.3%) and SAPS II had the highest specificity (82.9%).
Conclusions: All three scores performed well in predicting the mortality. Overall, APACHE II had highest sensitivity, hence was the best predictor of mortality in critically ill patients. SAPS II had the highest specificity, hence it predicted improvement better than death. SOFA had intermediate sensitivity and specificity.

Keywords: APACHE II, SAPS II, Sepsis, Sepsis scoring systems, SOFA

INTRODUCTION

Sepsis is one of the leading causes of in-hospital mortality and morbidity among medical and surgical patients. Spectrum of sepsis includes sepsis, severe sepsis and septic shock. Severe sepsis accounts for one in five admissions to ICUs and is the leading cause of death in the non-coronary ICU.[1] In spite of this information regarding early predictive factors is limited.

Data from western countries puts the overall incidence of sepsis ranging from 10% to 30% with mortality ranging from 10% to 56%.[2,3] Data from India suggest that the overall mortality of all sepsis patients is approximately 14% and that of severe sepsis alone is higher than 50%.[4] The early identification of sepsis and implementation of early evidence-based therapies have been documented to improve outcomes and decrease sepsis-related mortality.[5] Reducing the time to diagnosis of severe sepsis is thought to be a critical component of reducing mortality from sepsis-related multiple organ dysfunction.[6] Lack of early recognition is a major obstacle to sepsis bundle initiation. Sepsis screening tools have been developed to monitor ICU patients and their implementation has been associated with decreased sepsis-related mortality.[5,7]

This study is intended to determine the spectrum of sepsis and to identify early and reliable prognostic variables for

sepsis and compare the usefulness of three scores namely APACHE II (Acute Physiology and Chronic Health Evaluation), SAPS II (Simplified Acute Physiology Score), SOFA (Sequential Organ Failure Assessment) scoring system in the setting of sepsis in this hospital.

METHODS

The study was conducted in patients admitted to intensive care unit of a tertiary care hospital attached to a government medical college. This was a prospective study conducted between October 2015 to September 2017 with 100 patients who gave consent for study and satisfying the inclusion criteria in the ICU of a tertiary care referral hospital. All the patients admitted in ICU either with existing sepsis or those who developed new episode of sepsis/severe sepsis/septic shock within the ICU were enrolled. Excluded were those who died within 24h of admission and those who did not satisfy the sepsis criteria according to "Sepsis Surveillance Campaign" 2012 guidelines.

After obtaining informed consent, detailed demographic, clinical and laboratory data were recorded including arterial blood gas analysis and relevant cultures of blood, urine, sputum, tracheal aspirates or other samples as indicated. APACHE II, SAPS II and SOFA indices were calculated at baseline to assess the severity of illness. The total duration of ICU stays, mechanical ventilation and hospital stay were recorded. All patients recruited in the study were monitored until death or discharge, whichever occurs earlier and were compared with scoring systems result and appropriate statistical analysis.

Mean (standard deviation) or median (min-max) were calculated for continuous variables and frequency (%) for categorical variables. To compare the continuous and categorical variables with the primary outcome, that is, death/survival, paired t-test and Chi-square test were used, respectively. Univariate and stepwise multivariate logistic regression analysis was done to see the predictors of ICU death and duration of mechanical ventilation, respectively. The results for each parameter (numbers and percentages) for discrete data and averaged (mean+ standard deviation) for each parameter were presented in tables and figures. Proportions were compared using Chi-square test of significance. To compare the scoring systems results AUC-area under the curves were using ROC (Receiver Operating Characteristic) curves were used. Sensitivity and specificity for each of scores were calculated using the curves and results of each were compared.

RESULTS

A total of 100 patients were included in the study, out of 100 patients 65% (65 patients) improved and were discharged from the ICU and 35% (35 patients) expired during the ICU stay. Mean age among the survivors was 48.95±14.30years with youngest being 18years and eldest being 71years, mean age among non-survivors was 43.74±17.50years with youngest being 18years and eldest being 85years as illustrated in Table 1.

Table 1: Demographic and clinical data.

Study parameter	Number
Outcome	
Survivors	65
Non-survivors	35
Age	
Survivors	48.95±14.30 years
Non-survivors	43.74±17.50 years
Gender	
Male	67
Female	33
Organ failure (total)	32
Survivors	17
Non-survivors	15
Use of inotropes (total)	45
Survivors	12
Non-survivors	33
Ventilation support (NIV/Ventilator)	
Survivors	26
Non-survivors	27
Culture results	
Positive	49
Negative	51
Septic shock	
Survivors	10
Non-survivors	31

Out of 100 patients in this study 32 patients had various pre-existing organ failure. They constituted 26.2% (17 patients) of survivors and 42.9% (15 patients) of non-survivors. Statistical analysis for the presence of pre-existing organ dysfunction was not significant with p-value of 0.088, hence did not have any effect on outcome. In present study of 100 patients, 53% (53 patients) required ventilator support either in the form of invasive mechanical ventilation or non-invasive ventilation. They constituted, 40% (26 patients) of survivors and 77.1% (27 patients) of non-survivors as depicted in Table 1. Statistical analysis showed very significant p-value of <0.001.

Out of 100 sepsis cases, culture positive was 49% (49 patients) and rest 51% (51 patients) were culture negative. Culture positive patients constituted 56.9% (37 patients) of survivors and 34.3% (12 patients) of non-survivors. Culture negative patients constituted 43.1% (28 patients) of survivors and 65.7% (23 patients) of non-survivors. Statistical analysis was significant with a P-value of 0.031 suggesting that culture positive patients had better outcome. Among the 49 culture positive cases, 17 cases were positive for *Klebsiella*, followed by 12 cases for *E. Coli*. *Pseudomonas* and *Streptococcus* were positive for 4 patients each followed by *Proteus* and

Staphylococcus organisms which were positive in 3 patients each. 2 patients were positive were MRSA strain, so total of 5 patients were positive for staphylococcus species. 2 patients were positive for gram negative non-fermenters and one each were positive for *Enterococcus* and *Acinetobacter*. In present study, mean duration of hospital stay for 65 patients who survived was 147.562±71.9hours with least duration of stay being 26.5 hours and longest being 432hours. Mean duration of stay for the 35 patients who expired was 90.5±113.5hours with minimum duration of stay being 30hrs and maximum being 700hours.

All the three scores had significant statistical correlation in relation to the outcome of the patients as tabulated below in Table 2.

Table 2: Comparison of three scoring systems in relation to outcome.

Scores	Outcome	N	Mean	SD	Min.	Max.	P value
Apache II	Discharge	65	18.82	6.314	5	31	<0.001
	Death	35	27.66	5.688	15	37	
SAPS II	Discharge	65	37.45	12.035	10	65	<0.001
	Death	35	53.66	12.357	23	91	
SOFA score	Discharge	65	7.94	3.618	1	16	<0.001
	Death	35	12.91	3.346	5	19	

To compare and find out the better score among the three, ROC-Receiver Operating Characteristic curves were used. On ROC analysis, sensitivity and specificity of each score was calculated based on the cut-off values for each score.

Cut-off values were selected based on multivariate analysis of predictors of mortality, with odds ratio greater than 2. Based on this criterion, the cut-off scores for APACHE II was 27 and SAPS II was 43 and SOFA was 11.

Area under the curves for each of the scores were calculated and specificity and sensitivity for each of the scores were analysed. AUC values and sensitivity specificity for each of the scores have been represented in Table 3.

Table 3: Analysis of ROC.

Scores	AUC	Cut off value	Sensitivity	Specificity
Apache II	0.843	≤27	92.3	62.9
SAPS II	0.831	≤43	75.4	82.9
SOFA score	0.838	≤11	86.2	74.3

A rough guide for classifying the accuracy (AUC) is as follows:

- 0.90-1.00 =Excellent (A),
- 0.80-0.90=Good (B),
- 0.70-0.80=Fair (C),
- 0.60-0.70=Poor (D),
- 0.50-0.60=Fail (F).

Accordingly, APACHE II had the highest sensitivity-92.3% and specificity-62.9% (as depicted in Figure 1), i.e., it predicted the true positives (mortality) more accurately than other scoring systems, meaning APACHE II predicted death better than other scoring systems. SAPS II had sensitivity of 75.4% and specificity of 82.9% (as depicted in Figure 2). SAPS II had the highest specificity, meaning it had predicted the true negatives (those patients who improved) more precisely, hence SAPS II predicted patients who improved better than those who died.

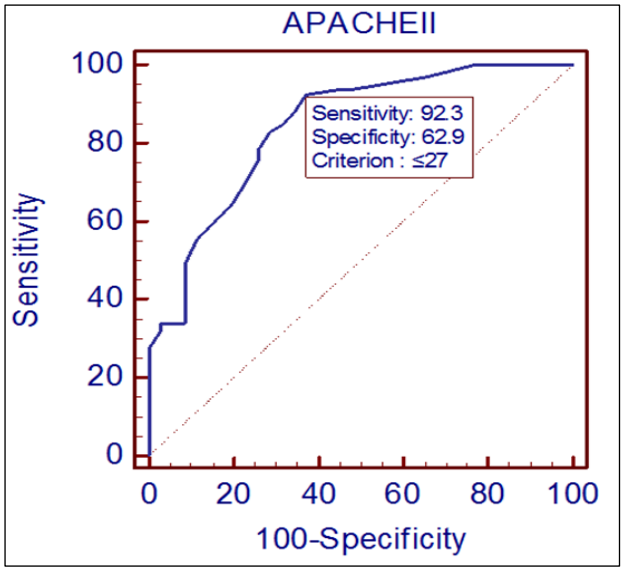

Figure 1: ROC curve for APACHE II.

Meanwhile SOFA had sensitivity of 86.2% and specificity of 74.3% (as depicted in Figure 3).

Hence, it had sensitivity more than SAPS II but less than APACHE II and specificity more than APACHE II and but less than SAPS II. Hence, author could conclude that SOFA predicted death and improvement equally well, when compared to SAPS II and APACHE II.

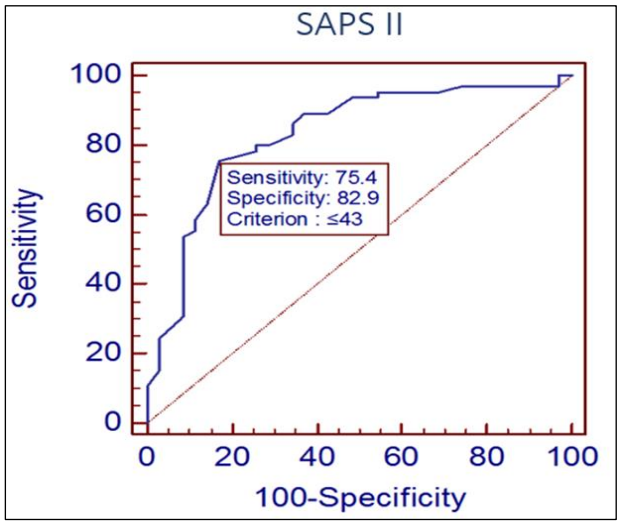

Figure 2: ROC curve for SAPS II.

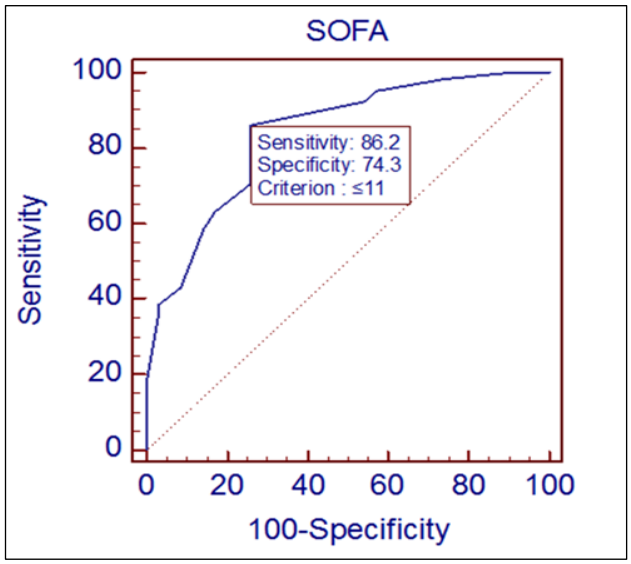

Figure 3: ROC curve for SOFA score.

DISCUSSION

Among the 100 patients, 65% improved during the hospital stay and were discharged from ICU whereas 35% expired during the ICU stay. Where as in a study by Khan MS et al, 60% of patients survived and mortality was 40%.[8] Study by Alejandria MM et al, had 66.3% survivors and 23.5% non-survivors.[2] In a similar study done by Mohan A et al, 47% of patients survived and 53% of patients expired.[9]

Out of 100 patients, 49 patients had positive culture reports and rest 51 were culture negative. Culture positive patients constituted 56.9% of survivors and 34.3% of non-survivors. Culture negative patients constituted 43.1% of survivors and 65.7% of non-survivors. P-value was significant with value of 0.031. Hence, author concluded that culture negative patients had worse prognosis. This could be because culture positive patients received targeted anti-microbial therapy which might have improved their survival. In the study by Alejandria et al, 34.6% were culture negative.[2] They constituted 38.2% of survivors and 27.3% of non- survivors. This is discordant with present study.

Among the 100 patients, 34 patients had sepsis, 21 patients had severe sepsis and 41 patients had septic shock. Out of the survivors, 52.3% had Sepsis, 32.3% had severe sepsis and 15.4% had septic shock. Out of the non-survivors, 11.4% had severe sepsis and 88.6% had septic shock. Hence, author concluded that septic shock had worse outcome which was statistically significant with P-value of <0.001.

In this study, mean APACHE II score in survivors was 18.82±6.31 and in non-survivors was 27.66±5.68, mean SAPS II score in survivors was 37.45±12.00 and in non-survivors was 53.66±12.3, mean SOFA score in survivors was 7.94±3.6 and in non-survivors was 12.9±3.34. P-value was significant for all the three scores <0.001.

Author observed that the mortality rate in this study was 35% which is lesser than Khan MS et al, and Mohan A et al, which are done in India, whereas it's higher than Alejandria et al, which was done in Philippines. Average mortality reported in previous studies in India is 40.3%.[2,8-10] A study by Bota PD et al, showed APACHE II to have better discriminative power than SOFA score and MODS, which is in accordance with this study for predicting the mortality.[11]

Study done by Badrinath K et al, showed that APACHE II score found to be more useful for stratifying sepsis patient as it considers laboratory parameters, chronic comorbidities and surgical status of the patient. The illness severity and predicted mortality among sepsis patients by APACHE II score were very close to observed mortality.[12]

According to this study, for prediction of death, the most reliable prognostic score is APACHE II scoring system since it had the highest sensitivity and SAPS II scoring system predicted well, those of who improved, since it had the highest specificity.

SOFA was equally good in both predicting mortality as well as those who improved. On ROC analysis, in the study done by Khan MS et al, highest sensitivity was for APACHE II (94.1%) scoring system which is concordant with this study but the highest specificity was for SOFA scoring (82.4%) which differs from this study in which SAPS II had the highest specificity.[8] According to analysis done by Mohan A et al, on comparison between

SAPS II and SOFA, sensitivity i.e. ability to correctly predict mortality, was higher for SAPS II (81.1%) and specificity i.e. ability to predict improvement was higher in SOFA (72.3%) scoring system.[9]

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