Comparison of Sequential Organ Failure Assessment (SOFA), Acute Physiology and Chronic Health Evaluation II and IV (APACHE) Scoring System Validity as Mortality Predictors in ICU Patients with Multiple Organ Dysfunction Syndrome in Sepsis

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ABSTRACT

BACKGROUND

Multiple organ dysfunction syndrome (MODS) has recently been considered as a defining syndrome of sepsis and is responsible for a high mortality rate among the patients in the intensive care units (ICUs). Prognostication of the ICU patients is an integral part of the management of the critically ill patients and many scoring systems, for that matter, have been devised and compared for their efficiency at predicting mortality. This study was conducted to evaluate and compare the validity of sequential organ failure assessment (SOFA), acute physiology and chronic health evaluation (APACHE II) and APACHE IV as mortality predictors in intensive care unit (ICU) patients suffering from MODS in sepsis.

METHODS

Hundred patients diagnosed with MODS in sepsis were carefully examined, followed by relevant laboratory investigations. The SOFA score was calculated daily, and the APACHE II and IV scores were calculated on the day of admission. The scores were further compared among the survivors and the non-survivors, followed by receiver operating characteristic (ROC) curve analysis of the SOFA D1, D2, and D3 and the APACHE II and IV scores to estimate their capability of mortality prediction.

RESULTS

The means of the APACHE II, IV and SOFA D1 were 16.57 ± 6.49, 71.91 ± 16.19 and 8.75 ± 2.20, respectively. There was a statistically significant difference in the mean APACHE II scores (14.23 ± 5.20 vs. 21.12 ± 6.38) and the mean APACHE IV scores (67.27 ± 13.21 vs. 80.91 ± 17.77) in the survivors and the non-survivors. A statistically significant difference was also evident in the mean ages of the survivors and the non-survivors (52.82 ± 14.67 years vs. 63.25 ± 16.98 years). The SOFA score was high among the non-survivors than the survivors right from day-1 (10.24 ± 2.08 vs. 7.98 ± 1.86) to day-20 (15.00 ± 0.00 vs. 3.14 ± 0.38). Furthermore, ROC analysis showed that the best discrimination was provided by SOFA D3 followed by the APACHE II and SOFA D1 scores, with APACHE IV score showing the least.

CONCLUSIONS

SOFA score on day 3 provides the best mortality prediction in patients with MODS in sepsis, as compared to APACHE II and IV scores.

KEYWORDS

SOFA, APACHE II, APACHE IV, Multiple Organ Dysfunction Syndrome, Sepsis

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BACKGROUND

Sepsis, recognised as a clinical condition since the ancient Greeks, occurs due to severe infectious events, with extreme and potentially unfavourable impact on a patient's health. Moreover, clinicians have been facing complications due to the multiple organ dysfunction syndrome (MODS) associated with sepsis, which recently has been designated as the defining syndrome of sepsis.[1,2] MODS is characterised by serial, incremental and detrimental physiological assaults on individual organs; not being limited as a single event. It is a range of processes, virtually and gradually involving all the organs, though the damage may vary from barely discernible or mild to completely irreversible.[3] In critically ill patients in the intensive care units (ICUs), an unresolving organ dysfunction becomes a dominant cause of death.[1] To ensure an absolute quality of care in the ICUs, prognostication of the patients in a systematic way plays a fundamental role. Conventionally, ICU physicians differentiate survivors and non-survivors based on their clinical proficiency. But prognostication is best achieved by the analysis of definite objective data. Thus, several severity of illness scoring systems have been developed, transforming the approach toward prognostication or mortality prediction into a more objective and reliable practice.[4] Beyond just estimating the prognosis, the scoring systems further help in resource allocation and comparison of the ICU performance.[5] One of the scoring systems that is extensively being used in the assessment of the severity of organ dysfunction in critically ill patients is the sequential (formerly 'sepsis-related') organ failure assessment (SOFA) score. An increase in the SOFA score by two points or more is indicative of a significant organ dysfunction and an associated high-risk of mortality.[6] Other widely used scoring system is the APACHE (acute physiology and chronic health evaluation) scoring system that encompasses various parameters like physiological variables, vital signs, urine output and neurological score, along with age-related parameters and comorbid conditions, which may have a significant impact on the outcome of the critically ill patients. APACHE II, devised by Kraus et al. in 1985, has been used worldwide for measuring ICU performance of critically ill patients.[7] It estimates the mortality risk based on data available within 24 hours of ICU stay. However, with the advancement of the treatment modalities and the quality of care rendered in the ICUs over the past three decades, the older scoring systems have started exhibiting inaccuracies in the present scenarios of the ICUs. The latest scoring system developed in 2006 by the APACHE foundation, the APACHE IV, attempts to address these inaccuracies, and this is attributable to the inclusion of 142 variables in the mortality equation, with 115 various disease groups. This also leads to its complexity in application.[8] Moreover, although the APACHE IV scoring system reveals good discrimination,[9] it exhibits a poorer calibration than the APACHE II as reported in the literature.[10] Acknowledging the vitality of prognostication of critically ill patients and the pros and cons of the various scoring systems, the present study was designed to evaluate the validity of SOFA, APACHE II and APACHE IV as mortality predictors in ICU patients suffering from MODS in sepsis. Going through the literature, we found there were not many studies comparing these three scoring systems. This study was conducted to evaluate and compare the validity of SOFA, APACHE II and APACHE IV as mortality predictors in ICU patients suffering from MODS in sepsis.

METHODS

This prospective observational study was conducted at the ICU of a tertiary care hospital from September to December 2019 and was approved by the institutional ethical committee. A total of 100 patients aged ≥ 18 years, of either gender, admitted to the ICU and diagnosed with MODS in sepsis, as defined by the American College of Chest Physicians / Society of Critical Care Medicine (ACCP / SCCM) Consensus Committee in 1992,[11] were included in the study. Pregnant patients or patients with retroviral infections or under immunosuppressive agents were excluded from the study. A detailed medical history was noted, followed by performing a thorough clinical examination and relevant laboratory investigations.

The patients were prognosticated on the basis of the SOFA and the APACHE II and IV scores. The SOFA score was calculated daily and the APACHE II and IV scores were calculated on the day of admission. Lastly, all the score profiles were analysed between two groups, the survivor group that comprised of patients discharged successfully after recovery and the non-survivor group that comprised of patients declared dead.

Statistical Analysis

The results were presented as percentages or means (± standard deviation (SD). Unpaired t-test was used to compare the variables between the survivor and the non-survivor group and a P-value < 0.05 was considered significant. Binary logistic regression analysis was used to evaluate the variables for their validity at mortality prediction. Further, the SOFA scores of day 1 (SOFA D1), day 2 (SOFA D2) and day 3 (SOFA D3) and the APACHE II and IV scores were compared by receiver operating characteristics (ROC) curve analysis (1- specificity plotted on X-axis and sensitivity on Y-axis). The area under the curve (AUC) indicated the capability of the scores of mortality prediction and was interpreted as:[12,13]

Non-predictive AUC = 0.49,
Less predictive AUC = 0.5 – 0.69,
Moderately predictive AUC = 0.7 – 0.89,
Highly predictive AUC = 0.9 – 0.99 and
Perfectly predictive AUC = 1.

RESULTS

The mean age of the patients in our study was 56.06 ± 16.06 years, with 76 % of the patients being males and 24 % being females. Comorbidity was evident in 74 % of the patients and mortality in 34 % of the patients. The means of the

APACHE II, IV and SOFA D1 were 16.57 ± 6.49, 71.91 ± 16.19 and 8.75 ± 2.20, respectively (Table 1). The mean age of the survivors was 52.82 ± 14.67 years and of the non-survivors was 63.25 ± 16.98 years, and the difference was statistically significant (P = 0.004). Moreover, there was a statistically significant difference between the gender of the survivors and non-survivors, with 39.5 % of the males and 16.7 % of the females being non-survivors (P = 0.049).

	Category	Mean ± SD / N (%)	Maximum Score
Age	--	**56.06 ± 16.06**	**-**
Gender	Male	76 (76 %)	-
	Female	24 (24 %)	-
Comorbidity	Yes	74 (74 %)	-
	No	26 (26 %)	-
Mortality	Survivors	66 (66 %)	-
	Non-survivors	34 (34 %)	-
APACHE II	--	16.57 ± 6.49	71
APACHE IV	--	71.91 ± 16.19	286
SOFA D1	--	8.75 ± 2.20	24

Table 1. Baseline Demographic and Clinical Characteristics

Variable		Survivor (N = 66)	Non-Survivor (N = 34)	P-Value
Age		52.82 ± 14.67	62.35 ± 16.98	0.004*
Gender	Male	46 (60.5 %)	30 (39.5 %)	0.049*
	Female	20 (83.3 %)	4 (16.7 %)	
APACHE II		14.23 ± 5.20	21.12 ± 6.38	0.001*
APACHE IV		67.27 ± 13.21	80.91 ± 17.77	0.001*

Table 2. Comparison among Survivors and Non-Survivors

Unpaired t-test; * indicates significant difference at p ≤ 0.05

SOFA	Survivor (N = 66)	Non-Survivor (N = 34)	Difference	t Value	P-Value
Day 1	7.98 ± 1.86	10.24 ± 2.08	- 2.25	- 5.508	0.001*
Day 2	7.94 ± 1.98	9.97 ± 2.04	- 2.03	- 4.921	0.001*
Day 3	7.23 ± 2.04	9.91 ± 2.28	- 2.68	- 5.999	0.001*
Day 4	6.86 ± 1.91	10.55 ± 2.32	- 3.68	- 8.400	0.001*
Day 5	6.30 ± 1.86	10.84 ± 2.73	- 4.54	- 9.591	0.001*
Day 6	5.62 ± 1.77	12.26 ± 2.60	- 6.64	- 14.224	0.001*
Day 7	5.16 ± 1.59	12.16 ± 2.59	- 7.00	- 14.04	0.001*
Day 8	4.91 ± 1.62	11.75 ± 2.53	- 6.84	- 11.45	0.001*
Day 9	5.00 ± 1.25	11.90 ± 2.96	- 6.90	- 10.78	0.001*
Day 10	4.43 ± 0.96	12.83 ± 2.64	- 8.41	- 13.68	0.001*
Day 15	3.95 ± 0.85	14.33 ± 1.16	- 10.39	- 18.92	0.001*
Day 20	3.14 ± 0.38	15.00 ± 0.00	- 11.86	- 29.34	0.001*

Table 3. Comparison of SOFA Scores

Unpaired t test; * indicates significant difference at P ≤ 0.05

Variable	Mortality		Exp (ß) [95 % Confidence Interval (CI)]	P-Value
	Alive	Death		
Age	55.5 (44.50 – 65)	67.5 (50 – 75)	1.043 (1.012 – 1.075)	0.007*
Gender	46 (60.5) 20 (83.3)	30 (39.5) 4 (16.7)	3.261 (1.014 – 10.484)	0.047*
Comorbidity	47 (63.5) 19 (73.1)	27 (36.5) 7 (26.9)	1.559 (0.581 – 4.185)	0.378 (NS)
APACHE II	14.50 (10 – 18)	22 (15 – 25)	1.231 (1.122 – 1.351)	0.001*
APACHE IV	68 (57 – 78.25)	79.50 (66 – 93)	1.063 (1.028 – 1.099)	0.001*
SOFA 1	8 (6 – 9)	10.50 (9 – 12)	1.750 (1.360 – 2.252)	0.001*
SOFA 2	8 (6 – 9)	10 (9 – 112)	1.655 (1.294 – 2.117)	0.001*
SOFA 3	7 (6 – 8.25)	10 (8 – 11)	1.794 (1.392 – 2.310)	0.001*

Table 4. Association of Mortality with Tested Variables

Binary logistic regression; * indicates significant difference at P ≤ 0.05; age, APACHE II, IV and SOFA scores presented as median † NS: non-significant

Test Result Variable (s)	Area under the Curve (95 % CI)	P-Value
APACHE II	0.7879 (0.693 – 0.883)	0.001*
APACHE IV	0.7063 (0.599 – 0.814)	0.001*
SOFA D1	0.7874 (0.690 – 0.885)	0.001*
SOFA D2	0.7669 (0.68 – 0.866)	0.001*
SOFA D3	0.8104 (0.719 – 0.902)	0.001*

Table 5. Area under the Curve on ROC Analysis Depicting the Capability of the APACHE II, IV and SOFA D1, D2 and D3 Scores

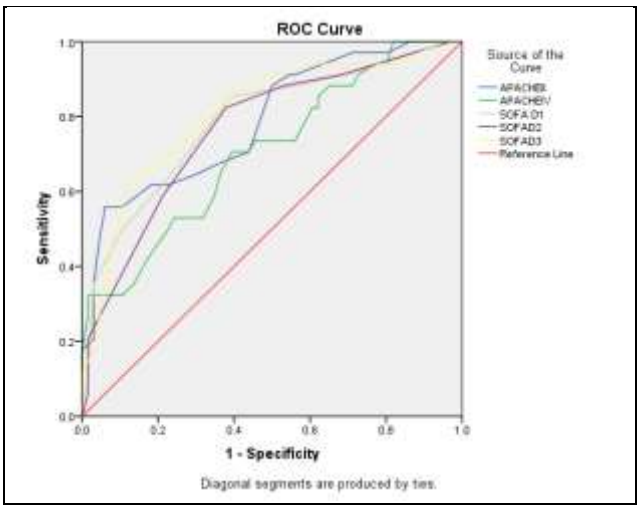

Figure 1. Diagonal Segments are Produced by Ties

The mean APACHE II scores in the survivors and non-survivors were 14.23 ± 5.20 and 21.12 ± 6.38, respectively, and the mean APACHE IV scores were 67.27 ± 13.21 and 80.91 ± 17.77, respectively. The differences in both the scores between the survivors and the non-survivors were statistically significant (P = 0.001). (Table 2). For all the patients, the SOFA score was calculated from day 1 to the last day. The SOFA score was high among the non-survivors than the survivors right from day 1 (10.24 ± 2.08 vs. 7.98 ± 1.86) to day 20 (15.00 ± 0.00 vs. 3.14 ± 0.38), and each day, the difference in the scores between the two groups was statistically significant (P = 0.001). Moreover, the SOFA scores among the survivors kept on gradually decreasing with each passing day (SOFA score on day 1, 7.98 ± 1.86; SOFA score on day 20, 3.14 ± 0.38), while those in the non-survivors kept on increasing (SOFA score on day 1, 10.24 ± 2.08; SOFA score on day 20, 15.00 ± 0.00) (Table 3).

On binary regression analysis of the tested variables for their association with mortality, it was found that age, gender and the APACHE II, IV and SOFA scores added significantly to the mortality prediction (Table 4).

The ROC analysis showed that the best discrimination was provided by SOFA D3 score [0.8104 (0.719 – 0.902)], followed by the APACHE II [0.7879 (0.693 – 0.883)] and SOFA D1 scores [0.7874 (0.690 – 0.885)]. The APACHE IV score showed the least AUC [0.7063 (0.599 – 0.814)] (Table 5 and Figure 1).

DISCUSSION

MODS is considered to be the main cause of death in the ICU patients diagnosed with sepsis. Prognostication is an important part of the management of such patients. The present study compared the SOFA, APACHE II and APACHE IV scoring systems in patients diagnosed with MODS in sepsis.

The mortality rate evident in our study was 34 %, which was slightly lesser than the rates evident in similar studies conducted by Abhinandan K et al.[14] and Anjana D et al.[15] where the mortality rates were 36 % among the patients. The mortality rate associated with sepsis ranges from 8 – 90

%, with rates towards the higher sides in patients with septic shock and MODS.[16]

In the present study, the mean age of the non-survivors was significantly higher than that of the survivors (63.25 vs. 52.82 years), and age was found to be a variable associated with mortality prediction. In a previous study conducted by Abhinandan K et al.[14] The mean age of the non-survivors was higher than that of the survivors, although the difference was not statistically significant. Dash L et al. in their study also found that mortality among the patients, diagnosed with a similar clinical condition as in the present study, was highest in the age group of 56 – 65 years. Moreover, previous literatures support this by stating that age is an important factor that increases the risk of death due to multiple organ failure and that worse prognoses are seen in patients older than 65 years of age.[17,18] However, Chen C et al.[19] through their study on patients suffering from severe sepsis proposed that age may not be an important predictor of mortality and that the physicians should consider other risk factors for the purpose.[19]

It was evident in the present study that gender was a variable associated with the prediction of mortality, with males being more among the non-survivors than females. This was in accordance with the results of a study conducted by Nasir N et al.[20] who showed that males with sepsis had a 70 % greater mortality rate, and the mortality was associated with high levels of plasma interleukin-6. However, in a regional Italian cohort of ICU patients with severe sepsis, female gender was independently associated with a higher risk of death, although the prevalence of severe sepsis was lower in women than in men.[21]

The APACHE II score among the non-survivors was significantly higher than that among the survivors (21.12 ± 6.38 vs. 14.23 ± 5.20). Abhninandan K et al.[14] in their study, stated that although the mean APACHE II score was higher among the non-survivors than the survivors (23.28 vs. 18.75), the difference was not statistically significant ($P = 0.068$). However, our results were in accordance with the study conducted by Bilevicius E et al.[22] who found that there was a significant difference between the mean APACHE II scores of the survivors (21 ± 18) and non-survivors (42 ± 26) ($P < 0.001$) and concluded that high mortality in patients with MODS in sepsis was associated with high APACHE II scores. Dash L et al.[23] in their study, also found that the mean APACHE II score was higher among the non-survivors than the survivors (22.55 vs. 10.16). Moreover, Pandya H et al.[24] concluded that in the era of many complex scoring systems, the age-old APACHE II still poses to be a user-friendly and inexpensive bedside method for mortality prediction in sepsis patients. Similarly, our study made it evident that APACHE II was significantly associated with mortality prediction and ranked the second most competent one at predicting mortality, preceded only by the SOFA D3 score.

The mean SOFA score was significantly higher in the non-survivors than the survivors, right from day one to the last. However, SOFA D3 exhibited the best capability to predict mortality. Similar findings were evident in the study conducted by Abhinandan K et al.[14] with most significant difference in the mean SOFA scores between the survivors and the non-survivors being evident on day 3. Vosylius S et al.[25] also proposed that the SOFA scores showed high accuracy in describing the course of organ dysfunction in patients with severe sepsis, with the best discrimination results being exhibited on day 3. Desai S et al.[26] compared SOFA and APACHE II, in rural-based ICU patients with sepsis, and concluded that SOFA score was better than APACHE II at predicting the outcome of the patients, with the SOFA score on day 3 being better at predicting mortality. This might be attributable to the differences in the included variables in both the scores. While APACHE II includes age and chronic health variables, the SOFA score does not consider these variables. Moreover, APACHE is an admission score and the worst parameter within 24 hours is included for the calculation of the score. Thus, in APACHE II, one-time data is considered, while in SOFA, the collection of data is sequential and repetitive, throughout the duration of ICU stay. In other words, APACHE II works as a static model, while SOFA, as a dynamic model.[27] The concept of dynamicity, i.e., changes in the SOFA score, is also considered in the new definition of sepsis. Sepsis now is defined as substantiation of infection along with life-threatening organ dysfunction, which is clinically evident by acute change of two-point score or more in the SOFA score.[28,29]

APACHE IV, although was significantly higher in the non-survivors than the survivors, its AUC was the least, indicative of least capability of predicting mortality as compared to the other scoring systems included in the study. Although not many studies in the literature have undertaken the use of APACHE IV in patients diagnosed with MODS in sepsis, there are studies that have tried to derive its utility in other similar conditions. Chan T et al.[30] evaluated the accuracy of APACHE IV in prediction of mortality in ICU patients with surgical abdominal sepsis and suggested it to be a poor predictor of mortality in those patients. Likewise, Sánchez-Casado M et al.[31] evaluated the mortality predicting capacity of few of the many scoring systems, with APACHE IV being one of them, and concluded that although APACHE IV showed the best discrimination as compared to the other systems evaluated in the study (APACHE II, simplified acute physiology score II and III and mortality probability models II), there were other problems that restricted its use in the ICUs, such as the large number of variables (142) needed to calculate APACHE IV and a poor calibration.

CONCLUSIONS

Among the SOFA, APACHE II and APACHE IV scores, SOFA score on day 3 provides the best mortality prediction in patients with MODS in sepsis. Thus, it is advisable that serial measurement of SOFA score, at least during the first three days of ICU admission, can be of great use at prognostication of patients. The APACHE II although exhibited a good ability at mortality prediction, is a static score and is less effective for prognostication as compared to the SOFA score on day 3. Further extensive studies are advisable in similar clinical settings to advise adequate modifications, if required, in the existing scoring systems.

Limitations

Different organ system failures were not considered for data analysis and relevant correlations. However, the strength of the present study lies in the incorporation of APACHE IV, as well, for the comparison between the different scoring systems in patients with MODS in sepsis, which, to the best of our knowledge, has not been included in the literature so far.

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REFERENCES

[1] Ziesmann MT, Marshall JC. Multiple organ dysfunction: the defining syndrome of sepsis. Surg Infect (Larchmt) 2018;19(2):184-190.
[2] Fujishima S. Organ dysfunction as a new standard for defining sepsis. Inflamm Regen 2016;36:24.
[3] Spapen HD, Jacobs R, Honore P. Sepsis-induced multi-organ dysfunction syndrome-a mechanistic approach. J Emerg Crit Care Med 2017;1(10):1-9.
[4] Sinuff T, Adhikari NKJ, Cook DJ, et al. Mortality predictions in the intensive care unit: comparing physicians with scoring systems. Crit Care Med 2006;34(3):878-885.
[5] Becker RB, Zimmerman JE. ICU scoring systems allow prediction of patient outcomes and comparison of ICU performance. Crit Care Clin 1996;12(3):503-514.
[6] Vincent JL, de Mendonça A, Cantraine F, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working Group On Sepsis-Related Problems of The European Society of Intensive Care Medicine. Crit Care Med 1998;26(11):1793-1800.
[7] Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. Crit Care Med 1985;13(10):818-829.
[8] Zimmerman JE, Kramer AA, McNair DS, et al. Acute Physiology and Chronic Health Evaluation (APACHE) IV: hospital mortality assessment for today's critically ill patients. Crit Care Med 2006;34(5):1297-1310.
[9] Lee H, Shon YJ, Kim H, et al. Validation of the APACHE IV model and its comparison with the APACHE II, SAPS 3 and Korean SAPS 3 models for the prediction of hospital mortality in a Korean surgical intensive care unit. Korean J Anesthesiol 2014;67(2):115-122.
[10] Parajuli BD, Shrestha GS, Pradhan B, et al. Comparison of acute physiology and chronic health evaluation II and acute physiology and chronic health evaluation IV to predict intensive care unit mortality. Indian J Crit Care Med 2015;19(2):87-91.
[11] Bone RC, Balk RA, Cerra FB, et al. Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/ Society of Critical Care Medicine Chest 1992;101(6):1644-1655.
[12] Ratanarat R, Thanakittiwirun M, Vilaichone W, et al. Prediction of mortality by using the standard scoring systems in a medical intensive care unit in Thailand. J Med Assoc Thai 2005;88(7):949-955.
[13] Wehler M, Kokoska J, Reulbach U, et al. Short-term prognosis in critically ill patients with cirrhosis assessed by prognostic scoring systems. Hepatology 2001;34(2):255-261.
[14] Abhinandan K, Vedavathi R. Usefulness of Sequential Organ Failure Assessment (SOFA) and acute physiology and chronic health evaluation II) score in analysing patients with multiple organ dysfunction syndrome in sepsis. Journal of Evolution of Medical and Dental Sciences 2013;2(49):9591-9605.
[15] Anjana D, Chandraprakash. A comparative study of APACHE II and SOFA scoring systems in critically ill patients with sepsis. IJHRMLP 2017;3(1):20-22.
[16] Balk RA. Severe sepsis and septic shock. Definitions, epidemiology and clinical manifestations. Crit Care Clin 2000;16(2):179-192.
[17] Zimmerman JE, Knaus WA, Sun X, et al. Severity stratification and outcome prediction for multisystem organ failure and dysfunction. World J Surg 1996;20(4):401-405.
[18] Hebert PC, Drummond AJ, Singer J, et al. A simple multiple system organ failure scoring system predicts mortality of patients who have sepsis syndrome. Chest 1993;104(1):230-235.
[19] Chen CM, Cheng KC, Chan KS, et al. Age may not influence the outcome of patients with severe sepsis in intensive care units. International Journal of Gerontology 2014;8(1):22-26.
[20] Nasir N, Jamil B, Siddiqui S, et al. Mortality in Sepsis and its relationship with Gender. Pak J Med Sci 2015;31(5):1201-1206.
[21] Sakr Y, Elia C, Mascia L, et al. The influence of gender on the epidemiology of and outcome from severe sepsis. Crit Care 2013;17(2):R50.
[22] Bilevicius E, Dragosavac D, Dragosavac S, et al. Multiple organ failure in septic patients. Braz J Infect Dis 2001;5(3):103-110.
[23] Dash L, Singh L, Murmu M, et al. Clinical profile and outcome of organ dysfunction in sepsis. Int J Res Med Sci 2018;6(6):1927-1933.
[24] Pandya H, Pabani N, Shah K, et al. Study of various prognostic factors for sepsis patients requiring intensive medical care with special emphasis on APACHE II score in prognostication. Journal of Integrated Health Sciences 2015;3(2):14-22.
[25] Jones AE, Trzeciak S, Kline JA. The sequential organ failure assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. Crit Care Med 2009;37(5):1649-1654.
[26] Desai S, Lakhani JD. Utility of SOFA and APACHE II score in sepsis in rural set up MICU. J Assoc Physicians India 2013;61(9):608-611.

[27] Ferreira FL, Bota DP, Bross A, et al. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA 2001;286(14):1754-1758.
[28] Abraham E. New Definitions for sepsis and septic shock: continuing evolution but with much still to be done. JAMA 2016;315(8):757-759.
[29] Shankar-Hari M, Phillips GS, Levy ML, et al. Developing a new definition and assessing new clinical criteria for septic shock: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315(8):775-787.
[30] Chan T, Bleszynski MS, Buczkowski AK. Evaluation of APACHE-IV predictive scoring in surgical abdominal sepsis: a retrospective cohort study. J Clin Diagn Res 2016;10(3):PC16-PC18.
[31] Sánchez-Casado M, Hostigüela-Martín VA, Raigal-Caño A, et al. Predictive scoring systems in multiorgan failure: a cohort study. Med Intensiva 2016;40(3):145-153.