THE CLINICAL PROFILE OF PATIENTS WITH SEPSIS ADMITTED TO THE MEDICAL INTENSIVE CARE UNIT AND THEIR OUTCOME BASED ON SEQUENTIAL ORGAN FAILURE ASSESSMENT (SOFA) SCORE AT ADMISSION

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ABSTRACT

BACKGROUND

Aims and Objectives

To study the clinical profile of patients with sepsis admitted to the medical intensive care unit.

To study the significance of SOFA score calculation of patients with sepsis to the outcome.

To ascertain the prognostic significance of repeated measurement of the SOFA score to refine outcome prediction in such patients.

MATERIALS AND METHODS

The study was conducted in 152 patients admitted with sepsis in the Medical Intensive Care Unit of Department of General Medicine, Govt. Medical College Hospital, Thiruvananthapuram. These patients were enrolled consecutively in the study and SOFA scores were calculated at zero hour and after 48 hours of admission to MICU, and followed till discharge/otherwise from the hospital.

RESULTS

Among the 152 cases, 51 patients expired showing the overall mortality of 33.6%. The maximum mortality was in 30 to 49 years age group (42.9%) followed by 50-69 years age group (34.5%), mortality among those with age >70 was 21.4% (This disparity may be because most number of patients entered in our study were of 30-69 years of age i.e. 121 patients). There was no significant statistical difference between the age in recovered patients and the expired. In this study, age has no correlation to outcome (i.e., death/discharge). The total number of death cases was more among males but there was no statistical difference between males and females (34.1% & 32.8%).

CONCLUSION

SOFA score at admission, delta SOFA score and repeat SOFA score at 48 hours are strong and independent predictors of mortality in sepsis patients. Average SOFA score of 8.5 at admission and 14.5 at 48 hours has 99% specificity for mortality prediction. Incidence of sepsis in MICU was 69.72%.

KEYWORDS

Sepsis, Outcome, MICU, SOFA Score.

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BACKGROUND

Sepsis is often lethal, killing 20 to 50 percent of severely affected patients.[1] It is the second leading cause of death among patients in non-coronary intensive care units (ICUs)[2] and the 10th leading cause of death overall in the United States.[3] Furthermore, sepsis substantially reduces the quality of life of those who survive.[4,5] Accurate national data on sepsis may be used to establish health care policy and to allocate health care resources.[6-8] Epidemiologic estimates are equally dependent on consistent defining criteria. By consensus, sepsis is defined as the combination of pathologic infection and physiological changes known collectively as the systemic inflammatory response syndrome.[9] Patients with acute organ dysfunction are considered to have severe sepsis. These consensus criteria have been applied in five epidemiologic surveys of sepsis.[10-14]

Brun-Buisson et al and Alberti et al[11,12] focused on microbial patterns and the ICU-specific incidence of severe sepsis in Europe. Rangel-Frausto et al[13] described the

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natural history of the systemic inflammatory response syndrome in a single-institution cohort during a nine-month period. Sands et al[14] in a study involving a sample of inpatients from eight hospitals during a 16-month period, observed that sepsis accounted for 2.0 percent of all hospitalisations, with 59 percent of patients with sepsis requiring intensive care and accounting for 10.4 percent of admissions to the ICU. Angus et al quantified severe sepsis in 1995, using state-hospital discharge records with codes from the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) that are indicative of infection and organ dysfunction. On the basis of the use of ICD-9-CM codes, a 2003 report from the Centres for Disease Control suggested that the incidence of sepsis was increasing.

MATERIALS AND METHODS

The study was conducted in 152 patients admitted with sepsis in the Medical Intensive Care Unit of Department of General Medicine, Govt. Medical College Hospital, Thiruvananthapuram, from 2010-2011 for a period of one year. These patients were enrolled consecutively in the study and SOFA scores were calculated at zero hour and at 48 hours of admission to MICU, and followed till discharge/otherwise from the hospital.

Sample Size

Sample size was fixed using the formula

$N = ((Z\alpha_{1/2})^2\ PQ\ ) / L^2$, where

P = proportion of clinical scenario under study,

Q = 100-P

$Z\alpha_{1/2} = 1.96$, if α error = 0.05

L = 20 % of P, if β error= 0.02.

This information from the study conducted by Jean-Louis Vincent, Yasser Sakr and others in One hundred and ninety-eight intensive care units in 24 European countries (Sepsis in European Intensive Care Units: Results of the SOAP Study) is used to estimate the sample size.

P = Proportion of patients with sepsis admitted to the Medical Intensive Care Unit i.e., 24.7%. Thus,

$N = ((1.96)^2 \text{ X } 32 \text{ X } 68)/(0.2 \text{ X } 32)^2 = 152$

The desired sample size is 152.

Inclusion Criteria

1. Patients admitted to the Medical Intensive Care Unit of Govt. Medical College Hospital, Thiruvananthapuram with Sepsis/severe sepsis/septic shock, within 24 hours of hospital admission.
2. Both male and female patients.

Exclusion Criteria

1. New sepsis - defined as sepsis that developed 48 hours after ICU admission.
2. Patients requiring mechanical ventilation at the time of admission.
3. HIV positive patients.
4. Suspected/proven Viral infection & Parasitic Infestations.
5. Age less than 13 years.
6. Post-operative and post-traumatic patients.

Data Collection

The patients were categorised by the number of organs failed, with septic shock, myocarditis, ARDS and the outcome noted.

	0	1	2	3	4
Respiration- PaO_2/FIO_2 (mmHg) SaO_2/FIO_2	>400	<400 221–301	<300 142–220	<200 67–141	<100 <67
Coagulation- Platelets $10^3/mm^3$	>150	<150	<100	<50	<20
Liver- Bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Cardiovascular Hypotension	No Hypotension	MAP <70	Dopamine </=5 or dobutamine (any)	Dopamine >5 or norepinephrine </=0.1	Dopamine >15 or norepinephrine >0.1
Renal-Creatinine (mg/dL) or urine output (mL/d)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9 or <500 mL/day	>5.0 or <200 mL/day
SOFA Score					

Data Analysis

The entire patient data were computerised and statistical analysis was done using software SPSS version 10 (Statistical Package for Social Sciences) for windows.

RESULTS

Age	Count	Percentage
<30	17	11.2
30 - 49	63	41.4
50 - 69	58	38.2
>=70	14	9.2
Mean±SD	47.8±14.3	
Median	49	

Table 1. Percentage Distribution of the Sample According to Age

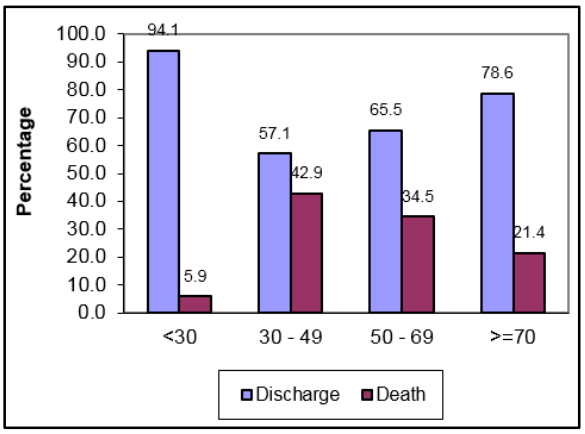

Figure 1. Distribution of Outcome According to Age

Maximum mortality was seen among 30 to 49 years of age, 21.4% death in >70 years.

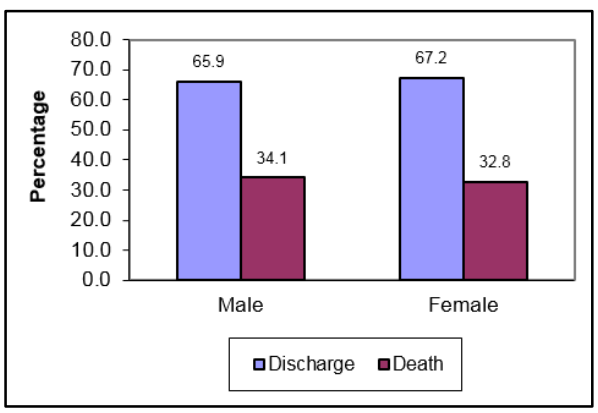

Figure 2. Comparison of Outcome Based on Sex

No significant sex difference in mortality.

Number of Organ Failures	Discharge		Death	
	Count	Percent	Count	Percent
0	36	100.0	0	0.0
1	49	87.5	7	12.5
2	15	36.6	26	63.4
3	1	5.3	18	94.7

Table 2. Distribution of Outcome According to Number of Organ Failures

x^2 = 77.61**, p = 0.000.

2 or more organ failures had more than 63% mortality.

SOFA Score at Admission	Discharge		Death	
	Count	Percent	Count	Percent
<5	71	86.6	11	13.4
5 - 9	29	55.8	23	44.2
10 - 14	1	5.9	16	94.1
>=15	0	0.0	1	100.0
Mean ± SD	4.1 ± 2		8 ± 3.2	
Median	4		8	

Table 3. Distribution of Outcome According to SOFA Score at Admission

x^2 = 47.53**, p = 0.000.

The more the SOFA score the higher the mortality rate.

SOFA at 48 Hours	Discharge		Death	
	Count	Percent	Count	Percent
<5	15	100.0	0	0.0
5 - 9	69	97.2	2	2.8
10 - 14	16	45.7	19	54.3
>=15	1	3.2	30	96.8
Mean ± SD	7.2 ± 2.8		15.5 ± 3.3	
Median	7		16	

Table 4. Distribution of Outcome According to SOFA at 48 hours

x^2 = 99.98**, p = 0.000.

Worsening of SOFA at 48 hours >5 predict higher mortality.

SOFA 0 minus SOFA 48	Discharge		Death	
	Count	Percent	Count	Percent
1 - 5	68	85.0	12	15.0
6 - 10	17	34.7	32	65.3
>10	1	12.5	7	87.5
Mean ± SD	3.2 ± 2.7		7.6 ± 2.8	
Median	3		7	

Table 5. Distribution of Outcome According to SOFA 0 minus SOFA 48

x^2 = 52.53**, p = 0.000.

Delta score of > 5 carries 65% or more mortality

Comorbidity	Discharge		Death	
	Count	Percent	Count	Percent
Normal	58	71.6	23	28.4
Diabetes	37	58.7	26	41.3
COPD	6	75.0	2	25.0

Table 6. Distribution of Outcome According to Comorbidity

x^2 = 2.91, p = 0.233

No significant for relation with co-morbidity.

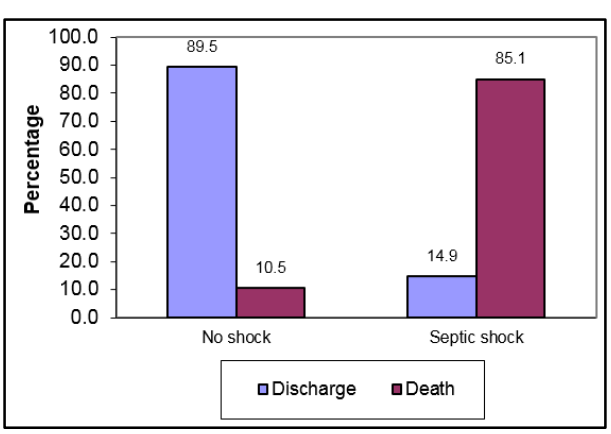

Figure 3. Comparison of Outcome Based on Shock

Septic shock indicate mortality of 85%.

Myocarditis	Discharge		Death		p#
	Count	Percent	Count	Percent	
Nil	93	70.5	39	29.5	p<0.01
Present	8	40.0	12	60.0	

Table 7. Comparison of Outcome Based on Myocarditis

: Fisher's Exact Test.

In Myocarditis mortality was 60%.

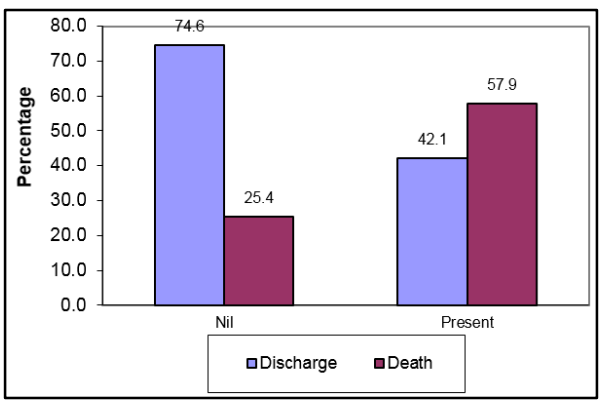

Figure 4. Comparison of Outcome Based on ARDS

ARDS caused 58% mortality.

Serology	Discharge		Death		p#
	Count	Percent	Count	Percent	
Positive	18	72.0	7	28.0	p>0.05
Negative	83	65.4	44	34.6	

Table 8. Comparison of Outcome Based on Serology

: Fisher's Exact Test.

Serology had no co-relation to outcome.

Number of Days' Stay in MICU	Discharge		Death	
	Count	Percent	Count	Percent
1 – 3	1	2.7	36	97.3
4 – 7	88	90.7	9	9.3
>7	12	66.7	6	33.3
Mean ± SD	5.9 ± 1.1		3.8 ± 3	
Median	6		3	

Table 9. Distribution of Outcome According to Number of days' stay in MICU

x^2 = 93.07**, p = 0.000.

Duration of MICU stay was of no significance.

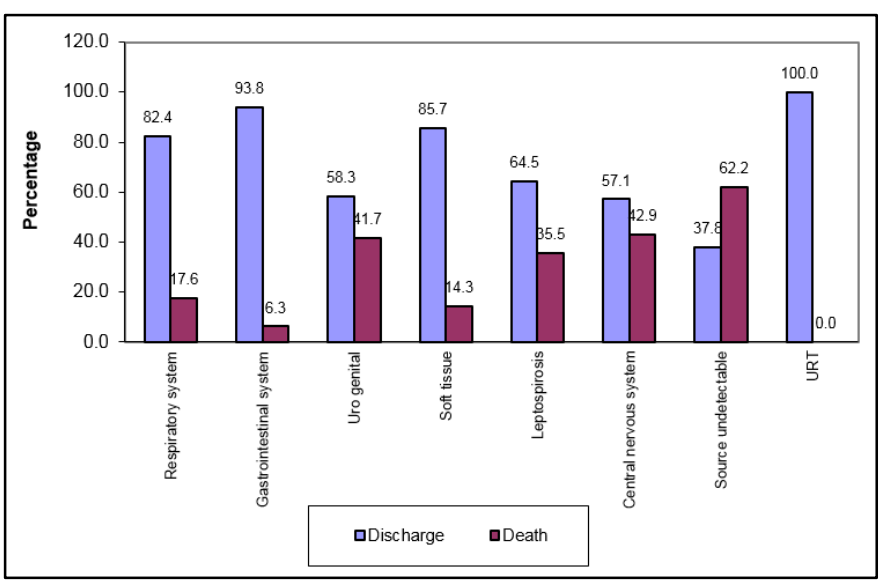

Figure 5. Distribution of Outcome According to Focus of Infection

Source was undetectable in 62% expired.

SOFA at 48 hours in Predicting Death			
SOFA at 48 hours	Outcome		
	Death	Discharge	Total
>=11.5	44	8	52
<11.5	7	93	100
Total	51	101	152
Sensitivity			86.3
Specificity			92.1
Accuracy			90.1

Table 10. Showing Sensitivity and Specificity of SOFA at 48 Hours in Predicting Death

SOFA 48 score has 92.1% specificity with 90.1% accuracy in mortality prediction.

Table SOFA 0 minus SOFA 48 in Predicting death			
SOFA 0 minus SOFA 48	Outcome		
	Death	Discharge	Total
>=5.5	39	18	57
<5.5	12	83	95
Total	**51**	**101**	**152**
Sensitivity	76.5		
Specificity	82.2		
Accuracy	80.3		

Table 11. Showing Sensitivity and Specificity of SOFA at 0 minus SOFA 48 in Predicting Death

Delta SOFA score was less specific and accurate as compared to SOFA 0 and SOFA 48.

DISCUSSION

The study was conducted in 152 patients admitted to the Medical Intensive Care Unit of Department of General Medicine, Medical College, and Thiruvananthapuram. The incidence of sepsis was 69.72%. The age of the patients varied from 15 years to 80 years with a mean of 47.8±14.3 years. Majority were male. Among these, 63 were diabetic (41.4%), 8 had COPD (5.1%) and the rest (53.3%) without any any significant comorbidity. 131 patients (86.2%) were hospitalised prior to admission at Medical college and of these 64.4% had taken antibiotics for <5 days and 25.7% for >5 days. Only 7.9% (12 patients) presented without taking antibiotics. Majority of them had fever (69.7%) as cardinal manifestation and 28.3% had respiratory symptoms.

Greg S. Martin, M.D., David M. Mannino[15] and others studied the epidemiology of sepsis in the United States from 1979 through 2000 which is one of the largest studies of sepsis, the average age of patients with sepsis increased consistently over time, from 57.4 years in the first subperiod to 60.8 years in the last subperiod, the mean change between these subperiods was an increase of 3.5 years and increasing age, male sex and comorbidities correlates to mortality. But in our study the average age was 47.8 years age, sex and comorbidities did not influence the outcome.

Of the total number of patients, 36 (23.7) had no organ failure at admission to MICU, 56 (36.8%) had one organ failure, 41 (27%) and 19 (12.5%) with two and three organ failures respectively.

SOFA score was calculated at the time of admission, varied from 1 to 16 with the mean score 5.4. 80 patients' (46.1%) score was >5 at admission and 18 (11.9%) had the score >9.

Of all patients, 131 (86.2%) showed sinus tachycardia or other arrhythmias and 45 (29.6%) had ST-T changes serially. 47 patients (30.9%) were in shock, 20 (13.2%) had myocarditis, 38 (25%) were in ARDS and 61 (40.1%) had evidence of MODS.

Mean SOFA score at 48 hours of admission was 10 ± 4.9 over a range of 2 to 21, 66 (43.4%) patients had a score >10 at 48 hours and 31 (20.4%) had the score more than 14 at 48 hours.

The average delta score (SOFA 0– SOFA 48) was 4.7 ± 3.4. 37.5% (57 patients) had a worsening of score beyond 5.

16 cases had a positive culture (10.5%) among all patients, the commonest being E. coli (9) followed by Staph (3) and Klebsiella (2). Serology was positive among 25 patients (16.4%), the great majority for leptospirosis (21) followed by S. typhi, paratyphi and Brucella (one patient each).

In our study, Respiratory tract (lung) was the most common source of infection clinically (22.4%) followed by GI tract (10.5%), soft tissue (9.2%) and urogenital in 7.9 %. The source was undetectable in 23.4%.

The mean MICU stay was 5.2 ± 2.2 days with more than 7 days' stay in 18 cases (11.8%) and >3 days in 105 cases (75.6%). 47.4% had platelet counts <1.5 lakhs (72 patients) and 25.7% (39 cases) had thrombocytopenia amounting to <1 lakh. The mean platelet count was 1.6 ± 0.7. 91 patients (59.9%) had leucocytosis > 12000 and only one patient had leucopenia. S. creatinine was elevated in 71.7% and the mean creatinine value 1.8 ± 1 mg%.

The total number of death cases was more among males but there was no statistical difference between males and females (34.1% & 32.8%).

Greg S. Martin et al[15] found in their US study, that the organ failure had a cumulative effect on mortality; approximately 1.5 percent of patients without organ failure died, whereas 70 percent of patients with three or more failing organs (classified as having severe sepsis and septic shock) died. The additive effect of organ failure on mortality was consistent over time, with improvements in survival being most evident among patients with fewer than three failing organs. The organs that failed most frequently in patients with sepsis were the lungs (in 18 percent of patients) and the kidneys (in 15 percent of patients).

Our study confirmed that the above finding is significant in our setup also. What we found was, regarding the number of organ failures, no mortality in patients without organ failure in our ICU and the mortality increased with increasing number of failed organs. In patients with three organs failure, the mortality was 94.7% (18 deaths among 19 patients), with two and one organ failure the mortality was 63.4% and 12.5% respectively. This is highly statistically significant (x^2=77.61 and p=0.000).

Similarly, the higher the SOFA score at admission, the higher was the mortality and those with total SOFA 0 score <5, 86.6% were discharged (71 out of 82 patients) but it declined to 5.9% in those with initial SOFA score of >10. This also had a positive correlation.

Repeat measurement of SOFA score at 48 hrs. had independent and statistically significant correlation to mortality among the studied patients, with only 15% mortality among those with score 1-5, 65.3% in those with score 6-10 and 87.5 in those with score >10.

Ferreira FL et al,[16] in their study titled 'Serial evaluation of the SOFA score to predict outcome in critically ill patients' in a 31-bed ICU at the University Hospital in Belgium, the results of which was published in JAMA, 2002 February,[17] concluded that independent of the initial score, an increase in SOFA score during the first 48 hours in the ICU predicts a mortality rate of at least 50%. They found that the initial, highest, and mean SOFA scores correlated well with mortality. Initial and highest scores of more than 11 or mean scores of more than 5 corresponded to mortality of more than 80%. In univariate analysis, mean and highest SOFA scores had the strongest correlation with mortality, followed by Delta-SOFA and initial SOFA scores. These findings were similar to results we obtained in our study.

There was no significant correlation of symptomatology at presentation or comorbidities to outcome (Chi square- x^2=1.72 & p=0.422, x^2 =2.91 & p=0.233). The mortality was

higher in those who had a prior hospitalisation of >5 days (48.9%) and prior antibiotic use of >5 days (51.3%), but this was not of high statistical value (p=0.027 and p=0.022 respectively).

The correlation and thus the predictive value of total WBC count, Platelet count, S. creatine, SGOT, SGPT, ECG changes at admission, focus of infection and the number of days' stay in MICU in our study group was not of statistical significance.

Of the 47 patients with septic shock at admission, mortality was 85.1% with P value <0.001. The mortality in patients with myocarditis (20 patients) was 60% (p<0.01), ARDS (38 patients)- 57.9% (p<0.001); MODS (61 patients) -67.2% (p<0.001), all being statistically significant.

Mortality in culture-positive cases was 25% (4 out of total 16 cases) and 34.6%. (47 out of 136 cases) in culture negative. Mortality among the patients with positive serology was 28% (7 out of 25 cases) and 34.6% in negative cases (44 out of 127 cases). So in our study both culture and serological evidence did not carry any positive correlation to the outcome.

In our study, the ROC curve for SOFA score at admission covered an area of 0.847 (same as the ESICM result) and 0.968 for SOFA score at 48 hrs. and 0.882 for the delta SOFA score (SOFA 0 minus SOFA 48), all of which were statistically highly significant and had positive correlation to outcome and these values correlate well with other studies mentioned above.[18,19]

The sensitivity and specificity of mortality prediction based on SOFA score at admission was found to be 76% for a score of 5.5 and 67% and 88% for an initial score of 6.5, with accuracy around 90%

Similarly, a score of 11.5 at 48 hrs. of admission has sensitivity of 86% and specificity of 92% for outcome prediction in terms of mortality, the specificity of which is 99% with a score 14.5 at 48 hrs. with accuracy of 90.1%.

CONCLUSIONS

1. SOFA score at admission, delta SOFA score and repeat SOFA score at 48 hours are strong and independent predictors of mortality in sepsis patients.
2. Average SOFA score of 8.5 at admission and 14.5 at 48 hours has 99% specificity for mortality prediction.
3. Incidence of sepsis in MICU is 69.72%.
4. There is significant involvement of lower age group (30 – 49 years) in our study.
5. Lung is the major focus of infection.
6. Prevalence of MODS is 59.9%, septic shock 30.9%, ARDS 25% and myocarditis 13.2% in sepsis patients and all these have significant association to mortality.
7. Comorbidities have no influence on outcome.
8. Culture was positive in 10.5% and culture positivity has no significant correlation to outcome.

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