Original Article

DOI: 10.7860/JCDR/2024/68367.19331

Comparison of qSOFA, MEDS, and APACHE II Scores in Early Identification of Sepsis for Patients with 28 Days Mortality and ICU Admission: A Cross-sectional Study

Internal Medicine Section

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ABSTRACT

Introduction: Sepsis is a life-threatening infection that results in organ dysfunction due to an increased pathogen load, necessitating urgent intervention. There is a gap in clinicians' ability to identify septic patients at high-risk with poor outcomes, highlighting the need for validated predictive scores for early intervention, favourable outcomes, and prompt recovery.

Aim: To validate the predictive capacity of the Sequential Organ Failure Assessment (qSOFA), Mortality in Emergency Department Sepsis (MEDS), and Acute Physiology and Chronic Health Evaluation (APACHE 2) scores in patients with 28-day mortality and in Intensive Care Unit (ICU) patients due to sepsis.

Materials and Methods: This cross-sectional study was conducted on 150 septic patients at the Department of Emergency Medicine, Sri Ramachandra Institute of Higher Education and Research in Chennai, India, between June and December 2022. Parameters assessed included Respiratory Rate (RR), Systolic Blood Pressure (SBP), Mean Arterial Pressure (MAP), temperature, White Blood Cell (WBC) count, platelet count, bilirubin, and creatinine. Descriptive analysis of age, gender, source, RR, GCS, SBP, qSOFA, MEDS, APACHE 2 in 28-day mortality, and ICU patients. Positive correlation and good predictivity of predictive scores (qSOFA, MEDS, APACHE 2) were analysed using Spearman's Rank Correlation Coefficient (SRCCRs) statistical test in 28-day mortality and ICU patients.

Results: A total of 150 septic patients (male: female-93:57) with an average age of 57.07±14.4 years were included. Urosepsis was the most common (n=51), followed by respiratory sepsis (n=48). Of these, 96 patients were admitted to the ICU, and 54 patients experienced 28-day mortality. The average and median values of RR were 27.1±7.64 breaths/minute (b/m) and 26 b/m, respectively. SBP values were 106.13±30.47 mmHg and 110 mmHg, respectively. Diastolic Blood Pressure (DBP) values were 66±16.51 mmHg and 60 mmHg, respectively. The average and median values of GCS were 12.75±3.92 and 15, respectively. The average for qSOFA was 29.1±0.025, with a median of 28; for MEDS, the average was 7.99±5.89, with a median of 7; and for APACHE 2, the average was 16.74±9.64, with a median of 15. Spearman's Rank Correlation Coefficient (SRCCRs) demonstrated a strong positive correlation and good predictive validity between qSOFA, MEDS, and APACHE 2 scores in 28-day mortality and ICU patients (<0.001). Receiver Operating Characteristic Curve (ROC) analysis indicated good predictive validity for qSOFA in 28-day mortality and ICU patients.

Conclusion: qSOFA exhibited a positive correlation and good predictive validity compared to MEDS and APACHE 2 in both 28-day mortality and ICU patients (<0.001). This study highlights the utility and applicability of qSOFA at the bedside for initial triage, as it can be quickly employed with minimal information.

Keywords: APACHE 2, MEDS, Predictive scores, qSOFA

INTRODUCTION

Sepsis is a potentially fatal disease that affects all organs of the body, caused by dysregulated host response or immunity to infection. Sepsis is a life-threatening and high-economic spending disease associated with organ dysfunction and requires immediate diagnosis of the source of sepsis [1]. Thus, predictive scores such as qSOFA, MEDS, and APACHE 2 supports the diagnosis of poor outcomes and high-risk.

According to the 2016 Third International Consensus Definition of Sepsis, septic shock is fatal organ dysfunction due to infection. Predictive scores such as the qSOFA score assess the level of organ dysfunction and identify those at high-risk of poor outcomes [2]. Sepsis causes six million deaths globally each year, surpassing tuberculosis (1.29 million deaths) and Human Immunodeficiency Virus (HIV) (1.3 million deaths), making it a significant global burden [3]. Sepsis is responsible for 20% of deaths worldwide, particularly in Low- and Middle-Income Countries (LMICs) [4]. Male elderly patients with lower extremity burns, scalds, total burns, delayed treatment, and co-morbidities such as diabetes are at high-risk [5]. Regarding the source of sepsis, patients with Urinary Tract Infection (UTI) and ureteroscopy are at higher risk, with post-operative urosepsis occurring in 5.0% of cases [6]. In recent times (during Coronavirus Disease-2019 (COVID-19), untreated respiratory tract infections have led to sepsis [7]. Abdominal sepsis is also a common source of infection resulting in high morbidity and mortality [8].

Cellulitis or skin sepsis can lead to bacteraemia and eventually trigger sepsis, accounting for 2 to 21.3% of cases [9]. Sepsis encephalopathy and septic encephalitis are common sources of neurosepsis [10]. Patients with Human Immunodeficiency Virus (HIV) also have a high-risk of developing sepsis [11]. Although several clinical investigations are conducted to stratify septic patients, confirmatory investigations take a longer duration, necessitating specific tools like predictive scores for early sepsis diagnosis. Among the predictive scoring systems, the MEDS score is widely used [12]. The qSOFA score often "rules out" sepsis in many wards and emergency departments [13]. The APACHE 2 scoring system also provides a good predictive score [14].

Due to the challenges faced in managing the high burden of sepsis in Low- and Middle-Income Countries (LMICs), predictive scores were not routinely utilised [15]. A study conducted among

residents of LMICs showed that predictive scores were employed in septic patients [16]. This publication underscores that India is also one of the LMIC countries where the prevalence of sepsis is under-reported.

Data and research publications from India are scarce, and they primarily focus on infections and microbiological resistance patterns rather than sepsis. Sepsis-related ICU mortality in India is underestimated due to the limited duration of the studies, such as 1-day or 4-day mortality, and the fact that not all sepsis-related deaths in ICU settings are captured, with very few studies testing the combination of predictive scores [17].

Hence, the authors here conducted the present study to test the combination of predictive scores of qSOFA, MEDS, and APACHE 2 in relation to 28-day mortality in ICU patients with the null hypothesis that the true area=0.5.

MATERIALS AND METHODS

This cross-sectional study was conducted at the Department of Emergency Medicine, Sri Ramachandra Institute of Higher Education and Research in Chennai, India, between June and December 2022. The ethical clearance certificate reference number is CSP-MED/21/NOV/40/150. The informed consent form was received from every patient's caregiver.

Sample size estimation: A total of 150 sepsis patients were selected with a population standard deviation value of 30, an error rate of 4, and a 95% confidence interval using the formula of

$$n=\frac{1.96^2\sigma^2}{E^2}$$

n-Sample Size

1.96^2-95% Confidence……1.96^2

σ^2-Standard Deviation……30^2

E^2-Error Rate……..…4^2

$$n=\frac{1.96^2\sigma^2}{E^2} \quad n=\frac{3.84\times30^2}{E^2} \quad n=\frac{3.84\times600}{16} \quad n=144$$

The sample size selected for this study was 150 septic patients to assess the validity of the predictive score.

Inclusion criteria: Those patients >18 years of age with clinically diagnosed infections such as pneumonia, abdominal sepsis, skin and soft-tissue infection, cerebral infection, and pyelonephritis were included in the study.

Exclusion criteria: Patients under 18 years of age and HIV-positive patients were excluded from the study.

Procedure

The patients' demographic and clinical details, such as the source of sepsis, Respiratory Rate (RR), Systolic Blood Pressure (SBP), Mean Arterial Pressure (MAP), temperature, White Blood Cell (WBC) count, platelet count, bilirubin, and creatinine levels, were recorded.

GCS: The Glasgow Coma Scale (GCS) measures three functional components: eye-opening (E), verbal response (V), and motor response (M). The person can be classified as mild with a GCS score of 13 to 15, moderate with a score of 9 to 12, and severe with a score of 3 to 8 [18].

qSOFA (≥2): The quick qSOFA score includes three clinical factors: RR ≥22 breaths/min, altered mental status with GCS <15, and SBP <100 mmHg [19]. A score of 2 or higher indicates a higher risk of death or extended stay in an ICU, especially in septic patients.

MEDS: The MEDS score considers factors such as terminal illness (<30 days survivor), age over 65 years, tachypnoea and/or hypoxia, lower respiratory infection, septic shock, altered cognitive state, platelet count <150,000/mm^3, and nursing home residency [20]. The MEDS score was created to risk stratify patients presenting to the ED with suspected sepsis.

APACHE 2: The Acute Physiology and Chronic Health Evaluation II (APACHE 2) score is calculated based on acute physiology score, age points, and chronic health points. The score ranges from 0 to 71 [21] and measures illness severity within the first twenty-four hours of admission.

Analysis: The patients' GCS, qSOFA, MEDS, and APACHE 2 scores were calculated from collected clinical markers, and average, mean, median, and standard deviation values were analysed and recorded. The Spearman's Rank Correlation Coefficient (SRCC) statistical test was used to determine positive correlation, predictivity, and accuracy with the ROC curve.

STATISTICAL ANALYSIS

The collected data were entered into Microsoft Excel 2016 and analysed using IBM SPSS Statistics for Windows, version 25.0 (Armonk, NY: IBM Corp). To describe the data, descriptive statistics, frequency analysis, and percentage analysis were utilised for categorical variables, while mean and Standard Deviation (SD) were used for continuous variables. Predictive scores (qSOFA, MEDS, APACHE 2), positive correlation, and good predictivity were analysed by SRCC statistical test for 28-day mortality and ICU patients, with a significance level set at <0.05. The overall performance and diagnostic accuracy of qSOFA compared to MEDS and APACHE 2 were assessed using the ROC curve and plotted.

RESULTS

A total of 150 septic patients were observed, and the basic details were tabulated in [Table/Fig-1]. There were 93 (62.0%) male patients, which was higher than the number of females, with an average age of 57.0±14.4 years. The analysis of biomarkers was conducted to determine mean and SD values and tabulated in [Table/Fig-2]. The mean and SD values for MAP were 76.0±18.3 mm Hg, WBC was 11866.0±3718.7 (mm^3), platelets were 137326.7±88948.0 mm^3, bilirubin was 3.4±3.0 mg/dL, and creatinine was 12.75±3.92 mg/dL.

Variables	No (%)
Gender (N=150)	
Males	93 (62.0)
Females	57 (38.0)
Age categories (in years) (N=150) 57.07±14.4 years, (95% CI, 54.74-59.39)	
≤30 years	9 (6.0)
31-60 years	73 (48.7)
61 years	68 (45.3)
Source of sepsis (N=150)	
Urosepsis	51 (34.0)
Respiratory sepsis	48 (32.0)
Abdominal sepsis	20 (13.3)
Skin sepsis	20 (13.3)
Encephalitis	11 (47.3)
ICU admission (N=150)	
Yes	96 (64.0)
Mortality rate (N=150)	
28 days mortality	54 (36.0)

[Table/Fig-1]: Basic profile of study patients infected with sepsis.

Parameter (N)	Mean±SD
MAP (mmHg) (N=150)	76.0±18.3
WBC (mm^3) (N=150)	11866.0±3718.7
Platelets (mm^3) (N=150)	137326.7±88948.0
Bilirubin (mg/dL) (N=150)	3.4±3.0
Creatinine (mg/dL) (N=150)	12.75±3.92

[Table/Fig-2]: Mean and standard deviation of bio-markers of septic study patients.

The mean, SD, and 95% Confidence Interval (CI) of the study population were analysed and tabulated in [Table/Fig-3] for age (57.0±14.4, median-60 years), RR (27.1±7.6, median-26.00 beats/minute), SBP (106.1±30.4, median-110.00 mm Hg), DBP (66±16.5, median-60.00 mm Hg), GCS score (average-12.7±3.9, median-15.00), MEDS score (7.95.8, median-7.00), and APACHE 2 score (16.7±9.6, median-15.00).

Parameter (N)	Mean± SD	Median	Minimum	Maximum	95% CI	
					Lower	Upper
Age (years) (N=150)	57.07± 14.4	60.00	20.00	85.00	54.74	59.39
Respiratory Rate (RR) (beats/minutes) (N=150)	27.11± 7.64	26.00	15.00	50.00	25.88	28.35
Systolic BP (SBP) (mmHg) (N=150)	106.13± 30.47	110.00	50.00	210.00	101.22	111.05
Diastolic BP (DBP) (mmHg) (N=150)	66± 16.51	60.00	40.00	110.00	63.34	68.66
GCS score (N=150)	12.75± 3.92	15.00	3.00	15.00	12.11	13.38
qSOFA score (N=150)	29.1± 0.025	28.00	0.00	29.00	0.837	0.939
Med's score (N=150)	7.99± 5.89	7.00	0.00	27.00	7.04	8.94
APACHE 2 score (N=150)	16.74± 9.64	15.00	2.00	43.00	15.18	18.30

[Table/Fig-3]: Mean and standard deviation of variables of study patients infected with sepsis.

The qSOFA scores were distributed as follows: score 0-43 (28.7%), score 1-38 (25.3%), score 2-44 (29.3%), MEDS score 3- 0 and score 4-25 (16.7%). The mean values of the predictive scores for 28-day mortality and ICU admission patients were analysed and tabulated in [Table/Fig-4].

Parameter (N)	In 28 days, mortality patients (N=54)	In ICU admission patients (N=96)
GCS score (N=150)	9.89	11.38
qSOFA score (N=150)	2.28	1.94
MEDS score (N=150)	13.31	11.21
APACHE 2 score (N=150)	25.31	21.41

[Table/Fig-4]: Mean value of predictive scores in 28-day mortality and ICU admission patients.

The SRCC statistical test was employed to analyse the positive correlation and good predictivity between predictivity in 28-day mortality and ICU patients, as shown in [Table/Fig-5]. qSOFA and MEDS (AUC-0.888-0.939, AUC-0.907-0.954, p<0.001) demonstrated a positive correlation and good predictivity in 28-day mortality and ICU patients, respectively. qSOFA and APACHE 2 (AUC-0.963-1.014, AUC-0.912-0.963, p<0.001) showed positive correlation and good predictivity in 28-day mortality and ICU patients, respectively. MEDS and APACHE 2 exhibited positive correlation and good predictivity in 28-day mortality and ICU admitted patients (p<0.001).

The strong positive correlation of qSOFA score with MEDS and APACHE 2 was confirmed by ROC analysis for 28-day mortality and ICU patients, showing good predictive accuracy validity (AUC-0.888-0.907), [Table/Fig-6].

DISCUSSION

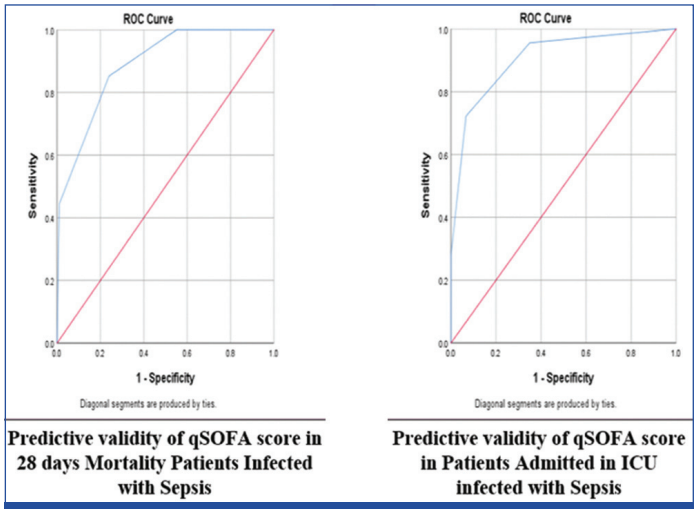
In the current study, the median age of the patients was 60 years, while Yu H et al.'s study also reported a median age of 62 years for their study patients [22]. Urosepsis was more prevalent at 51 (34%) in the present study, whereas Dimitrijevic Z et al., reported that among 489 CKD study patients, 70 (14.3%) developed urosepsis, which is a much higher percentage than in the present study [23]. The average RR in the current study was 27.1 (7.64), whereas Wang X et al.'s study presented patients with Neutrophil Percentage Albumin Ratio (NPAR) elevation, an inflammatory predictor marker associated with all causes of illness and lengthy ICU stay, at 18.70±3.72 (<0.001) [24].

In the present study, the respiratory source of sepsis and cellulitis source accounted for 32% and 13%, respectively, which aligns with Mustafa AK et al.'s study on 3406 COVID-19 patients where 59 patients died due to excess ventilation alone, with 29 patients dying from respiratory failure and 27 from sepsis. Abdelhamid AM et al.'s study indicated that cellulitis with tissue inflammation was the third source of sepsis, around 20% [25,26].

The current study found a positive correlation between qSOFA and MEDS in 28-day mortality and ICU patients, with a correlation coefficient of 0.888-0.907 (<0.001), while Velissaris D et al.'s study reported MEDS and qSOFA after antibiotic initiation within <3 hours and >3 hours [27]. Li Y et al.'s research showed a qSOFA ROC score of 0.558 (0.548, 0.568) [28]. In a retrospective cohort study on 10,811 patients, the qSOFA score for 28-day mortality was 5.1 (3.4) for patients receiving antibiotics within <3 hours and 3.9 (3.1) for those receiving antibiotics after three hours [29]. Ruangsomboon O et al.'s study on all-cause mortality found that qSOFA (AUROC 0.58; 95% CI 0.55-0.61) had the highest predictive performance [30].

Predictive scores (N)	Predictive validity (N)	Area under the curve	Std. Error	95% Confidence interval of AUC		p-value (Spearman's rank correlation (R_s))
				Lower bound	Upper bound	
qSOFA (≥1) and Meds (N=150)	In 28 days, Mortality Patients (N=54)	0.888	0.025	0.837	0.939	**<0.001***
	In ICU Admission Patients (N=96)	0.907	0.024	0.859	0.954	**<0.001***
qSOFA (≥1) and APACHE2 (N=150)	In 28 days, Mortality Patients (N=54)	0.963	0.024	0.912	1.014	**<0.001***
	In ICU Admission Patients (N=96)	0.912	0.923	0.961	0.963	**<0.001***
MEDS and APACHE2 (N=150)	In 28 days, Mortality Patients (N=54)	0.8804	0.023	0.8753	0.8855	**0.001***
	In ICU Admission Patients (N=96)	0.7701	0.027	0.7649	0.7753	**0.001***

[Table/Fig-5]: Correlation between predictive scores in study patients infected with sepsis.
Spearman's rank correlation (Rs) test-*-Statistically Significant



[Table/Fig-6]: ROC curve of qSOFA (≥1) predictive score in 28-day mortality patients and ICU patients with sepsis.

The present study reported a strong positive correlation between qSOFA and MEDS (AUC-0.888, 95% CI 0.837-0.939) (<0.001), while Wattanasit P and Khwannimit B; study showed correlation values of qSOFA (0.657, 95% CI 0.609-0.706) and MEDS (0.608, 95% CI 0.551-0.665) with p<0.001 [31]. Liu S et al.'s study suggested that Lactate-enhanced qSOFA (LqSOFA) outperformed qSOFA and MEDS with AUC and 95% CI of LqSOFA (AUC-0.751, 95% CI 0.720-0.780), qSOFA (AUC-0.717, 95% CI 0.685-0.748), and MEDS (AUC-0.670, 95% CI 0.636-0.702) [32].

One of the studies conducted and published by Falsetti L et al., in 390 elderly patients aged ≥65 years with suspected infection showed that both SOFA (AUC: 0.686; 95% CI 0.637-0.732; p<0.0001) and qSOFA (AUC: 0.680; 95% CI 0.641-0.735; p<0.0001) in predicting in-hospital death was low in this population [33]. The current study presented the ROC of qSOFA which showed good predictive validity in 28 days mortality and ICU patients. Compared to the current study, Liu YC et al.'s study also reported good sensitivity to qSOFA (CI 0.59-0.88 vs. 0.58; CI 0.47-0.67) [34].

When predicting the performance of predictivity of qSOFA in 28-day mortality patients (AUROC 0.833 vs. 0.795, Z=1.378, p=0.168), in ICU admission patients (AUROC 0.868 vs. 0.895, Z=1.022, p=0.307), in patients with mechanical ventilation (AUROC 0.868 vs. 0.845, Z=0.921, p=0.357), and in patients with vasopressor usage (AUROC 0.875 vs. 0.821, Z=2.12, p=0.034) [35]. The area under the curve (ROC) for the study by Shahsavarinia K et al., qSOFA outcome prediction was 0.59 (p-value is 0.04). In this study, the time it took to diagnose sepsis was ≤16 minutes when qSOFA was used for predicting outcomes [36].

A retrospective study conducted by Koch C et al., in 13,780 surgical patients both admitted in the ICU and intermediate ICU were assessed for predicting both suspected infection and mortality using SOFA and qSOFA score. In this retrospective study, in critically sick patients, SOFA score prediction accuracy was higher, and prediction of mortality was strong in qSOFA score in both ICU {AUCROC SIRS 0.54 (0.53-0.54); SOFA 0.73 (0.70-0.77); qSOFA 0.59 (0.58-0.59)}, and IMCU {AUCROC SIRS 0.72 (0.71-0.72); SOFA 0.52 (0.51-0.53); qSOFA 0.82 (0.79-0.84)} patients [37].

This current study found the combination of predictive scores such as qSOFA with MEDS and APACHE 2 showed a strong positive correlation and good predictivity (p<0.001), whereas the study by Morkar DN et al., presented the combination of predictive scores, sensitivity of SOFA vs. APACHE 2 was 74.36%, and SOFA vs. SAPS II was 93.94% [38].

Limitation(s)

As this study is a comparative analysis of predictive scores for sepsis, the comparison of other vital markers such as procalcitonin level and other predictive scores such as the Epic Sepsis Model (ESM) and SIRS would have given further insights. This was a limitation of this study.

CONCLUSION(S)

The present study concluded that a higher number of male patients above 31 years of age group suffered due to sepsis, and urosepsis was the higher source of sepsis. qSOFA showed accuracy, positive correlation, and good predictive values with MEDS and APACHE 2 predictive scores. Therefore, based on institutional protocol, individualised patient's clinical findings, and the usage of swift predictive scores such as the qSOFA score, and the usage of a combination of predictive scores, clinicians can initiate several planned strategic approaches and innovations for the improvement in sepsis adherence protocol. Effective strategies to prevent deaths due to sepsis include early recognition of the source of the sepsis, usage of a quick predictive score for the identification of disease progression, and appropriate treatment approaches that will reduce the mortality rate due to sepsis. Sepsis is not only life-threatening but also economy-threatening, and hence healthcare settings must practice these predictive scores to improve patients' quality of life along with their economy.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Nov 14, 2023
- Manual Googling: Jan 18, 2024
- iThenticate Software: Feb 23, 2024 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Oct 30, 2023**
Date of Peer Review: **Jan 08, 2024**
Date of Acceptance: **Feb 29, 2024**
Date of Publishing: **Apr 01, 2024**