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Original Research Article

Utility of Sofa and Sofa in Predicting Outcomes in Patients Presenting with Sepsis with Acute Febrile Illness in a Tertiary Care Hospital in Rural Rajasthan

Maninder Patni[1], Tasha Purohit[2], Vijay Kumar[3], Nilesh Kumar Patira[4]

[1]MD, Anaesthesia. Associate Professor, Pacific Medical College and Hospital, Bhilon Ka Bedla, Udaipur, Rajasthan. 313001)

[2]MD, Anaesthesia. Associate Professor, Pacific Medical College and Hospital, Bhilon Ka Bedla, Udaipur, Rajasthan, 313001)

[3]MD, Anaesthesia, Associate Professor, Pacific Medical College and Hospital, Bhilon Ka Bedla,Udaipur,Rajasthan, 313001)

[4]MD, General Medicine, Associate Professor, Pacific Medical College and Hospital, Bhilon Ka Bedla, Udaipur, Rajasthan,313001)

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Corresponding author: Nilesh Kumar Patira

Conflict of interest: Nil

Abstract

Introduction: SOFA SCORE has been used to predict outcomes in patients with sepsis. The present study aims to assess utility of SOFA in predicting outcomes in septic patients at a tertiary care hospital in rural Rajasthan. Literature available on assessing the utility of SOFA SCORE in predicting outcomes in septic patients from rural background is very scanty. The study intends to assess the utility of SOFA SCORE in predicting outcomes in patients in an ICU in a tertiary care hospital in rural Rajasthan.

Aim: The objective was to determine the utility of Sequential Organ Failure Assessment (SOFA) score to predict outcome of patients in Intensive Care Unit (ICU) of a tertiary care hospital in rural Rajasthan.

Material and Methods: This was an observational prospective study performed in an ICU of a medical college in rural Rajasthan from August 01,2021 till November 30, 2021. 79 patients admitted in MICU with diagnosis of sepsis were studied and their SOFA score was calculated on day of admission and 72 hours after admission. Change in SOFA score (Δ SOFA) at 72 hours was also calculated. Data was analysed using Chi-square test and an independent t- test. To assess the performance of SOFA and Δ SOFA sensitivity and specificity was calculated.

Result: A total of 79 patients were included with mean age of 46.3 out of which 58 were men and remaining were women. Mean SOFA score at admission amongst survivors was 7.49± 4.16 and amongst non survivors was 11.90±4.134. Mean SOFA score at 72 hours among survivors was 4.60±4.089 and among non survivors was 9.33±5.972. The difference in SOFA score at admission and at 72 hours between survivors and non survivors was significant ($p < 0.05$). Area under the curve for SOFA on day 1 and day 3 predicting mortality in sepsis was 0.744 and 0.743. Area under ROC curve for Δ SOFA was 0.651.

Conclusion: Sofa score at time of admission, after 72 hours of admission have at best only moderate accuracy in predicting outcomes in patients with sepsis in a rural population where majority of infections are vector borne.

Keywords: Sepsis, Intensive Care Unit, Sequential Organ Failure Assessment Score, Rural

Introduction

Although common and associated with high morbidity and mortality, sepsis and related terms remain difficult to define. [1,2] Though two international consensus conferences (1991,2001) used expert opinions to generate current opinions, [3,4] advances in the understanding of the pathobiology and an appreciation that elements of the definition may be outdated, inaccurate and confusing prompted the ESICM and SCCM to convene a 3rd international consensus task force to re-examine the definitions. The task force recommended elimination of terms Sepsis syndrome, septicaemia and severe sepsis and instead defined Sepsis as "life threatening organ dysfunction due to dysregulated host response to infection. [5]

The task force recommended that sepsis could be defined as life threatening organ dysfunction caused by dysregulated host response to infection. The taskforce also recommended that for clinical operationalization, organ dysfunction could be represented by an increase in SOFA SCORE of two points or more (which is associated with an in-hospital mortality greater than 10%). SOFA score is a simple and objective score that allows for calculation of both the number and severity of organ dysfunction in six organ systems (respiratory, coagulation, hepatic, CVS, renal, neurological) and the score can be measured in divided/ aggregate organ dysfunction. [6]

Many other investigators have identified a link between the number of dysfunctional organs and both short term and long term mortality among Emergency Department patients with infection. [7] We could not come across many studies which assessed the utility of SOFA scoring in predicting outcomes in sepsis in a primarily rural/tribal population affected by vector borne infections. Race and ethnicity have been described to be associated with the outcome of sepsis, hence we decided to study the utility of SOFA scoring in this population. [8,9,10] A study done by national vital statistics system on sepsis related mortality among adults aged 65 years and over in USA 2019 found that sepsis related death rates among adults aged 65 years and over were higher among non-hispanic black adults than among other race and Hispanic origin groups. This study also found that sepsis related death among adults aged 65 years and over were higher in rural areas compared to urban areas. [9]

A study done at a remote north Australian emergency department concluded that remote indigenous patients have worse clinical sepsis scores. [10] Although the epidemiology and outcomes of sepsis in high income countries have widely been reported [3,4], there is very limited data available from the rural India. In high income countries, where the largest part of the current scientific evidence on sepsis care originates from, the predominant cause of sepsis is bacterial. [3,4]

Many lower –middle- income countries like India, are geographically located in tropical regions where pathogens other than bacteria commonly cause infectious diseases. [7] International guidelines including the ones prescribed by ESICM and SCCM which redefined sepsis and suggested using SOFA score to define organ dysfunction have been formulated with strong focus on sepsis by bacterial infections. [6] We could find only one study from rural India which assessed the utility of SOFA score in predicting outcomes in sepsis in rural India. [11] Hence we decided to study the utility of SOFA score in this population.

Material and Methods

The study was a prospective observational study performed between August and November 2021 at a private tertiary care teaching hospital in rural Udaipur, Rajasthan. It was carried out in 15 bedded Medical ICU. The study has been approved by the hospital ethics committee.

(IEC/186A/2021). Included patients were ≥ 18 years of age who were admitted to the Medical ICU whose evaluation showed any symptom consistent with an infection including fever, cough, burning micturition, sputum production, difficulty in breathing, altered sensorium.

Exclusion criteria:

- Age <18 years
- Patient with chronic kidney disease ,chronic heart failure, stroke, chronic liver disease, chronic respiratory failure, malignancies
- Surgical patients

An aggregate total maximum SOFA score (range 0-24) was derived from the maximum SOFA score for each individual. The data was first entered into a Microsoft excel spread sheet and was then exported into a statistical software for analysis. SOFA scores on day of admission, at 72 hours of admission and the change in SOFA score at 72 hours was compared between the survivors and non survivors. The predicting discriminatory abilities of the SOFA scores for identifying survivors were done using tests of diagnostic accuracy including specificity, sensitivity and area under Receiver Operator Characteristic (ROC) curve.

Patients who died or were transferred out of the MICU in less than 24 hours were not included in the study. For patients who stayed for more than 24 hours but less than 72 hours only, the SOFA score on the day of admission was calculated.

"Surviving sepsis campaign: International guidelines for management of Sepsis and Shock: 2016 "were followed for the management of patients presenting with sepsis.

Regular biochemical tests including serum electrolytes, kidney function tests, liver function tests, complete blood counts were done. Other tests such as coagulation profile, serum albumin was done wherever indicated. Endotracheal tube secretions, blood and urine were sent for culture and sensitivity in patients wherever indicated. Cases presenting with acute encephalitis syndrome underwent neuroimaging (CT/ MRI) followed by CSF analysis. Patients presenting with respiratory complaints underwent chest X rays/ CT scans whenever indicated. Arterial blood gas analysis was done whenever required. A rapid diagnostic card test for malaria and dengue was carried out in patients who were suspected to be suffering from these infections.

IgM antibody testing against *O.tsutsugamushi* by ELISA was also carried out whenever indicated. Out of a total of 150 admissions in the MICU during the study period 79 fulfilled the inclusion criteria. SOFA SCORE of all 79 patients were calculated on the day of admission and after 72 hours of admission. The patients were followed till their discharge from the hospital or till their death in ICU. We studied outcomes of ICU stay and had two groups depending upon the outcome: survivors and non survivors.

Outcome of ICU stay was studied and thus two groups were created: survivors and non Survivors. SOFA score on day of admission and 72 hours after admission was calculated. Change in SOFA score at 72 hours (ΔSOFA) was also calculated. A maximum SOFA score was determined (range from 0-4, 4 being the worst score) for each of the six organ systems: respiratory, hepatic, cardiovascular, coagulation, neurologic and renal.

Statistical Analysis

The data were first entered in to Microsoft excel spread sheet and was then exported to epi info version 7.2. SOFA scores of survivors and non survivors were compared by Chi-square test. The predictive and discriminatory abilities of the SOFA scores for identifying survivors were ascertained using tests of diagnostic effectiveness, including sensitivity, specificity and area under Receiver Operator Curve (ROC). Statistical significance was defined at p value < 0.05.

Results

In our study we classified sepsis on the basis of etiology into malaria, dengue, scrub typhus, gram positive sepsis, gram negative sepsis. Majority of the cases (>50%) were vector borne

diseases such as malaria *(plasmodium vivax, plasmodium falciparum), dengue (aedes aegypti),* scrub typhus *(orientia tsutsugamushi).* A total of 79 patients were included in the analysis. We found no significant association between age and survival status and between gender and survival status. The mean age of the patients among survivors was 48.26±19.23 years and non survivors was 41±15.84. The mortality rate in our study was 26.5%. The cause of sepsis could not be ascertained in 21.50 % patients. Mean SOFA SCORE on day 1 amongst survivors was 7.09 ± 4.16 and amongst non survivors was 11.90 ± 4.13 and the difference was significant (p≤ 0.001). Mean SOFA SCORE on Day 3 among survivors was 4.60 ± 4.08 and among non survivors was 9.33 ± 5.972 and this difference was statistically significant too (p=0.001). The change in SOFA SCORE (Δ SOFA) was also significantly more amongst non survivors (p = 0.022).

Discrimination for SOFA on day 1 and day 3 were acceptable with area under ROC curve of 0.744 and 0.743. Discrimination for ΔSOFA is poor with area under ROC curve of 0.651.The gold standard was taken as survival status at ICU discharge. Based on this SOFA on day 1 is sensitive and on day 3 is specific. Delta SOFA was neither sensitive nor specific.

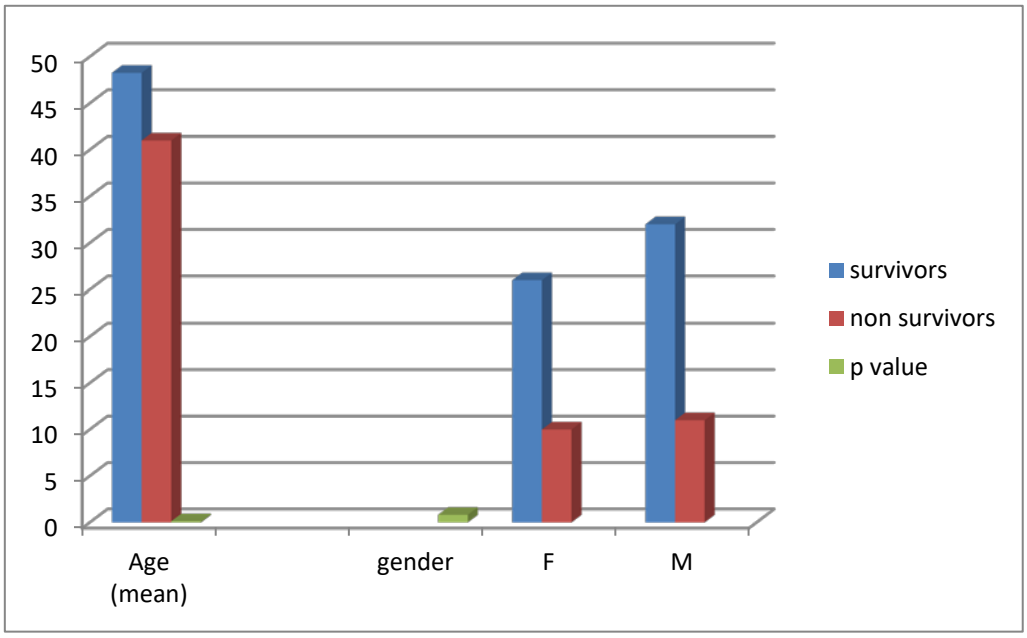

Figure 1: Showing demographic data among survivors and non survivors

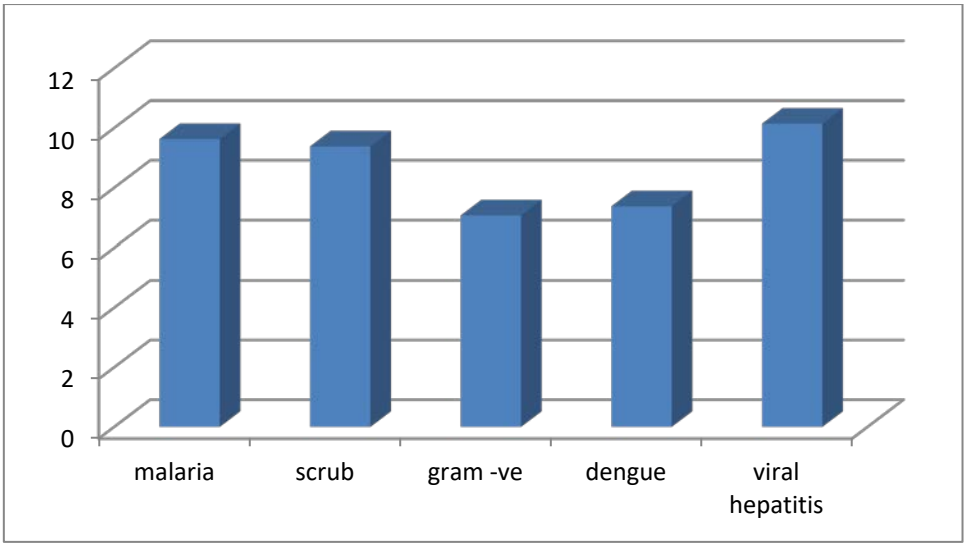

Figure 2: Showing Mean SOFA score of different etiology of sepsis

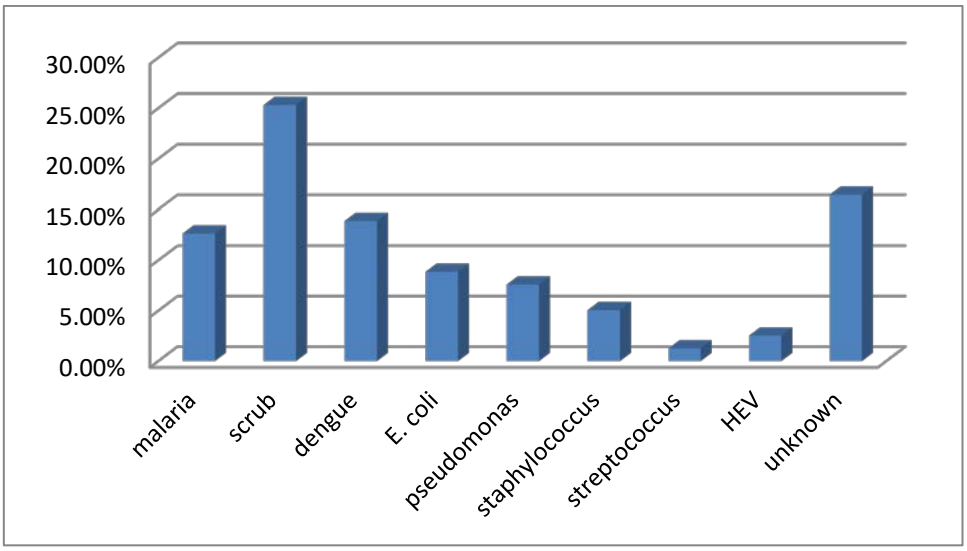

Figure 3: Showing percentage of different etiologies of sepsis

Table 1: Showing Interpretation of SOFA score on Day 1 and 3

	Outcome of ICU stay	N	Mean	Standard Deviation	Standard Error Mean	P value
SOFA 1	Survivors	58	7.09	4.160	0.546	0.001
	Non survivors	21	11.90	4.134	0.902	
SOFA 3	Survivors	52	4.60	4.089	0.567	0.001
	Non survivors	15	9.33	5.972	1.542	

Table 2: Showing sensitivity, specificity and area under receiver operator characteristic curve of sofa score on day 1, day 3 and Δ SOFA to predict mortality in patients with sepsis

	Area under ROC	P value	Cut-off value	Sensitivity	Specificity	Positive Predictive value	Negative predictive value	LR +	LR-
SOFA Day 1	0.744	0.003	7.5	90.5%	60.3%	45.2%	94.6%	2.27	0.16
SOFA Day 3	0.743	0.004	6.5	68.8%	78.4%	50.0%	88.9%	3.19	0.40
Delta SOFA	0.651	0.070	2.5	75.0%	64.7%	40.0%	89.2%	2.12	0.39

Discussion

SOFA score on day 1 and at 72 hours in our study was found to be moderately accurate at best in predicting mortality in patients with sepsis. The adaptation of ICU based scoring systems (e.g. APACHE III) to application in the Emergency department has been studied in previous investigations. [12,13] These studies found the predictive abilities of these scoring systems to be modest at best and these scores are complex and require special software and hence their utility in real time in an emergency department is difficult. SOFA is more practical for use in the emergency department as it includes only vital signs and laboratory data that are routinely available and does not require a definitive final diagnosis of the acute process.

The area under the ROC curve for SOFA score on admission in our study is 0.744 which suggests that SOFA score has a low to moderate accuracy in predicting mortality. Jean Louis Vincent performed a prospective, observational study at a 31 bedded medicosurgical ICU at a university hospital in Belgium to determine the usefulness of repeated measurement of SOFA score for prediction of mortality in the ICU patients. [14] They concluded that initial, highest, and mean SOFA scores correlated well with mortality. They found mean and highest SOFA score to have strongest correlation with mortality followed by Δ SOFA and initial SOFA scores. The area under ROC for initial SOFA score in their study was 0.79 which is higher than our study. Area under ROC at 48 hours in their study was 0.84 which

is much higher than area under ROC at 72 hours in our study (0.743). Unlike us they did not calculate the SOFA score at 72 hours. The area under ROC for change in SOFA score at 48 hours in their study was 0.78 which is much higher than the area under ROC for Δ SOFA at 72 hours in our study. The highest SOFA score in their study had the highest area under ROC (0.90).

April et al in 2017 found the area under the ROC curve for SOFA at admission is 0.70 which is similar to our findings. [15]

Seymour et al in 2016 found that area under the ROC curve for SOFA on day 1 is 0.74 in ICU patients which is similar to our study. [16] Giamarellos et al in 2017 concluded that SOFA score could be used to validate unfavourable outcome. [17]

Raith et al in 2017 did a retrospective cohort analysis of 1,84,875 adults and found the SOFA

score had an area under the ROC curve of 0.753 which is similar to our study and showed that SOFA score had greater discrimination for in-hospital mortality than SIRS criteria or qSOFA. [18] Donelly et al in 2017 did a retrospective analysis using data from 30239 participants and supported the use of SOFA scoring in identifying patients with infection who are at elevated risk of poor outcome. [19] The AUC for SOFA score in their study was 0.77 which is slightly higher than our study. This study was carried out in non ICU patients unlike our study.

Cheng et al in 2017 performed a retrospective multicenter study in six ICUs in China and found that the AUROC for SOFA score was 0.69 which was lower than our findings. [20]

This study is one of the few large studies done to assess the applicability of SOFA score in predicting mortality in sepsis in Asian population. S.Gaini et al in a retrospective study in 2018 found that the AUROC of SOFA score in predicting mortality was 0.83 which is higher than our study. The main difference of this study from our study is that it was carried out in non ICU patients. [21] Ritesh Lal et al in 2017 performed a study and found that the AUROC of SOFA score for predicting survival to be 0.911 which suggests that discriminatory power of SOFA score in predicting mortality is very high. [22]

Alan E et al in 2005 did a prospective observational study to examine the utility of SOFA score for assessing outcome of patients with severe evidence of hypoperfusion. The area under ROC of SOFA at admission predicting mortality at admission was 0.75 which is similar to our study but the area under ROC of SOFA at 72 hours was 0.84 which is much higher than what we found in our study. [23]

Prasanth et al in their study concluded that among the three critical illness severity scores which were QUICK SOFA, APACHE & SOFA; the SOFA score correlated with in hospital mortality and duration. Their study was though limited only to patients with Scrub typhus unlike ours where we studied patients with sepsis irrespective of etiology. [24]

All the severity scoring systems have been developed using large cohorts of critically ill patients admitted to American and European ICUs. Validation is essential before routine application of any predicting model in a group of patients different from the one originally used for model development. [25]

Our study is probably the only study which has assessed the utility of SOFA scores in predicting outcome in a tertiary care hospital in rural India where majority of infections are parasitic infections.

There are limitations in our study. First, the sample size was small. Our observations need to be confirmed in larger prospective studies. Ours is a single center study and more such studies need to

be carried out at multiple centres to reach a definite conclusion.

Conclusion

SOFA score at admission is significantly higher amongst non survivors than survivors. Most of the literature on assessing the predictive ability of SOFA score has come from western ICUs. SOFA score has been found to be highly accurate (AUROC ∞ 0.911) to be very less accurate (AUROC 0.69) in the existing medical literature, though most studies have found it to have moderate accuracy (AUROC ∞ 0.74- 0.81). Our study also concluded that the SOFA score is at best moderately accurate in predicting outcomes. Unlike most studies delta SOFA at 72 hours has very low accuracy in predicting outcomes. More efforts are needed to devise scoring systems with higher accuracy and also to test the accuracy of SOFA scoring in rural Indian population affected by parasitic infections.

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