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UTILITY OF APACHEII, SAPS II, AND SOFA SCORES AS INDICATORS OF SEVERITY OF SEPSIS AND PREDICTORS OF MORTALITY IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Objectives: The aim of the study was to predict the outcome and mortality of patients with sepsis in a tertiary care hospital using defined scores such as APACHE II, SAPS II, and SOFA scores.

Methods: This prospective and observational study was carried out in intensive care units (ICUs) setup of multispecialty hospital in Western Maharashtra. Sample size was 90 patients with sepsis who were admitted to ICU (surgical) directly or indirectly, during the duration of 1 1/2 month. The study was approved by the Institutional Ethical Committee and written informed consent from all the patients or their guardians/legal representatives. The detailed history, clinical examination, and all the relevant laboratory investigations were done including blood culture. The parameters as mentioned in APACHEII, SAPS II, and SOFA scores were recorded daily. For statistical analysis, Chi-square test, Fisher's exact test, MannWhitney test, and Binary Logistic Regression were used. SPSS software was used for analysis.

Results: Out of these 90 patients, 64 (71.1%) were males and 26 (28.8%) were females. Mean age of the study population was 61.86 years. Mean duration of stay in the ICU was found out to be 3.33 days. Culture positivity was found in 53 cases (58.8%). Gram-negative organisms were responsible for 37 (69.8%) cases while Gram-positive organisms were responsible for 16 (30.1%) cases. Statistics of various variables among cases and other detailed results were studied. SOFA score (p=0.046) and APACHE II score (p=0.00042) have been found to be statistically significant predictors of "Death"; higher the SOFA score and APACHE II score-more probability of patient dying. However, mortality as per SAPS II (p=0.202) was not found to be statistically significant predictor of death.

Conclusions: APACHE II, SAPS II, and SOFA scores can be used for prediction of mortality by using appropriate statistical tests. People of older age, male gender, and preexisting chronic health conditions are chiefly prone to develop Septic shock; hence, prevention strategies should be targeted at these susceptible populations. The epidemiology of Septic shock in developing countries warrants greater attention in the future studies.

Keywords: APACHEII, SAPS II, SOFA score, Sepsis, Predictors, Mortality.

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INTRODUCTION

The load of sepsis on our health-care delivery system is huge, with approximately 750,000 cases per year in the United States, 215,000 consequential deaths, and annual costs of $16.7 billion nationally [1]. Recent studies estimate an incidence of sepsis requiring intensive care admission of 0.25–0.38 per 1000 population, suggesting ~2 million admissions to intensive care units (ICUs) alone [2,3] A more recent US study estimated 3.0 cases to occur per 1000 population per year [1], or ~20 million cases per year. With a mortality of 35%, this would mean ~20,000 deaths per day worldwide and 64,000 deaths annually in the UK. Clinicians are confronted to manage this disease in an aging population with numerous comorbidities, immunosuppression, and a changing pattern of causative microorganisms [4].

Age has a strong influence on the incidence of sepsis. In the first retrospective epidemiology study concerning all ages, the incidence was lowest in children aged 5–14 years and in young adults (15–24 years), increasing slowly until the age of 59 years [5]. After 60 years, the incidence increased sharply and was 130 times higher in the elderly over 85 years compared with children. The majority of patients in intensive care are male [6] and the proportion of men with sepsis or Septic shock varies from 5.1% to 66.8% [7,8]. Ethnic variation also influences the incidence of sepsis and Septic shock [9,10]. The incidence is nearly double in black people compared to white people (6.08 vs. 3.58/1000 population, respectively) [11].

Patients with Septic shock often have more than one organ dysfunction or failure. Organ dysfunction has been defined as SOFA score <2 and organ failure as SOFA score >3 [12]. The most prevalent organ dysfunctions are acute respiratory failure (50–96%) [13] followed by septic shock (46–72%) [14], acute renal failure (16–51%), hematological dysfunction (12–22%), and hepatic failure (0.6–1.3%) [15]. Central nervous system dysfunction is most difficult to prove to be of septic origin and the occurrence varies widely from 9% to 30%.

A 2016 Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) task force has defined sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection (Sepsis-3) as evidenced by the organ dysfunction and infection. Septic shock is a type of vasodilatory or distributive shock. Septic shock is defined as sepsis that has circulatory, cellular, and metabolic abnormalities that are associated with a greater risk of mortality than sepsis alone. Clinically, this includes patients who

fulfill the criteria for sepsis (see 'Sepsis' above) who, despite adequate fluid resuscitation, require vasopressors to maintain a mean arterial pressure (MAP) ≥65 mmHg and have a lactate >2 mmol/L (>18 mg/dL). Organ dysfunction is defined by the 2016 SCCM/ESICM task force as an increase of two or more points in the SOFA score. The validity of this score was derived from critically-ill patients with suspected sepsis by interrogating over a million intensive care unit (ICU) electronic health record encounters from ICUs both inside and outside the United States. The most prevalent organ dysfunctions are acute respiratory failure (50-96%) [13] followed by septic shock (46-72%) [14], acute renal failure (16-51%). Hematological dysfunction (12-22%) and hepatic failure (0.6-1.3%) [15]. Central nervous system dysfunction is most difficult to prove to be of septic origin and the occurrence varies widely from 9-30%.

The evaluation of severity of illness of the patients in the critically care units is made through the use of severity scores and prognostic models. Severity scores are tools that aim at stratifying patients based on the severity of illness, assigning to each patient an increasing score as their severity of illness increases. Prognostic models, apart from their ability to stratify patients according to their severity, predict a certain outcome as mentioned earlier based on a given set of prognostic variables and a certain modeling equation [16]. These systems enable the health services comparative audit and evaluative research of intensive care units [17]. The ideal components of a scoring system include the data collected during the course of routine patient management which includes numerous parameters and variables that are easily measured, objective, and reproducible [18]. In view of above, we carried out this study to predict the outcome and mortality of patients with sepsis in a tertiary care hospital using defined scores such as APACHE II, SAPS II, and SOFA scores.

METHODS

This prospective and observational study was carried out in ICU setup of multispecialty hospital in Western Maharashtra. Since all the consecutive patients with sepsis who were admitted to ICU (surgical) directly or indirectly, during the duration of 1 1/2 month were included in the study, no sample size was calculated. Overall 90 patients were admitted during that duration and thus were included in the study after taking written informed consent from all the patients or their guardians/legal representatives. The study was approved by the Institutional Ethical Committee.

Inclusion criteria were all patients above 18 years of age of either sex and admitted in ICU fulfilling the criteria of sepsis as per American College of Chest Physician/Society of Critical Care Medicine Consensus Criteria. The detailed history, clinical examination, and all the relevant laboratory investigations were done including blood culture. In this study, the conditions were defined according to standard practice and based on relevant literature. All patients with age <18 years, length of stay at the ICU <8 h, patients with burns, post-coronary artery bypass graft of heart valve after myocardial infarction, patients on treatment with immunosuppressive agents, patients with retroviral infection, and pregnant patients were excluded from the study. For statistical analysis, Chi-square test, Fisher's exact test, MannWhitney test, and Binary Logistic Regression were used. SPSS Statistics for Windows, version 19. 0 (SPSS Inc., Chicago, Ill., USA) was used for analysis.

The patients were assessed daily for the purpose of study. The parameters as mentioned in the different scoring systems were recorded daily. The worst values of different parameters were finally selected and recorded in the scoring charts. Blood tests including the complete hemogram, liver function tests, renal function tests, and arterial blood gas analysis GCS recording were done on the 1st day of admission or the day of diagnosis of sepsis in surgical ICU for the purpose of study and also as and when indicated depending on the condition of the patient. Apart from the various laboratory parameters, age of the patients, their various comorbid conditions, and reason for admission in the ICU whether elective or emergency post-operative or non-operative admissions were also considered for the various scoring systems used in the study.

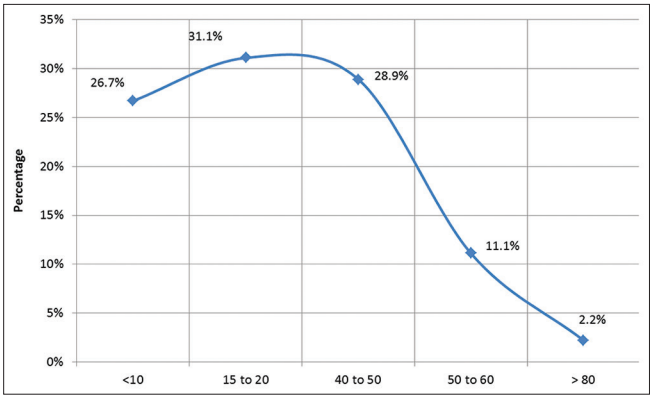

Fig. 1: Distribution of mortality as per SOFA % among cases

RESULTS

Out of these 90 patients, 64 (71.1%) were males and 26 (28.8%) were females. Mean age of the study population was 61.86 years. Mean duration of stay in the ICU was found out to be 3.33 days. Culture positivity was found in 53 cases (58.8%). Gram-negative organisms were responsible for 37 (69.8%) cases while Gram-positive organisms were responsible for 16 (30.1%) cases. Statistics of various variables among cases and other detailed results are summarized in Tables 1-3 and Fig. 1

DISCUSSION

Sepsis is among the main causes of mortality in critically ill patients admitted in ICUs of hospitals worldwide. Out of these 90 patients, 60 patients (66.7%) finally succumbed to death during the course of ICU admission while 30 patients (33.3%) finally survived. A multicenter, prospective, and observational study was conducted in four intensive therapy units (ITUs) in India from June 2006 to June 2009 to determine the incidence and outcome of Septic shock among adult patients. Hospital mortality and 28-day mortality of Septic shock in the study were 65.2% and 64.6%, respectively. Septic shock is associated with high mortality, both in ICU as well as in Hospital, ranging from 27% to 59% [19,20]. Various studies showing ICU and hospital Mortalities in patients with Septic shock are shown in Table.

The lung was the predominant source of sepsis (57.45%) in that study. In our study also, it was found that lungs were the predominant source of infection contributing to about 31 cases (34.4%) of sepsis, followed by limbs 21 cases (23.3%) and pressure sores – 13 cases (14.4%).

APACHE II

The APACHE II score ranges from 0 to 71 points; however, it is unusual for any patient to accrue more than 55 points. A mounting score (range 0 to 71) was intimately correlated with the ensuing peril of hospital death for 5815 intensive care admissions from 13 hospitals [21]. This association was also found for many common diseases. When APACHE II scores are combined with precise explanation of disease, they can prognostically stratify acutely ill patients and assist investigators comparing the accomplishment of new or differing forms of therapy. This scoring index can be used to assess the use of hospital resources and compare the effectiveness of intensive care in different hospitals or over time.

SAPS II

SAPS II consists of 17 physiological variables and three disease-related variables. The worst physiological variables were gathered within the first 24 h of ICU admission [22]. The "worst" measurement was defined as the measure that correlated to the highest number of

Table 1: Statistics of various variables among cases (n=90)

Variables	Mean	SD	Median	IQR	Mode	Minimum	Maximum
Age (years)	61.62	17.72	66.00	22.75	66.00	20.00	92.00
Age points as per APACHE II	3.74	2.12	5.00	3.25	5.00	0.00	6.00
Age points as per SAPS II	10.71	5.62	12.00	8.25	12.00	0.00	18.00
Temperature (°C)	38.39	0.67	38.60	0.85	38.60	37.00	39.60
Systolic BP (mmHg)	113.51	24.05	110.00	36.00	110.00	76.00	180.00
MAP (mmHg)	81.68	21.59	78.00	32.00	53.00	51.00	140.00
HR (b/min)	125.70	22.40	120.00	28.50	110.00	92.00	184.00
RR (b/min)	30.40	4.54	30.00	5.50	28.00	23.00	44.00
PaO_2	82.09	8.38	80.00	14.00	76.00	64.00	98.00
FiO_2	31.28	8.23	30.00	19.00	21.00	21.00	46.00
Arterial pH	7.46	0.13	7.45	0.19	7.45	7.16	7.78
Sodium (mmol/L)	133.22	4.24	133.00	6.00	132.00	126.00	145.00
Potassium (mmol/L)	3.46	0.40	3.30	0.50	3.20	3.00	4.50
Urinary output (ml/d)	730.89	432.06	675.00	842.5	600.00	100.00	1700.00
Blood urea nitrogen (mg/dl)	38.26	9.34	39.00	15.25	40.00	18.00	58.00
Serum creatinine	1.40	0.30	1.40	0.40	1.40	0.80	2.40
Serum HCO_3 (mEq/L)	25.96	4.32	25.50	8.00	21.00	20.00	36.00
WBCs (1000/cmm)	15058.11	4147.88	16000.00	5575.00	16500.00	6500.00	26000.00
Platelets (1000/cumm)	122.61	24.89	129.00	49.00	141.00	78.00	164.00
Serum bilirubin (mg/dl)	1.28	0.38	1.20	0.20	1.30	1.00	4.60
GCS	12.76	2.83	15.00	4.25	15.00	5.00	15.00
Hematocrit (%)	37.62	2.80	37.35	4.78	36.80	31.00	43.20
Vasopressors			0.00	0.00			
Chronic disease	0.90	2.72	0.00	0.00	0.00	0.00	9.00
Chronic health points as per APACHE II	4.40	1.21	5.00	0.00	5.00	2.00	5.00
Type of admission	7.11	2.53	8.00	0.00	8.00	0.00	8.00
APACHE II Score/mortality	19.40	4.75	19.50	7.25	19.00	10.00	34.00
Mortality as per APACHE II (%)	0.34	0.19	0.29	0.30	0.15	0.04	0.81
SAPS II score	36.08	10.65	35.50	14.00	33.00	9.00	63.00
Mortality as per SAPS II (%)	28.65	18.76	24.70	25.20	14.00	0.80	78.40
SOFA score	8.77	3.02	9.00	5.00	10.00	2.00	15.00

IQR: Interquartile range, SD: Standard deviation, APACHE II: Acute Physiology and Chronic Health Evaluation II, SAPS II: Simplified Acute Physiology Score II, SOFA: Sequential organ failure assessment, GCS: Glasgow Coma Scale, WBCs: White blood cell, MAP: Mean arterial pressure, HR: Heart rate, RR: Respiratory rate, BP: Blood pressure

Table 2: Variables in the equation on basic parameters and sequential organ failure assessment, Acute Physiology and Chronic Health Evaluation II and Simplified Acute Physiology Score II scores

Variables in the equation	*B*	SE	Wald	df	Significance	Exp (B)
Temperature (°C)	5.160	2.282	5.112	1	0.02376	174.085
Systolic BP (mmHg)	0.124	0.051	5.968	1	0.01456	1.132
WBCs (1000/cumm)	0.001	0	6.12	1	0.01336	1.001
Vasopressor use	9.620	3.368	8.161	1	0.00428	15068.694
Constant	−226.58	94.481	5.751	1	0.01648	0

Thus, temperature, systolic BP, WBC count and vasopressor use are statistically significant predictors of "Death"; higher the temperature, Systolic BP, WBC count and use of vasopressor-more probability of patient dying. WBCs: White blood cell, BP: Blood pressure, SE: Standard error

Variables	*B*	SE	Wald	df	Significance	Exp (B)
SOFA score	0.439	0.124	12.44	1	0.00042	1.55
APACHE II score	0.163	0.082	3.996	1	0.0456	1.178
SAPS II score	−0.027	0.032	0.692	1	0.406	0.974
Constant	−4.991	1.432	12.145	1	0.000	0.007

Thus, SOFA score and APACHE II score are statistically significant predictors of "Death"; higher the SOFA Score and APACHE II score-more probability of patient dying. APACHE II: Acute Physiology and Chronic Health Evaluation II, SAPS II: Simplified Acute Physiology Score II, SOFA: Sequential organ failure assessment, SE: Standard error

Variables	*B*	SE	Wald	df	Significance	Exp (B)
Mortality as per SOFA score	1.691	0.403	17.614	1	0.0000271	5.425
Mortality as per APACHE II score	0.055	0.019	8.435	1	0.00368	1.057
Mortality as per SAPS II score	−0.041	0.02	4.168	1	0.04119	0.959
Constant	−3.422	0.893	14.693	1	0.000	0.033

Thus, mortality as per SOFA score and APACHE II score are statistically significant predictors of "Death"; higher the Mortality as per SOFA score and APACHE II score (%) - more probability of patient dying. APACHE II: Acute Physiology and Chronic Health Evaluation II, SAPS II: Simplified Acute Physiology Score II, SOFA: Sequential organ failure assessment, SE: Standard error

points. The study did not continually calculate SAPS II scores beyond the first 24 h of ICU admission. The SAPS II score ranges from 0 to 163 points.

SOFA

The SOFA score is composed of six variables, each representing an organ system. Each organ system is allocated a point value from 0 (normal)

Table 3: Comparison of various scores by mortality status among the cases

Variables	Mortality status	n	Mean	SD	Median	IQR	*Z*	*P*
APACHE II score#	Died	60	20.78	4.54	20.00	5.00	−4.024	5.71E-05
	Survived	30	16.63	3.93	16.50	5.00	Difference is significant	
Mortality as per APACHE II (%)^	Died	60	39.17	19.87	0.36	0.31	−3.531	0.0004
	Survived	30	23.54	13.14	0.22	0.18	Difference is significant	
SAPS II score#	Died	60	37.65	10.65	37.00	13.00	−1.996	0.046
	Survived	30	32.93	10.10	34.00	14.00	Difference is significant	
Mortality as per SAPS II (%)^	Died	60	30.54	19.85	27.40	30.60	−1.276	0.202
	Survived	30	24.86	16.00	24.10	19.00	Difference is not significant	
SOFA score#	Died	60	9.88	2.73	10.00	4.00	−5.024	5.07E-07
	Survived	30	6.53	2.27	6.00	3.00	Difference is significant	

#Ordinal data. Hence Mann–Whitney test applied, ^Data failed "Normality" test. Hence Mann–Whitney test applied. IQR: Interquartile range, SD: Standard deviation, APACHE II: Acute Physiology and Chronic Health Evaluation II, SAPS II: Simplified Acute Physiology Score II, SOFA: Sequential organ failure assessment

to 4 (high degree of dysfunction/failure). The worst physiological variables were collected serially every 24 h of a patient's ICU admission. The "worst" measurement was defined as the measure that correlated to the highest number of points. The SOFA score ranges from 0 to 24.

Unlike other ICU mortality systems, SOFA was not designed to precisely forecast mortality and was initially developed examining ICU mortality (not hospital mortality). While there is no direct conversion of SOFA score to mortality, an approximate and rough estimate of mortality risk may be made based on two prospective papers that have been published [23,24]. Note that this estimation is based on the maximum (highest) SOFA score during a patient's ICU stay.

Scoring systems versus mortality prediction

As opposed to APACHE II, SAPS II, and SOFA score is calculated daily for the patients. However, among the various types of transformations of SOFA score available, maximum SOFA score was used for the final calculation and mortality prediction in this study. Maximum SOFA score in the cohort was 15 which was found in 2.2 % patients while minimum SOFA score was 2 which was found in 1.1 5 patients. Most of the patients had a SOFA score of around 10 which was found in 14.4% patients.

APACHE II and SAPS II scores can be converted into a prediction of mortality by means of, respectively, the APACHE II and the SAPS II logistic regression model. There exists no standard model to establish a probability from the SOFA score. However, as per the various studies, trend has been found between the SOFA score and estimate of mortality. Higher the SOFA score, higher the mortality. Twenty-four patients (26.7%) had a mortality prediction of <10%, 28 (31.1%) 15–20%, 26 (28.9%) 40–50%, 10 (11.1%) 50–60%, and 2 patients (2.2%) had a mortality prediction of >80%.

Two patients who had the mortality prediction of >80% by SOFA score eventually died. Furthermore, 10 patients who were predicted to have mortality of 50–60% died (100% mortality). Twenty-six patients (88.5%) were predicted to have mortality of around 40–50%, 23 of them (88.5%) died and only 3 (11.5%) survived. Twenty-four patients were predicted to have <10% mortality, 17 of them (70.8%) survived and 7 (29.2%) died. Pearson Chi-square test was applied with continuity correction and mortality prediction as per SOFA score was found to have statistically significant correlation with mortality (p=1.72E-05).

When the various scores were compared by mortality status among the cases, mean APACHE II score was 20.78 among those who died and 16.63 among those who survived, mean SAPS II score was 37.65 among those who died and 32.93 among those who survived, mean SOFA score was 9.88 among those who died and 6.53 among those who survived.

As calculated, mean mortality as per APACHE II was 39.17 among those who died and 23.54 among those who survived. Mann–Whitney test was applied and APACHE II score (p=5.71E-05) and mortality as per APACHE II (p=0.0004) were found to be the significant predictors of death. Mean mortality as per SAPS II was 30.54 among those who died and 24.86 among those who survived. MannWhitney test was applied and SAPS II score (p=0.046) found to be significant predictor of death. However, mortality as per SAPS II (p=0.202) was not found to be statistically significant predictor of death. Mean SOFA score was also found to be statistically significant predictor of death (p=5.07E-07).

As per Binary Logistic Regression with mortality as dependent variable and various scores as independent (Predictor) variables, SOFA score (p=0.046) and APACHE II score (p=0.00042) have been found to be statistically significant predictors of "Death"; higher the SOFA score and APACHE II score-more probability of patient dying. Furthermore, as per Binary Logistic Regression with mortality as dependent variable and mortality as per various scores as independent (Predictor) variables, mortality as per SOFA Score and APACHE II Score has been found to be statistically significant predictors of "Death"; higher the mortality as per SOFA Score and APACHE II Score (%) – more probability of patient dying.

CONCLUSIONS

Sepsis and Septic shock are foremost causes of death and the most common cause of death among gravely ill patients. Recent studies also advocate that acute infections deteriorate pre-existing chronic diseases or result in new chronic diseases, hence, leading to pitiable long-term outcomes in acute illness survivors. APACHE II, SAPS II, and SOFA scores can be used for prediction of mortality in them using appropriate statistical tests. People of older age, male gender, and preexisting chronic health conditions are chiefly prone to develop Septic shock; hence, prevention strategies should be targeted at these susceptible populations. The epidemiology of Septic shock in developing countries warrants greater attention in the future studies.

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AUTHORS CONTRIBUTION

All authors have contributed to preparation of manuscript

CONFLICT OF INTEREST

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REFERENCES

1. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of Septic shock in the United States: Analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001;29:1303-10.
2. Karlsson S, Varpula M, Ruokonen E. Incidence, treatment and outcome

of Septic shock in ICU-treated adults in Finland – The Finnsepsis study. Int Care Med 2007;33:435-43.
3. Blanco J, Muriel-Bombin A, Sagredo V, Taboada F, Gandía F, Tamayo L, *et al*. Incidence, organ dysfunction and mortality in Septic shock: A Spanish multi-centre study. Crit Care 2008;12:R158.
4. Annane D, Aegerter P, Jars-Guincestre MC, Guidet B. Current epidemiology in septic shock: The CUB-REA Network. Am J Respir Crit Care Med 2003;168:165-72.
5. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of Septic shock in the United States: Analysis of incidence, outcome, and associated costs of care. Crit Care Med 2001;29:1303-10. doi: 10.1097/00003246-200107000-00002
6. Reinikainen M, Uusaro A, Ruokonen E, Niskanen M. Impact of gender on treatment and outcome of ICU patients. Acta Anaesthesiol Scand 2005;49:984-90.
7. Flaatten H. Epidemiology of sepsis in Norway in 1999. Crit Care 2004;8:180-4.
8. Brun-Buisson C, Meshaka P, Pinton P, Vallet B; EPISEPSIS Study Group. EPISEPSIS: A reappraisal of the epidemiology and outcome of Septic shock in French intensive care units. Intensive Care Med 2004;30:580-8.
9. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med 2003;348:1546-54.
10. Dombrovskiy VY, Martin AA, Sunderram J, Paz HL. Occurrence and outcomes of sepsis: Influence of race. Crit Care Med 2007;35:763-8.
11. Barnato AE, Alexander SL, Linde-Zwirble WT, Angus DC. Racial variation in the incidence, care, and outcomes of Septic shock: Analysis of population, patient, and hospital characteristics. Am J Respir Crit Care Med 2008;177:279-84.
12. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, *et al*. Sepsis in European intensive care units: Results of the SOAP study. Crit Care Med 2006;34:344-53.
13. Guidet B, Aegerter P, Gauzit R, Meshaka P, Dreyfuss D; CUB-Réa Study Group. Incidence and impact of organ dysfunctions associated with sepsis. Chest 2005;127:942-51.
14. Van Gestel A, Bakker J, Veraart CP, van Hout BA. Prevalence and incidence of Septic shock in Dutch intensive care units. Crit Care 2004;8:153-62.
15. Alberti C, Brun-Buisson C, Chevret S, Antonelli M, Goodman SV, Martin C, *et al*. Systemic inflammatory response and progression to Septic shock in critically ill infected patients. Am J Respir Critic Care Med 2005;171:461-8.
16. Gullo A, Lumb PD. Intensive and Critical Care Medicine – Reflections, Recommendations and Perspectives (WFSICCM). Springer Publications; 2005.
17. Gunning K, Rowan K. ABC of intensive care outcome data and scoring systems. BMJ 1999;319:241244.
18. Hall JB, Schmidt GA, Wood LD. Principles of Critical Care. 3rd ed. McGraw-Hill Publications; 2015. p. 63-78.
19. Flaatten H. Epidemiology of sepsis in Norway. Crit Care 1999;8:180-4.
20. Brun-Buisson C, Doyon F, Carlet J, Dellamonica P, Gouin F, Lepoutre A, *et al*. Incidence, risk factors, and outcome of Septic shock and septic shock in adults. A multicenter prospective study in intensive care units. French ICU Group for Septic shock. JAMA 1995;274:968-74.
21. Knaus WA, Draper EA, Wagner DP. APACHE II: A severity of disease classification system. Crit Care Med 1985;13:818-29. PMID 3928249
22. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American multicenter study. JAMA 1993;270:2957-63. PMID 8254858
23. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, *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;26:1793-800. PMID 9824069
24. Ferreira FL, Bota DP, Bross A, Mélot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA 2001;286:1754-8. PMID 11594901