Original Article

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Anaesthesia Section

Value of SOFA Scores in Predicting Prognosis in Patients with Ventilator Associated Pneumonia

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ABSTRACT

Introduction: Ventilator-associated pneumonia (VAP) is a frequent infection in patients on mechanical ventilators in intensive care units (ICU) .The prediction of its outcome is important in the decision-making process and management. Critical care scoring system derives a value which helps in the prediction and prognosis of the patient in ICU.

Aim: The objective of this study was to assess the value of Sequential Organ Failure Assessment (SOFA) score in prediction of mortality in patients with VAP, to outline the incidence, type of infection, morbidity outcome and mortality and to correlate SOFA score with mortality in VAP in mechanically ventilated patients.

Study Design: Prospective observational study.

Materials and Methods: Fifty patients who were admitted to the ICU and who were on mechanical ventilation for more than 48 hours and developed ventilator associated pneumonia were included in the study. Patients were followed till discharge/death.

Clinical and laboratory data conforming to the SOFA scores were recorded on day of admission and SOFA and CPIS scores recorded on the day of the diagnosis of VAP and correlated with mortality and duration of stay in ICU.

Statistical Analysis: Following test were used to analyze the data: Mann-Whitney test, Pearson Chi-Square and Fisher's Exact Test. The continuous variable SOFA score was categorized into classes by selecting the best cut-offs (Receiver-operating characteristic analysis, ROC).

Results: Mortality rate was 54%. Eight patients had bacteraemia at the same time with the same organisms as those causing VAP. The mean SOFA in survivors (3.57) and non survivors (5.19) and the sofa score in survivors (8.09) and non survivors (11.67) scores determined at the time of VAP diagnosis were significantly higher in non survivors than in survivors. Area under receiver operating characteristic (ROC) curve for SOFA score on day of diagnosis of VAP was 0.816 with SOFA > 11 (sensitivity: 78, specificity: 83), p = 0.005).

Conclusion: Thus, we concluded that SOFA score is a very useful score to predict the mortality and morbidity of patients admitted in ICU. It is a simple, but effective prognostic indicator and evaluator for patient progress in ICU.

Keywords: Intubation, ICU Scores, Mechanical ventilation.

INTRODUCTION

Pneumonia is the leading cause of nosocomial infection in ICUs, (>90% of cases). Ventilator-associated pneumonia (VAP) is the most frequent infectious complication among mechanically ventilated patients in the intensive care unit (ICU). Since it is clinically significant and one of the major challenges faced by intensivist in intensive care , VAP is studied as an individual clinical entity [1,2]. VAP is prolonging the length of stay at the ICU and increasing the risk of death in critically ill patients [3].

VAP is defined as pneumonia occurring after more than 48 hours of intubation and initiation of mechanical ventilation (MV) including pneumonia developing even after extubation [1]. VAP occurs in 9 to 24% of patients intubated for longer than 48 hours [4,5]. Prognosis of VAP is based on its onset. Early-onset VAP occurs during the first four days of MV, usually less severe and associated with better prognosis. It is more likely to be caused by antibiotic sensitive bacteria. Late-onset VAP, develops five or more days after initiation of MV, is associated with increased morbidity and mortality and usually caused by multidrug-resistant (MDR) pathogens [6].

Scoring system for the illness severity, such as Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) score, have been developed and validated [3,7,8]. Although the SOFA

score was originally a tool for describing the severity of organ dysfunction, Vincent et al., [7] demonstrated that a high SOFA score for any individual organ is associated with increased mortality.

Cravens in his study concluded that the mortality rate of VAP was 27% and could increase to 43% if antibiotic resistant microorganisms were involved. Thus, the length of stay in the ICU increases by 5 to 7 days and hospital length of stay increases by 2- to 3 times in these patients [9]. The risk of VAP is highest during the early phase of hospital stay. It is estimated to be 3% /day during the first 5 days of ventilation, 2% /day during days 5–10 of ventilation and 1% /day after this [2].

The objective of this study was to assess the value of SOFA score in prediction of mortality in patients with VAP, to outline the incidence, type of infection, morbidity outcome and mortality and to correlate SOFA score with mortality in VAP in mechanically ventilated patients.

AIMS

1. To assess the value of the SOFA score in the prediction of mortality during VAP episodes in mechanically ventilated patients.
2. To evaluate the occurrence of risk factors (comatose, aspiration, re intubation and tracheostomy) in patients with VAP.
3. To study the organism involved in critically ill patients with VAP.
4. To assess the outcome of patients from VAP using SOFA scores.

MATERIALS AND METHODS

It was a prospective observational study with no intervention. Study was conducted over a period of 1 year (2010-2011) in intensive care unit of a Seth GS Medical College and KEM Hospital, after obtaining the ethics committee approval.

All patients above 12 years of age and below 85 years of age who were on mechanical ventilation for more than 48 hours and who developed ventilator associated pneumonia were included in the study.

Patients with advanced neoplastic disease and with a previously established permanent artificial airway were excluded from the study. Those on mechanical ventilation for less than 48 hours were also not included. Total of 50 patients were recruited in the study.

The Institutional Review Board waived the need for informed consent since the study did not evaluate additional variables compared to those used in clinical practice and did not influence clinical treatment.

In the case record form detailed history, investigations, clinical examination and outcomes were entered.

Primary outcomes were demographic data, admission diagnosis of the patients, time on mechanical ventilation, time in ICU, day when VAP developed, pathogens responsible for VAP and risk factors (for VAP acquisition, overall length of hospital stay and in-ICU mortality). Secondary outcomes were survival and non- survival.

SOFA scores were also determined on the day of VAP diagnosis (the day on which quantitative endotracheal aspirate (ETA) cultures were positive and the CPIS score >6).

ETA cultures were obtained routinely. Urine (from the catheter) and blood cultures were obtained weekly. Further samples were taken as required.

Cases of VAP were defined as those in which there was new or progressive infiltrate on chest X-ray accompanied by fever (> 38ºC) or changes in leukocyte counts (>12,000 or < 4,000 cells/mm^3) and at least one of the following findings: purulent tracheal secretions; isolation of a likely pulmonary pathogen in a sample from the lower respiratory tract; or PaO_2/FiO_2 ratio < 240. BAL cultures was used to analyze the etiologic profile of VAP [6]. We used CPIS >6 and positive quantitative culture of ETA sample at a threshold of 10^5 for the confirmation of diagnosis of VAP.

End Points

1. Discharge
2. Death

Statistics analysis was done using SPSS version 16.0 and Minitab version 17.1.0

Following test were used to analyze the data as applicable

1. Mann Whitney test
2. Pearson Chi-Square
3. Fisher's Exact Test

The continuous variable SOFA score was categorized into classes by selecting the best cut-offs (receiver-operating characteristic analysis, ROC).

RESULTS

Demographics, risk factors, comorbidities and ICU characteristics of the patient is given in the [Table/Fig-1]

Sex: In the present study the sex distribution (male/female) was 28/22. Although the males were more than females the results were statistically not significant (p value- 0.945) [Table/Fig-1].

Age: The mean age group was 33.5 years. The young population in our set up is due to number of cases of tetanus, poisonings, and Guillian-Barre in this age group [Table/Fig-2].

Variables	Survivor	Non-survivor	Total	p value
Age				
<18 yrs	5 (100%)	0 (0%)	5 (100%)	—
18 – 30 yrs	8 (38.1%)	13 (61.9%)	21 (100%	
30 – 40	3 (42.9%)	4 (57.1%)	7 (100%)	
40-50	5 (55.6%)	4 (44.4%)	9 (100%)	
50-60	1 (20%)	4 (80%)	5 (100%)	
>60	1 (33.3 %)	2 (66.7%)	3 (100%)	
Sex				
Male	13 (46.4%)	15 (53.6%)	28 (100%)	0.945
Female	10 (45.5)	12 (54.5%)	22 (100%)	
Risk Factors				
No risk factors	10 (62.5%)	6 (37.5%)	16 (100%)	—
Comatose	0 (0%)	10 (100%)	10 (100%)	
Aspiration	2 (66.66%)	1 (33.33%)	3 (100%)	
Re intubation	1 (50 %)	1 (50%)	2 (100%)	
Tracheostomy	8 (66.6%)	4 (33.33%)	12 (100%)	
Comatose+ Tracheostomy	1 (20%)	4 (80%)	5 (100%)	
Comatose+ Re-intubation+ Tracheostomy	1 (100%)	0 (0%)	1 (100%)	
Re intubation+ Tracheostomy	0 (0%0	1 (100%)	1 (100%)	
Co morbidities				
Diabetes (DM)	0 (0%)	2 (100%)	2 (100%)	—
COPD	2 (66.7	1 (33.3%)	3 (100%)	
Hypertension (HTN)	1 (33.3	2 (66.7%)	3 (100%)	
CVA	0 (0%)	1 (100%)	1 (100%)	
Others	1 (25%)	3 (75%)	4 (100%)	
DM + COPD + HTN	0 (0%)	1 (100%)	1 (100%)	
HTN + CVA	0 (0%)	2 (100%)	2 (100%)	
No	19 (55.9)	15 (44.1)	34 (100%)	
Total	23	27	50	

[Table/Fig-1]: Demographics, risk factors, co morbidities and ICU characteristics.

Parameter	Age (Years)
Number	50
Mean	33.5
Minimum	14
Maximum	65

[Table/Fig-2]: Descriptive statistics of age.

Early onset VAP and Late onset VAP: There was not a significant difference between early onset VAP and late onset VAP in survivors and non survivors [Table/Fig-3].

VAP		Mortality		Total
		Survivors	Non-Survivors	
Early	Count	5	12	17
	Percent	29.40%	70.60%	100.00%
Late	Count	18	15	33
	Percent	54.50%	45.50%	100.00%
Total	Count	23	27	50
	Percent	46.00%	54.00%	100.00%

Chi-Square Tests	Value	df	p value	Association is (p>0.05)
Pearson Chi-Square	2.85	1	0.091	Not significant
Fisher's Exact Test			0.136	Not significant

[Table/Fig-3]: Association between VAP onset and mortality among study group.

Pathogens: The most common organism associated with VAP was *Klebsiella pneumoniae* (76%) followed by *Pseudomonas aeruginosa* (54%), ESBL (*e.coli*) (34%), *Acinetobacter baumanii* 30%, MRSA (10%). It was also observed that *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were more in early VAP and ESBL, *Klebsiella pneumoniae, Acinetobacter baumanii* and *Candida* in late VAP [Table/Fig-4].

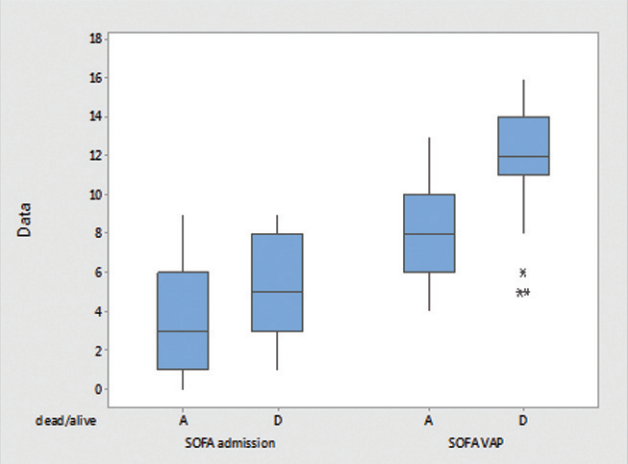
SOFA on day of admission and on day of VAP: There was a significant difference in SOFA score on admission and on day of VAP between survivors and non-survivors [Table/Fig-5,6].

The sensitivity and specificity values were calculated and cutoff points giving the best sensitivity and specificity for the mortality were determined for SOFA scores at the time of diagnosis of VAP. SOFA > 11 (sensitivity: 78, specificity: 83) [Table/Fig-7].

There was no significant difference between the duration of mechanical ventilation in survivors and non-survivors. There was no significant difference between day of occurrence of VAP between survivors and non survivors.

Organisms Involved	No. Of cases		Total No. Of Cases [N=50(100%)]
	Outcome : Mortality	Outcome: Alive	
Staphylococcus Aureus	1	1	2 (4%)
Enterococci	2	1	3 (6%)
Acinetobacter baumannii	10	5	15 (30%)
Klebsiella pneumonia	20	18	38 (76%)
Pseudomonas aeruginsa	14	13	27 (54%)
ESBL (*E.coli*)	10	7	17 (34%)
MRSA	2	3	5 (10%)
VRE	2	1	3 (6%)
Candida	2	1	3 (6%)

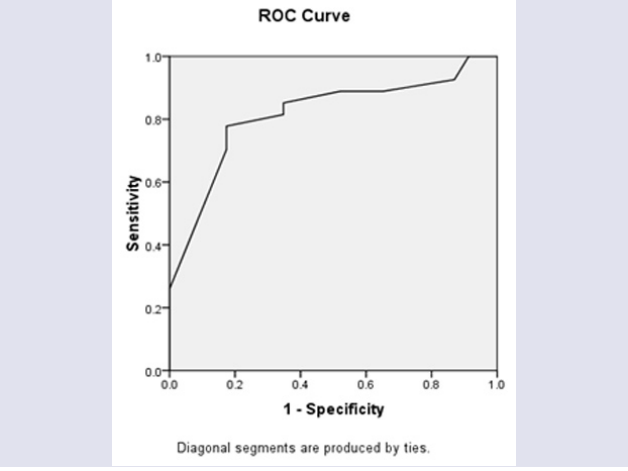
[Table/Fig-4]: Organisms involved.



[Table/Fig-5]: Sofa score on admission and on day of diagnosis of VAP (A-alive,D-dead.).

Variable	Mean		Mean Rank		p value
	Outcome: Mortality	Outcome: Survival	Outcome: Mortality:	Outcome Survival	
SOFA at admission	5.19	3.57	29.52	20.78	0.033* (Mann-Whitney Test)
SOFA at onset of VAP	11.67	8.09	32.76	16.98	≤0.001* (Mann-Whitney Test)

[Table/Fig-6]: SOFA Score on Day of Admission and on day of diagnosis of VAP.
*p<0.05 Significant difference



Area under the curve = 0.816

SOFA (at onset of VAP) cutoff	Sensitivity	Specificity
8	88.9	47.8
9	85.2	65.2
10	81.5	65.2
11	77.8	82.6

[Table/Fig-7]: ROC curve of SOFA at onset of VAP
*Area under the curve = 0.816.

The survivors had a mean ICU stay of 25 days while the non survivors had a mean ICU stay of 16 days.

The survivors had a mean hospital stay of 35 days while the non survivors had a mean hospital stay of 18 days.

There was statistically significant difference between length of ICU stay (p-value ≤0.001) and hospital stay (p≤0.001) in survivors and non survivors [Table/Fig-8].

	Minimum	Maximum	Mean	SD (±)
Duration of Mechanical Ventilation	5	45	16.68	8.938
Occurrence of VAP	3	25	8.12	4.605
Length of ICU stay	5	55	21.16	12.136
Length of Hospital stay	5	80	26.32	17.014
CPIS VAP	7	10	8.40	0.948
DURATION OF MECHANICAL VENTILATION				
Mann-Whitney U	p Value	Unpaired T test	p value	
278	0.524	0.421	0.676	
Difference is not significant		Difference is not significant		
Occurrence of VAP				
Mann-Whitney U	p Value	Unpaired T test	p value	
262	0.336	0.504	0.617	
Difference is not significant		Difference is not significant		
Length Of ICU Stay				
Mann-Whitney U	p Value	Unpaired T test	p value	
562	0.001	5.599	≤0.001	
Difference is significant		Difference is significant		
Length Of Hospital Stay				
Mann-Whitney U	p Value	Unpaired T test	p value	
141	0.001	3.919	≤0.001	
Difference is significant		Difference is significant		

[Table/Fig-8]: Descriptive statistics of duration of mechanical ventilation, day of occurrence of VAP, length of ICU stay, length of hospital stay, CPIS VAP.

DISCUSSION

Pneumonia is the 2nd most common nosocomial infection in ICU patients [10]. There is a higher risk of mortality (20-30%) associated with VAP than that due to the underlying disease alone. Mortality depends on various parameters which includes patient-specific characteristics, diagnostic criteria, and the pathogens involved.

SOFA score is one of the more recent organ failure indices, which help to predict severity status and impact of organ failure to the mortality outcome [11]. The SOFA score is a useful tool to stratify and compare patients in clinical trials [12]. Moreno et al., in their study showed a strong correlation of all the parameters of SOFA score with mortality outcome. The initial SOFA score can be used to measure the degree of

organ dysfunction or failure present on admission [13,14]. In spite of various improvements in prevention and treatment of VAP, diagnosis and prediction still remains a challenge [15].

Compared to the other scoring systems like APACHE, SAPS II, SOFA scoring systems requires less data collection. Calculations are easily made from published equations [16].

Clinical Pulmonary Infection Score >6 and positive quantitative culture of ETA sample at a threshold of 10^5 cfu /ml was used for the confirmation of diagnosis of VAP.

Pugin et al., introduced CPIS and found that threshold score of ≥ 6 was a fairly accurate indicator of VAP [17].

The mortality rate was 54% in our study. Demographic data was non-significant. The mean age group was 33.5 years. The young population in our set up was due to number of cases of tetanus, poisonings, acute febrile illness and neuromuscular disease like Guillian barre syndrome in this age group.

We had 8 patients who had bacteremia at the same time with the same organisms as those causing VAP during their ICU stay.

Initial SOFA score can triage the patients into risk categories for further management and resource planning. The highest SOFA score can identify the critical point at which patients exhibit the highest degree of organ dysfunction.

There was a significant difference of sofa score on admission between survivors and non-survivors. The mean sofa score on admission was 3.57 for survivors and 5.19 for non survivors. SOFA score at admission can be used to quantify the degree of dysfunction/failure already present on ICU admission, and can predict the future course. Hence, initial SOFA score can triage the patients into risk categories for further management and resource planning.

There was a significant difference of sofa score on day of VAP between survivors and non-survivors. The mean sofa score in survivors were 8.09 and in non survivors was 11.09. These results were significant with Vincent JL et al., Ferreira et al., [11,14]

Jain et al., and Moreno et al., also demonstrated a strong correlation of maximum SOFA score with mortality outcome [13,16]. An increase in the SOFA score during the first 48 hours in ICU predicts a mortality rate of at least 50% irrespective of the initial value [3,12].

Gul Gursel et al., showed that the mean SOFA score was significantly higher in non-survivors (7±3) (p=0.002) compared to survivor (4±2) at the time of diagnosis of VAP even though there was no significance difference in mean sofa score between the survivors (5±3) and non-survivors (6±3) (p=0.082) at the time of admission [3].

The sensitivity and specificity values were calculated and cutoff points giving the best sensitivity and specificity for the mortality were determined for SOFA scores at the time of diagnosis of VAP .SOFA > 11 (sensitivity: 78, specificity: 83).These were comparable to the study of Ferreira et al.,[11] Acharya SP et al., [18] and Ceriani et al.,[19].

Patients developed VAP on an average of 8 days in our study. The survivors developed on VAP on day 7 while the non-survivors developed on VAP on day 8.These were statistically not significant.

The most common organism associated with VAP is *Klebsiella* (76%) followed by *Pseudomonas* (54%) followed by ESBL (*E.coli*) (30%), MRSA (10%) Also, the overall mortality rate was high in the *Klebsiella* and *Pseudomonas* group. Many of our patients had polymicrobial infection. It was observed that *Klebsiella pneumoniae*, *Pseudomonas* aeruginosa were more in early VAP and ESBL, MRSA, *Klebsiella pneumonia, Acinetobacter baumanii* and *Candida* in late VAP. Though the etiology of organism in each ICU set up is different, many studies like -Steven M. Koenig ,Gadani et al., Gul Gursel et al., Joseph et al., – have shown *klebsiella* and *Pseudomonas* as the leading organism in VAP. [3,10,12,5]

The mortality of the early-onset type was found to be 70.6% and of the late-onset type was found to be 45.5% though statistically non-significant. Few studies have shown higher rate of late onset VAP mortality. Patients developed VAP on an average of 8 days in our study.

The survivors had a mean ICU stay of 25 days while the non survivors had a mean ICU stay of 16 days. The survivors had a mean hospital stay of 35 days while the non survivors had a mean hospital stay of 18 days This was because we had patients of tetanus, Guillian-barre syndrome, porphyria who needed mechanical ventilation for a prolong time.

Mechanical ventilation for more than 48 hours is a risk factor for developing VAP. As the criteria for inclusion in this study is to have mechanical ventilation for more than 48 hours, we have not included them in the risk factors. Other factors like enteral feeding was also not included in our study as all our patients had medical and neurological diseases like tetanus, Guillian barre syndrome, acute febrile illness etc., and were on enteral feeds. Apart from this 38% of patients had tracheostomy, 32% were comatose or sedated, 8% were re-intubated and 6% had aspirated.

Gadani et al., [12] have shown that comatose patients have a high risk of VAP development. Re-intubation also has a high risk of developing VAP. This could be due to the altered level of consciousness increasing the risk of aspiration or due to impaired reflexes due to prolong intubation.

LIMITATIONS

The small sample size is the most important limitation of the study since it may influence the evaluation of calibration and

discrimination of the scores. Serial, SOFA max and ΔSOFA scores were not measured.

Any of the scoring systems can never be 100% accurate, thus intensivist must learn to integrate data into clinical decision making.

CONCLUSION

Thus, we concluded that SOFA score is a very useful score to predict the mortality and morbidity of patients admitted in ICU. Among the parameters, low PaO2/FiO2 ratio correlates well with VAP episodes and found to be a good indicator. The SOFA scoring system can help the ICU physicians in admitting patients, monitoring the clinical course, assessment of organ dysfunction, predicting mortality, and for transferring patients out from the ICU and thus in proper utilization of ICU resources.

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