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Prediction of Early Ventilator Associated Pneumonia using Clinical Pulmonary Infection Score and C-Reactive Protein- A Prospective Observational Study

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Abstract
Background & Objectives: *Ventilator associated pneumonia (VAP) is an important form of hospital acquired pneumonia (HAP), specifically developing in a mechanically ventilated patient more than 48 hours after tracheal intubation. The overall or crude mortality associated with VAP ranges from 40% to 70% varying with underlying illness. Recent studies have shown that Clinical pulmonary infection score and CRP are valuable tool in detection of early VAP. The aim of the study was correlate clinical pulmonary infection score and c-reactive protein in the prediction of early ventilator associated pneumonia*
Methods: *In this study we have taken 30 patients who were above 18 yrs diagnosed to have Early Ventilator associated pneumonia and subjects on immunosuppressive therapy, chemotherapy and AIDS, Patient intubated outside hospital and refered were excluded. Serial CRP levels were measured later CPIS was calculated With the onset of chest infilterate, ET Tube Aspirate culture was obtained for confirmation of VAP.*
Results: *30 patients were enrolled. CPIS Score was calculated in 22 patients who developed early VAP which is confirmed by ET tube aspirate culture and sensitivity. CPIS Score of > 6 in cases who developed early VAP which is confirmed by ET Culture and sensitivity was statistically significant on Day 4 with p value of 0.016 , But it was not significant on Day 3 and 5 .Over all statistical analysis of CPIS Value of >6 in 18 patients who developed early VAP was significant (P value 0.003). There was serial rise in the titers of CRP levels but CRP levels did not show any stastical significance with CPIS score in VAP patients.*
Conclusion: *Study showed when the CPIS exceeded 6, there was an association with the presence of pneumonia in mechanically ventilated patients which was confirmed by ET tube aspiration culture. serum CRP is an easy, available and cheap test so serial rise in titres of CRP in mechanically ventilated patients along with CPIS helps in the early diagnosis of pneumonia and aggressive treatment to prevent mortality and morbidity.*
Keywords: *Ventilator associated pneumonia; C reactive protein; Clinical pulmonary infection score; Hospital acquired pneumonia.*

Introduction

Ventilator associated pneumonia (VAP) is an important form of hospital acquired pneumonia (HAP), specifically developing in a mechanically ventilated patient more than 48 hours after tracheal intubation[1].

VAP results from aspiration of stomach contents and aspiration or migration of bacteria contain-

ing secretions down the endotracheal tube (ETT) from the oropharynx into the lungs[2,3,4,13].

The overall or crude mortality associated with VAP ranges from 40% to 70% varying with underlying illness[10].

Most clinicians continue to rely on a clinical diagnosis of HAP because it is convenient.

The presence of pneumonia is defined by new lung infiltrate plus clinical evidence that the infiltrate is of an infectious origin. The presence of a new or progressive radiographic infiltrate plus at least two of three clinical features

1) fever greater than 38 degree C
2) leucocytosis or leucopenia, and
3) purulent secretions

These represents the most accurate combination of criteria for starting empiric antibiotic therapy[10].

Requiring all three clinical criteria is too insensitive and it will result in many patients with true pneumonia not receiving therapy.

Ventilator-associated pneumonia is usually suspected when the individual develops a new or progressive infiltrate on chest radiograph, leukocytosis, and purulent tracheobronchial secretions. Unfortunately, and unlike for community-acquired pneumonia, accepted clinical criteria for pneumonia are of limited diagnostic value in definitively establishing the presence of VAP[4].

It is the second most common nosocomial infection in the intensive care unit (ICU) and the most common in mechanically ventilated patients[5,6,7]. VAP rates range from 1.2 to 8.5 per 1,000 ventilator days and are reliant on the definition used for diagnosis . Risk for VAP is greatest during the first 5 days of mechanical ventilation (3 %) with the mean duration between intubation and development of VAP being 3.3 days This risk declines to 2 %/day between days 5 to 10 of ventilation, and 1 %/day thereafter [5,8].

Early onset VAP is defined as pneumonia that occurs within 5 days and this is usually attributed to antibiotic sensitive pathogens whereas late onset VAP is more likely caused by multidrug resistant (MDR) bacteria and emerges after 5 days of intubation[6,8].

In an effort to improve the specificity of clinical diagnosis, Pugin et al. developed the clinical pulmonary infection score (CPIS)[10,11]. It has been observed that when CPIS exceeded 6, good correlation with the presence of pneumonia in ventilated patients, which is evident by quantitative cultures of bronchoscopic and non bronchoscopic BAL (Broncho alveolar lavage) specimens [10,13]

Materials and methods

This was prospective observational study conducted in Kempegowda Institute of Medical Sciences & Research centre, Bengaluru which is a tertiary care teaching hospital. The study was carried out for a period of 24 months (from January 2015 to December 2016). It is a prospective observational study. The Ethical Committee clearance was obtained and informed consent was taken from the participating patients.

All adults both males and females with age more than 18 years admitted mechanically ventilated in ICU KIMS Hospital Bangalore without chest infilterate for 48hours after mechanical ventilation were included in study . Patient intubated outside, who are on immunosuppressive therapy, chemotherapy, who is diagnosed to have HIV infection and elevated total count at admission were excluded from the study.

Detailed history including age, sex and history of other diseases were obtained, Thorough clinical examination including general examination and local chest examination was conducted, Daily Laboratory investigations, Radiological evaluation for new pulmonary infiltrates was carried out by Plain X-rays. Serum C-reactive protein (CRP) assessment was done 1st 3rd, 4th and 5 th day during the first 5 days of intubation. Clinical pulmonary infection score (CPIS) at the onset of chest infilterate was calculated. ET Tube culture/ET Tube aspirate culture was done at the onset of chest infilterate. Patient were followed up, outcome noted as discharged, died and discharged against medical advice.

Figure 1: Clinical pulmonary infection

Clinical Pulmonary Infection Score (CPIS) criteria used in this study.

Component	Value	Point
Temperature ^0C		
	≥36.5 and ≤38.4	0
	≥38.5 and ≤38.9	1
	≥39.0 and ≤36.0	2
Blood leukocytes (mm3)	≥4000 and ≤11000	0
	<4000 or >11000	1
Tracheal secretions	Few	0
	Moderate	1
	Large and purulent (>25 PNL per LPF)	2
Oxygenation (Pa02/Fi02, mm Hg)	>240 or presence of ARDS	0
	≤240 and absence of ARDS	2
Chest radiograph	No infiltrate	0
	Patchy or diffuse infiltrate	1
	Localized infiltrate	2
Progression of pulmonary Infiltrate	No radiographic progression	0
	Radiographic progression (After CHF and ARDS excluded)	2
Culture	<10000 cfu bacteria per ml BAL or no growth	0
	≥10000 cfu bacteria per ml BAL	1

ARDS, Acute Respiratory Distress Syndrome; BAL, Bronchoalveolar Lavage; CFU, Colony Forming Unit; CHF, Congestive Heart Failure; CPIS, Clinical Pulmonary Infection Score; $Fi0_2$, Fraction of inspired oxygen; LPF, Low Power Field; $Pa0_2$, Partial arterial oxygen; PNL, Polymorphonuclear Neutrophils

Statistical Analysis

The resultsfor each parameter (numbers and percentage) for discrete data and averaged (mean+/-standard deviation) for continuous data are presented in Table and figures. Student t test , one way Analysis of Variance (Anova) and pearson correlation were used . p value less than 0.05 was considered as statistically significant. Data analysis was carried out using statistical package for social science (SPSS V 10.5)

Results

In this study 30 patients who were admitted to KIMS hospital ICU and mechanically ventilated who developed Ventilator associated Pneumonia were enrolled. All patients were above 18 years and most of them were in the age group of 41-50 age group (30%) and out of 30 patients 25 were male and 05 were female patients, Male to Female ratio is 5:1.

Table 1: Distribution of cases according to Diagnosis

DIAGNOSIS	N	%
OP COMPOUND	10	33.3
UNKNOWN POISON	5	16.7
RTA HEAD INJUY	4	13.3
CVA-ISCHEMIC STROKE	4	13.3
CVA-HEM STROKE	2	6.7
GB SYNDROME	1	3.3
HEAD INJURY -SELF FALL	2	6.7
METABOLIC ENCEPHALOPATHY	1	3.3
ALCOHOL INTOXICATION	1	3.3
TOTAL	30	100.0

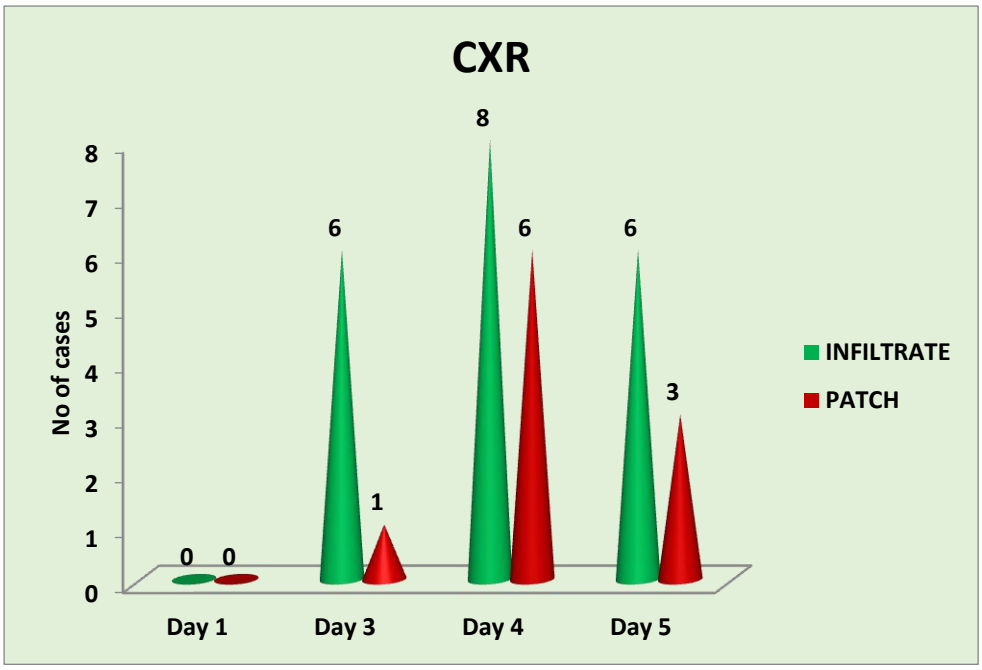
33.3% cases had Organo phosphorus compound poisoning, 16.7% cases had unknown compound poisoning, 13.3% cases had head injury, 13.3% cases had ischemic stroke, 6.7% cases had hemmorrhegic stroke. These were major number of cases in study

Table 2: Distribution of cases according to Co-Morbidities

CO-MORBIDITIES	N	%
TYPE2 DM	8	26.7
HYPERTENSION	7	23.3
THYROID DISORDER	4	13.3
CORONARY ARTERY DISEASE	5	16.7
COPD	2	6.7
OLD TB	2	6.7
SEIZZURE DISORDER	1	3.3
OLD CVA	3	10
BRONCHIAL ASTHMA	3	10

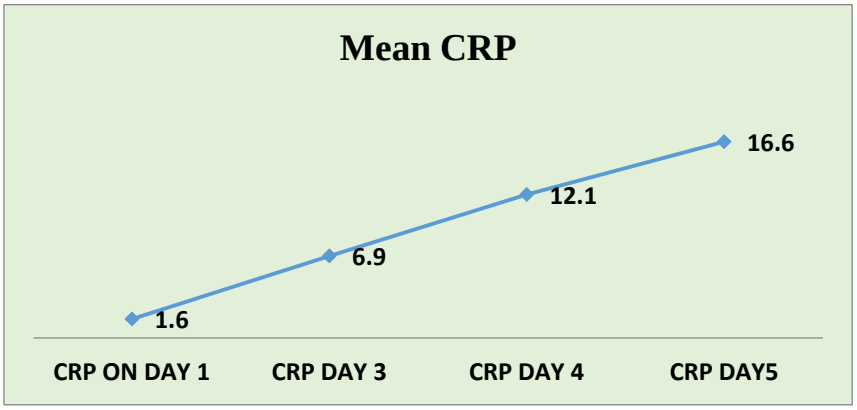
In our study 26.7% had Type 2 Diabetes , 23.3% of them had HTN followed by IHD 16.7% as the commonest co-morbidity.

Figure 2: Distribution CXR findings among the study population (N=30)



On Day 1 all cases had normal chest X Ray, On Day 3 chest X Ray showed infilterate in 6(20%) cases and patch(3.3%) in 1 case, On Day 4 inflitrates were present in 8(26.7%) cases and patch was present in 6 (20%) cases, On Day 5 infilterates were present in 6(20%) cases and patch in 3(10%) cases.

Figure 3: Mean CRP by days among study population



Mean CRP was 1.6 ±1.3 on Day 1, 6.9±3.2 on Day 3, 12.1±4.8 on Day 4 and was 16.6±6.9 on Day 5.

Table 3: ET Culture Growth and CPIS among study population

CPIS	≤6		>6		p value
ET CULTURE GROWTH	N	%	N	%	
Day 3	1	25	3	75	0.486
Day 4	**1**	**10**	**9**	**90**	**0.016***
Day 5	2	25	6	75	1.000

Note: *means significant difference at 5% level of significance

ET culture growth was found in 22(73.33%) of 30 patients who developed chest X ray infiltrate and patch.

Table 4: ET Culture Growth and CPIS among study population

CPIS	≤6		>6		p value
ET CULTURE GROWTH TOTAL	N	%	N	%	
	4	40	18	90	0.003* (SIG)

Note: *means significant difference at 5% level of significance

CPIS Score was calculated in 22 patients who developed early VAP which is confirmed by ET tube aspirate culture and sensitivity, CPIS Score was ≤6 in 1 case on Day 3, 1 case on Day 4 and in 2 cases on Day 5, CPIS Score was >6 in 3 cases on Day 3, 9 cases on Day 4 and 6 cases on Day 5, CPIS Score of > 6 in cases who developed early VAP which is confirmed by ET Culture and sensitivity was statistically significant on Day 4 with p value of 0.016 , But it was not significant on Day 3 and 5.

Over all statistical analysis of CPIS Value of >6 in 18 patients who developed early VAP was significant (P value 0.003).

Table 5: Mean CRP level by CPIS categories among study population

CPIS	≤6		>6		p value
CRP	Mean	SD	Mean	SD	
Day 3	6.8	2.0	7.9	1.8	0.491
Day 4	14.0	6.5	11.5	4.1	0.369
Day 5	12.4	2.6	18.0	7.5	0.362

Mean CRP and Clinical pulmonary infection score levels were not statistical significance, but there was serial rise in titre of CRP value from day 1 to day 5.

Table 6: ET Aspirate culture of the studied patients

Organism Isolated	No of patients (n=22)	%
Klebsiella pneumonia	12	54.5
Pseudomonas aeruginosa	10	45.5
Streptococcus pneumoniae	4	18.2
MRSA	8	36.4
Acinatobacter	6	27.3

ET Culture growth showed Klebsiella pneumonia in 12(54.5%) cases, Pseudomonas aeruginosa in 10(45.5%) cases, MRSA in 8(36.4%) cases, Acinatobacter in 6(27.3%) cases and streptococcus pneumonia in 4 (18.2%) cases. Multiple organisms have been isolated from same cases. Most of the organisms were multi drug resistant.

Table 7: Outcome among study population

OUTCOME	N	%
DEATH	12	40
DISCHARGE	17	56.7
DAMA	1	3.3
TOTAL	30	100

(DAMA-Discharge against medical advice)

Of 30 cases 17(40%) were discharged after treating, 12(56.7%) cases died and 1 (3.3%) diacharged against medical advice.

Figure 4: Comparison of CXR and CPIS among study population (N=30)

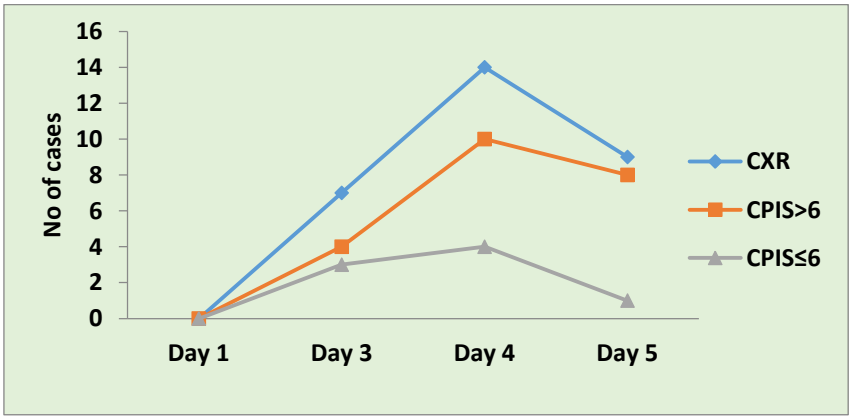


Table 8: Descriptive statistics of Subjects

Variables	Range	Mean	SD
AGE (IN YEARS)	24-79	45.9	15.8
HR/MIN @ADMISSION	56-120	94.1	18.1
RR cpm	12-38	21.2	7.9
SPo2 AT RA	64-97	88.3	7.4
GCS @ADMISSION	3-13	7.7	2.3
HB gm/dl	7.8-17.4	12.9	2.1
WBC COUNT	4170-16440	8687.3	3102.8
PLATELET COUNT (LACKS)	0.73-3.99	2.2	0.9
B.UREA	12-103	33.9	18.7
S.CREATINE mg/dl	0.5-4.3	1.0	0.7
LENGTH OF ICU STAY	6-40	16.2	9.7

Discussion

Ventilator associated pneumonia is important form of hospital acquired pneumonia, The single greatest risk factor for VAP is related to the duration of mechanical ventilation. Early VAP occurs within the first 5 days of intubation. Late-onset VAP occurs after 5 days, is more commonly caused by multidrug resistant (MDR) pathogens, and carries higher morbidity and mortality [10]. In our study, out of 30 cases who developed VAP on chest X ray, 22 (73.33%) cases had ET culture aspirate growth. CPIS Score was calculated in 22 patients who developed early VAP which is confirmed by ET tube culture and sensitivity CPIS Score was ≤6 in 4 patients , CPIS Score was >6 in18 patients . CPIS Score of > 6 in cases who developed early VAP which is confirmed by ET Culture and sensitivity was statistically significant on Day 4 with p value of 0.016 , But it was not significant on Day 3 and 5 .Over all statistical analysis of CPIS Value of >6 in 18 patients who developed early VAP was significant (P value 0.003). Out of 30 cases 12 patients succumbed to death. Most common factors associated with mortality includes VAP due to Multi drug resistant organism, underlying other co morbid conditions.

Ventilator-associated pneumonia is an important cause of morbidity and mortality in critically ill patients. Evidence-based clinical practice guidelines for the prevention, diagnosis, and treatment of ventilator-associated pneumonia may improve outcomes.

Enas Elsayed Mohamed et al in 2013 reported, serum CRP increased in 32 patients. CPIS of the studied patients at the onset of rising serum CRP ranged from 7 to 10 in 24 patients. In the first 5 days of intubation, 32 patients out of 80 patients had high CRP, those were 40% of the study population and 24 patients of those 32 patients had high CPIS; those were 30% of the study population and 75% of patients had high CRP[10] .

Pham et al reached a similar conclusion in their assessment of CPIS in the treatment of burn patients. These investigators retrospectively calculated the CPIS for 28 patients who had 46 quantitative cultures performed to diagnose VAP and tested the characteristics of a CPIS threshold of 6 for the diagnosis of VAP. They found that the CPIS had poor discrimination; patients with positive and negative culture results had a similar CPIS (the mean CPIS was 5.7 and 5.5, respectively), and the sensitivity and specificity of the CPIS was 30% and80%, respectively[14].

Smith et al used CRP as a useful sensitive marker of bacterial infection in cases of pneumonia. There was marked elevation of serum level of CRP within a few hours of Infection[15].

In this study CRP levels did not show any stastical significance with CPIS score in VAP patients, the reason mostly because CRP will be elevated in many condition like acute stress and associated infections like urinary tract infection, catheter related infections etc, but serial rise in CRP levels with CPIS score will be useful in detection of early VAP.

Conclusion

Clinical pulmonary infection score is an easy scoring system for the diagnosis of early Ventilator associated pneumonia. When the CPIS exceeded 6, there was an association with the presence of pneumonia in mechanically ventilated patients which was confirmed by ET tube aspiration culture .Serum CRP is an easy, available and cheap test so serial rise in titres of CRP in mechanically ventilated patients along with CPIS helps in the early diagnosis of pneumonia and aggressive treatment to prevent mortality and morbidity.

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