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Original Research Article

Comparison of clinical parameters with APACHE-II, Sequential Organ Failure Assessment and Clinical Pulmonary Infection Score scores in predicting treatment outcome of patients with ventilator associated pneumonia

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ABSTRACT

Background: The objective of this study was to study the multiple clinical parameters in patients with VAP and to compare the 3 scores namely, APACHE II, SOFA and CPIS in predicting the treatment outcome of patients with ventilator associated pneumonia.
Methods: It was a cross sectional observational study conducted on forty patients admitted in ICU between June 2018 and July 2019, who developed VAP after admission to ICU. Logistic regression analysis was applied to estimate the predictive ability of the APACHE II, SOFA and CPIS scoring systems in assessing VAP-related mortality. A p value of <0.05 was considered significant. All analyses were performed using SPSS software version 10.
Results: The sample size in our study was 40 patients. The mean age of patients was 43.4±15.9. The mean duration of mechanical ventilation before VAP onset was 8±2 days. *Klebsiella species* was the most common organism isolated from ET aspirate. Of the three scores only APACHE II was independent predictor of the mortality in the logistic regression analysis.
Conclusions: APACHE II score is better at predicting mortality in patients with VAP as compared to SOFA and CPIS scores. Age, co-morbidities, duration of ICU stay, time of acquiring VAP, multi organ dysfunction, need for ionotropes and multi drug resistant organisms play an important role in predicting the outcome of patients.

Keywords: APACHE II, Clinical pulmonary infection score, Sequential organ failure assessment, Ventilator associated pneumonia

INTRODUCTION

Ventilator associated pneumonia (VAP) is the most frequent intensive care unit acquired infection and is one of the leading causes of morbidity and mortality in ICUs.[1,2] VAP is defined as pneumonia occurring more than 48 hours after endotracheal intubation and initiation of mechanical ventilation, including pneumonia developing after extubation.[1] Incidence of VAP is approximately 9-27% of all intubated patients.[3]

Early onset VAP, which occurs during the first four days of mechanical ventilation, usually is less severe, associated with better prognosis, and is more likely to be caused by antibiotic sensitive bacteria. Late onset VAP, which develops five or more days after initiation of mechanical

ventilation, is caused by multidrug resistant pathogens and is associated with increased morbidity and mortality.[1]

Pseudomonas species, *Acinetobacter species*, *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus* have been identified as the common VAP pathogens. Predominance of gram-negative bacteria in isolates from ICU was observed in several studies. The etiology of VAP varies with different patient populations and types of ICUs. The local microbial flora causing VAP needs to be studied in each setting to guide more effective and rational utilization of antimicrobial agents.[1]

Information regarding early predictive factors of mortality in VAP is limited. The presence of pre-existing disease and organ dysfunction and severity of illness scores have been associated with poorer outcome in majority of reports. This information, along with a knowledge of early and reliable prognostic markers, is essential for optimum clinical management and prediction of outcome.

Early recognition and aggressive treatment play an important role in the management of VAP. Many scoring systems are available, especially to determine the severity of VAP. Some of the scoring systems unfortunately do not include the chronic health status of the patients which includes their co-morbid conditions. Hence it becomes very difficult to predict the prognosis accurately. This study is an attempt to compare the usefulness of the above scoring systems namely APACHE II (Acute physiology and chronic health evaluation), CPIS (Clinical Pulmonary Infection Score) and SOFA(Sequential organ failure assessment) scoring system with the clinical parameters of the patients in the setting of ventilator associated pneumonia (VAP) in this hospital.

Aims and objectives is to study the spectrum of organisms causing VAP in ICU setting, to study the multiple clinical parameters in VAP and to compare the usefulness of three scores namely APACHE II (Acute physiology and chronic health evaluation), CPIS (Clinical Pulmonary Infection Score) and SOFA (Sequential organ failure assessment) scoring system in the setting of ventilator associated pneumonia (VAP).

METHODS

This observational and cross sectional study was conducted for 12 months, from June 2018 to July 2019, in the medical ICU attached to the Department of Medicine, Victoria Hospital, Bangalore medical college, Bangalore. Prior to this, an institutional ethics committee approval was obtained. 40 VAP patients (culture positive) satisfying the inclusion and exclusion criteria were included in the study, after duly obtaining a written informed consent from the patient/ patient's relatives.

All patients were treated as per protocol, evaluated and followed up for treatment outcome.

Inclusion criteria

- Age more than 18 years.
- Diagnosed culture positive VAP patients who were intubated and on mechanical ventilation for more than 48 hours.
- Patient/ patient attenders who gave written informed consent.

All forty culture positive VAP patients (admitted at ICU and intubated for different etiologies) were evaluated with detailed history and clinical examination. Routine and specific lab and radiological investigations were carried out for VAP diagnosis and for the assessment of the etiology. Important details like demographic data, admission diagnosis of the patients, duration of mechanical ventilation, length of ICU and hospital stay, circumstances leading to VAP, pathogens responsible for VAP, multidrug resistance of the microorganisms and appropriateness of the antibiotic therapy were recorded and analysed. APACHE II, SOFA and CPIS scores were determined by the worst value (out of multiple values) found during the initial 24 hr after ICU admission. Microbiological data in regard to ET aspirate (quantitative culture), blood cultures, and catheter specimens of urine were recorded. All patients received protocol line of treatment - empirical antibiotics to start with and later changed according to culture sensitivity reports. All patients were followed up for 30 days after discharge/till in-hospital death.

Statistical analysis

Differences in parametric values were tested with Student's t test. Some continuous variables (APACHE II, SOFA, CPIS) were categorized into classes by selecting the best cut-offs (receiver-operating characteristic analysis, ROC). Discrimination was tested using the ROC curves and by evaluating areas under the curve (AUC). Logistic regression analysis was applied to estimate the predictive ability of the APACHE II, SOFA and CPIS scoring systems in assessing VAP-related mortality. The dependent variable was the mortality and the potential independent variables were age, APACHE II, SOFA, CPIS and sepsis. A p value of <0.05 was considered significant. All analyses were performed using SPSS software version 10.

RESULTS

Forty culture positive VAP patients were systematically studied for the etiology and treatment outcome. The mean age of patients was 43.4±15.9 years and majority of patients were males (67.5%). Admission SOFA, CPIS and APACHE II scores were recorded (Table 1). 37.5% of our patients were chronic smokers (Duration more than 5 years) and 30% of patients were chronic alcoholics (Duration more than 5 years). The baseline demographic characteristics of study population is given in Table 1.

Table 1: Baseline characteristics of study population.

Characteristics	
Age, in years	43.4±15.9
Gender (M/F)	27/13
Admission APACHE II	19.76±9.05
Admission SOFA	5±3
Admission CPIS	7.7±2
Length of ICU stay	8.49±4.79
Mortality	22.5%

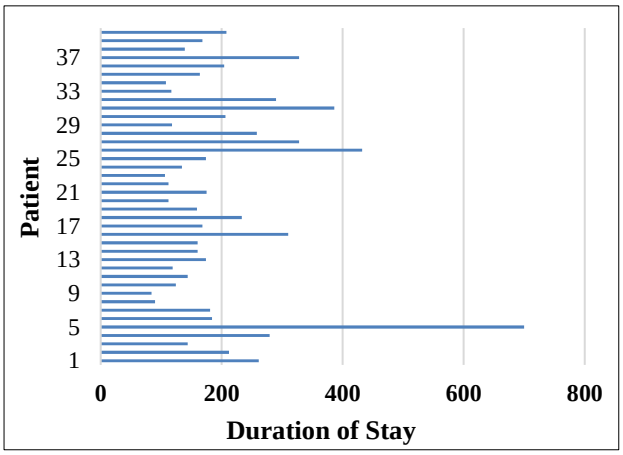

Figure 1: Duration of stay (in hours).

The mean duration of mechanical ventilation before VAP onset was 8±2 days. The mean duration of stay in ICU of patients in the study population was 8.49±4.79 days (203.83±114.9 hours). The maximum and minimum duration of stay being 29.17(700 hours) and 3.5(84 hours) days respectively. The mean duration of stay in patients who died was 330.89 hours as compared to 208.7 hours in patients who improved. The duration of ICU stays of each patient depicted in the Figure 1.

Table 2: Baseline diagnosis of patients in the study group.

Diagnosis	Number of patients
Acute alcohol intoxication	2
COPD	8
Assault with bowel injury	1
CAP	2
DKA	2
Diabetic foot	1
Viral fever	4
CVA	5
Hollow viscus perforation	2
IHD in failure	1
Poisoning	10
Polytrauma	1
TBM	1

The mean duration of mechanical ventilation among patients who improved was 183.9±73.37 hours as compared to 283.5±199.6 hours among those who died.

Table 2 gives the baseline diagnosis of patients at the time of admission to ICU.

The pathogens responsible for VAP are given in the Table 3.

Table 3: Organisms isolated from et secretions.

Organism	Number
Klebsiella sp.	19
E. coli	5
Pseudomonas aeruginosa	6
Streptococcus pneumoniae	2
MRSA	3
Acinetobacter baumanii	5
Total	40

Commonest organisms isolated (Table 3) included *Klebsiella* (47.5%), *Pseudomonas* (15%), *E. coli* (12.5%), *Acinetobacter* (12.5%) etc. For *Klebsiella*, low resistance was seen for tigecycline and minocycline. The highest level of resistance was found against levofloxacin and the lowest level of resistance was observed against tobramycin. Majority of *Klebsiella, Pseudomonas, E coli* and *Acinetobacter* species were resistant to the routine antibiotics namely ceftriaxone, ciprofloxacin, meropenem, piptaz and gentamycin. 40% of *Klebsiella* species and 60% of *Pseudomonas* species showed resistance to amikacin. MDR strains were noted (Resistant to more than three groups of antibiotics) in patients who had longer ICU stay, late VAP patients and in those who had exposed/ abused antibiotics frequently. 14 patients out of 40 had previous history of antibiotic usage for different infections, 7 each from survivors and non survivors group. 4 patients in the non survivors group habitually abused antibiotics (self-antibiotic usage) for the last 3 to 4 years.

Nearly 50% of study population (19 patients) required two antibiotics. 8 patients required three antibiotics during their course in ICU. Common antibiotics used were ceftriaxone, meropenem, piperacillin-tazobactam, and aminoglycosides. Empirical antibiotic was chosen according to the baseline diagnosis of the individual. Based on the culture sensitivity report, antibiotics were changed or added for better treatment outcome.

In this study 32.5% of the study population had co-morbidities (Figure 2). 55.6% of the study population who eventually died had comorbidities as compared to 29.03% of study population who improved. Comorbidities included diabetes, hypertension, COPD, bronchial asthma and alcoholism. 1 patient in the study group had retroviral disease, 8 patients had diabetes and 12 patients had hypertension. Many comorbid conditions were noted, mainly type 2 diabetes (20%), hypertension

(30%), IHD (7.5%), COPD (20%), CVA (5%) etc. Consideration should be given to multi organ dysfunction and need for interventions while predicting the outcomes in patients with VAP. 3 of the 9 patients who died in this study had diabetic ketoacidosis during their ICU stay. All 9 of them developed acute kidney injury at some point during their ICU stay.

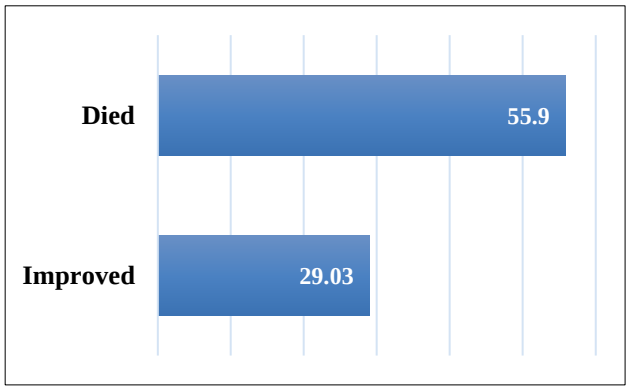

Figure 2: Percentage of population with comorbidities.

A total of 17 patients developed early VAP and 23 patients late VAP. 35.29% of patients with late VAP died as compared to 21.42% of patients with early VAP (Figure 3).

Nine out of the forty patients in the study population died. The mortality rate in the study population was 22.5%. All of them who died were on ionotrope support. Out of the 9 patients who died, ET culture of 4 had grown Acinetobacter, 2 MRSA, 1 each had Pseudomonas and Klebsiella infections. 6 had late VAP and 3 had early VAP as described above. The mean APACHE, SOFA and CPIS scores of patients who died are mentioned in Table 4.

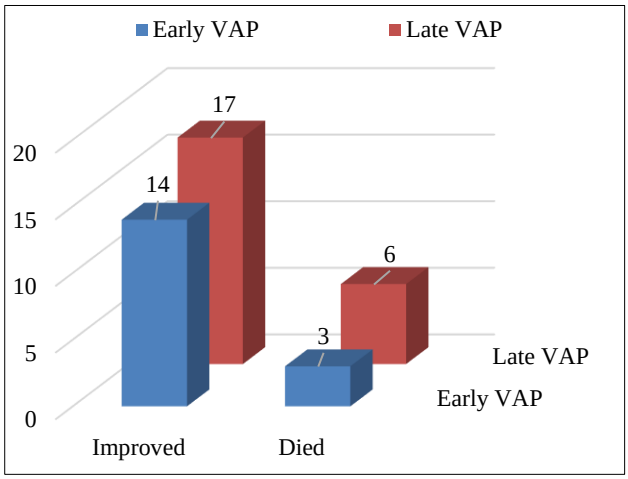

Figure 3: Outcomes of early vs late VAP.

Table 4: Comparison of scores among various patient groups.

Scores	Survived	Dead	Early VAP	Late VAP
APACHE II	16.84±7.17	31.5±5.16	15.82±7.27	29.32±9.11
SOFA	7.59±3.49	12.64±2.78	8.21±2.14	11.89±4.41
CPIS	7.63±3.1	8±1.71	8.12±2.69	8.86±3.42

Although the mean SOFA scores determined at the time of admission were not significantly different between the survivors and non survivors (p=0.082) they were significantly higher in non survivors and late VAP when they were measured at the time of VAP diagnosis (Table 4). APACHE II scores were significantly higher in non survivors and late VAP both at admission (p=0.004) and at the time of VAP diagnosis (p=0.001) as seen in Table 4. Mean CPIS scores of the non survivors were also significantly higher than of the survivors. Discrimination was excellent for APACHE II (AUC: 0.84, CI: 0.70-0.92, p=0.001), acceptable for SOFA (AUC: 0.75, CI: 0.58-0.84, p=0.004) but poor for CPIS (AUC: 0.61, CI: 0.50-0.77, p=0.068) score. Of the three scores only APACHE II was identified as a good predictor of mortality in the logistic regression analysis.

DISCUSSION

VAP is a dangerous disease and carries poor prognosis even with best of treatment. Many factors contribute to the high mortality and morbidity. Early diagnosis with a great suspicion still holds the key for better treatment outcomes. Many clinical parameters and scores like SOFA, APACHE II and CPIS are available for the assessment of severity of VAP. The main aim was to compare these scores with the clinical parameters and to predict the treatment outcome in VAP patients.

Forty culture positive VAP patients were evaluated for treatment outcome. In this study, males were the predominant study population (67.5%). The mean age group in this study was 43.4 years which was similar to Hina G et al, and several other studies conducted to assess outcomes in patients with VAP.[4]

The mean duration of mechanical ventilation before VAP onset was 8±2 days which was comparable with other studies.[4-6] The mean duration of mechanical ventilation among patients who improved was 183.9±73.37 hours as compared to 283.5±199.6 hours among those who died. The mean duration of mechanical ventilation is an

important risk factor for prognosis in VAP, which is similar to other studies.[7]

Set R et al, in a study conducted in a tertiary care centre in Mumbai studied ninety patients on mechanical ventilation. 25 out of the 90 patients developed VAP. The incidence of VAP was 27.7%. Out of these 25 VAP patients, 68% developed late onset VAP and 32% developed early onset VAP.[5] In this study, 57.5% patients developed late VAP and 42.5% developed early VAP. This was similar to the studies conducted by Dey et al, and Joseph et al.[6,8]

Re-intubation was done in 3 patients in this study and all of them developed VAP with poor outcome. A case-control study of 135 patients following heart surgery also found re-intubation to be a major risk factor as VAP occurred in 92% of the re-intubated patients versus 12% of the control subjects.[9]

Acinetobacter and Pseudomonas aeruginosa were the most commonly isolated pathogens of VAP in the studies conducted by Dey A et al, Rajasekhar. T et al, and Kanafani Z et al. This is in contrast to this study where *Klebsiella sp.* is the most common organism isolated followed by *Pseudomonas* and *Acinetobacter species*. Gram negative organisms are more commonly implicated in VAP as evidenced by several studies, including thiss.[6,10,11] Moreira and Gontijo Filho carried out a case-control study using patients with VAP by MDR pathogens (case) and non-MDR pathogens (control). They found that 25.3% developed VAP and 47.3% due to MDR pathogens.[12] The risk factors for MDR organisms causing VAP were length of hospital stay, use of steroids, prior use of antibiotics, inappropriate empirical antimicrobial therapy, and mixed/poly-microbial etiology. In the present study, 18% of patients with VAP had received prior antibiotics for other source of infection before developing VAP. The administration of broad-spectrum antibiotics is a risk factor for developing MDR VAP. Ranjan et al. observed that the prior use of antibiotics increases the risk of acquiring drug resistant pathogens (*P. aeruginosa* and *Acinetobacter sp.*).[13] Similarly, Joseph et al, stated that prior antibiotic therapy was independent risk factors for VAP by MDR pathogens.[14] MRSA had a poor treatment outcome in this study, 2 out of 3 patients who developed MRSA infection died**.**

Of 40 VAP patients, 9 patients (22.5%) died. 6 were in late VAP group and the remaining 3 were from early VAP group. Majority of the deaths occurred in Acinetobacter group (4 out of 9). Among deaths, 55.9% of patients had multiple co-morbid conditions.

With regard to the scores, several studies show that APACHE II is better at predicting 30 day mortality in patients with VAP. CPIS and SOFA scores do not have good discrimination and calibration for predicting mortality. The same has been elucidated in this study. As per statistics from this study, APACHE II was considered as a better predictor of mortality in VAP patients.

CONCLUSION

VAP occurs more frequently than expected in critically ill patients on mechanical ventilation. Predicting the treatment outcome of patients who develop VAP during their stay in ICU presents several difficulties. The prognosis of patients with VAP depends on several factors. Age, comorbidities, duration of ICU stay, time of acquiring VAP, multi organ dysfunction, need for ionotropes and multi drug resistant organisms play an important role in predicting the treatment outcome of patients. APACHE II scores over other scores and is better at predicting mortality of patients with VAP compared to SOFA and CPIS scores.

Clinical assessment may be supplemented by scores like APACHE II for better prognostication of patients with VAP. Since VAP is associated with significant morbidity and mortality, the age old proverb ‘Prevention is better than cure’ holds true for all times. Hence, all steps to prevent VAP in mechanically ventilated patients is the need of the hour. However, large, multi-centric randomized controlled studies are required to strengthen this proposal - the importance of clinical parameters and different scoring systems to evaluate the prognosis in VAP patients.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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