ORIGINAL ARTICLE

The Role of APACHE II Scoring System On The Development And Outcome Of VAP In Intensive Care Unit

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ABSTARCT:

OBJECTIVE: is to find out the role of APACHE II scoring system on the development and outcome of VAP, and also to investigate the pathogens with their susceptibility pattern related with VAP.

METHODOLOGY: This prospective cohort study of 90 patients was conducted in ICU of Lady Reading Hospital, Peshawar. **APACHE II** ("Acute Physiology and Chronic Health Evaluation II") score was calculated for every patient and is a severity of disease classification system, one of several ICU scoring systems. It was applied within 24 hours of admission of a patient to an ICU. VAP was recognized using CPIS of greater than 6. The incidence of VAP, death, frequency organisms isolated, their antibiotic sensitivity pattern, length of hospital stay & mechanical ventilation were evaluated.

RESULTS: Elevated APACHE II score was associated with high mortality rate and increased incidence of VAP. Mortality in non-VAP group was 44%, while 68.29% was in VAP group. Majority strains of *Pseudomonas* (38.46%) were resistant to beta-lactam antibiotics. All strains of *staphylococcus aureus* were MRSA and majority isolates of *Klebsiella pneumoniae* (54.54%) were extended-spectrum beta–lactamase generating. Mortality was greatest for infections of *Acinetobacter baumannii* (83.33%) and *Klebsiella pneumoniae* (54.53%).

CONCLUSION: APACHE II score can be used to stratify the risk of development of VAP and overall risk of death. Drug-resistant strains of a variety of pathogens are the main cause of VAP in our set up.

KEY WORDS: Ventilator-associated pneumonia (VAP); Mechanical ventilation; Clinical Pulmonary Infection Score (CPIS); APACHE II score;

INTRODUCTION:

Pneumonia in a mechanically ventilated patient, which develops 48 hours after endotracheal intubation, is called as Ventilator Associated Pneumonia **(VAP).** Clinical Pulmonary Infection Score **(CPIS)** of greater than six was used as diagnostic criteria for VAP [1, 2] **(Table II, III)**. VAP is a leading cause of morbidity and mortality in Intensive Care Unit (ICU) patients [3, 4, 5, 6]. Several countries have reported mortality rates ranging from 24% to 76%[7, 8]. Prevention of VAP was identified as a priority area for national action by the institute of medicine [9].

Acute Physiology and Chronic Health Evaluation II (APACHE II) is a severity of disease classification system, one of several ICU Scoring Systems. It is applied within 24 hours of admission of a patient to an ICU: an integer score from 0 to 71 is computed based on several measurements; higher scores correspond to more severe disease and a higher risk of death **(Table I).**

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APACHE II was designed to measure the severity of disease for adult patients admitted to intensive care units and can be used to stratify the risk of development of VAP. The lower age bound is not specified, but a good limit is to use Apache II only for patients aged 15 or older [10].

Patients acquiring VAP have poorer outcomes, longer lengths of stay in hospital and ICU [5], and higher mortality rate [1, 7, 8], but in one huge prospective cohort of mechanically ventilated patients, VAP is more expected in patients with underlying lung disease (acute or chronic), and VAP was associated with a noteworthy increase in ICU duration of stay but no increase in mortality [8].

Extended and haphazard use of antibiotics has affected antibiotic resistance patterns and the sensitivities of organisms frequently encountered in ICU. In this context, the objective of this study was planned to find out the role of APACHE II scoring system on the development and outcome of VAP; and also to investigate the pathogens with their susceptibility pattern related with VAP. This information will facilitate us in preparing an institutional antimicrobial therapy guideline, which will help us to decrease morbidity and mortality, length of treatment and stay in hospital, and also assisted us in cost reduction and prevention of development of multi-drug resistant strains.

METHODOLOGY:

This prospective cohort study was carried out in Intensive Care Unit (ICU), Post Graduate Medical Institute, Lady Reading Hospital of Peshawar, Pakistan over a period of two year from April 2010 to April 2012. Sample size was 90 patients, using estimated 8% prevalence of ventilator-associated pneumonia in ICU of Lady Reading Hospital, Peshawar, 95% confidence interval and 2.1% margin of error, using WHO software for sample size determination. Patients above 15 years of age regardless of any gender with normal chest x-rays, with no previous history of exposure to mechanical ventilation and were not suffering from pneumonia prior to taking on mechanical ventilator were included in the study. Moreover, Patients with Snake bites, Food poisoning, Drug Poisoning, Diabetic Ketoacidosis, Bilateral Diaphragmatic Paralysis, Post Traumatic Tetanus, Status epilipticus, Different kinds of Myopathies, Eclampsia, Guillan-barre Syndrome, Myasthenia Gravis and Bronchial Asthma were included in the Study, while those patients with sepsis/septic shock, cerebrovascular disease **(CVA),** chronic kidney disease **(CKD)** and patients with hepatic encephalopathy secondary to chronic liver disease **(CLD)** were excluded from the study. Informed written consent was taken from the close relative of every patient. Ethical Approval was obtained from Institutional Research and Ethics Board (IREB) before starting the study on VAP.

The patient related factors such as age, associated diseases, immune suppression, indication for mechanical ventilation, and the severity of illness based on APACHE II score were calculated during first 24 hours of admission in ICU with the help of APACHE II Calculator. APACHE II score can be used to describe the morbidity of a patient when comparing the outcome with other patients. Predicted mortalities are averaged for groups of patients in order to specify the group's morbidity **(Table I)**.

The diagnosis of VAP was established using Clinical Pulmonary Infection Score (CPIS) Calculator or Clinical Pulmonary Infection Score Calculation Method **(Table II, III),** which was assessed on every day until the patient was on ventilator support. CPIS of greater than six was used as diagnostic criteria for VAP. Early-onset VAP was defined as VAP

taking place within the first 04 days of hospitalization and Late-onset VAP was defined as VAP taking place after the first 04 days of hospitalization. Endotracheal aspirate was favored over protected specimen brush (PSB) sampling and broncho-alveolar lavage (BAL), as these methods are more invasive and studies have shown no mortality advantage of using these over endotracheal aspirate[11, 12, 13].

Endotracheal aspirate was obtained under aseptic method using a 22-inches (12F) suction catheter with a mucus Extractor, which was smoothly introduced through the endotracheal tube for a distance of approximately 25 centimeter. Every sample was processed in only one laboratory to reduce the chances of bias in the study results. The patients diagnosed with VAP on the basis of **CPIS** were started on early empirical antibiotic therapy, which was guided by the fact whether a multi-drug resistant pathogen was predictable. Later on, based on culture and sensitivity statement the management was modified.

The primary outcomes were to investigate out whether there is any association found between the severity of the underlying disease in a patient as assessed by APACHE II scoring system and mortality in patients with VAP. Other variables that were also assessed comprised frequency of different pathogens isolated, and their antibiotic sensitivity pattern, the incidence of VAP, age and gender of the patients, length of hospital stay and length of mechanical ventilation. Patients were divided into VAP, non-VAP, Survivors, and non-Survivors. Data was entered in Statistical Package for Social Sciences (SPSS) Versions 16 and was used for analysis. Data was subjected to univariate analysis using chi-square test and paired “t” test and “P” value $\leq$ 0.05 was considered statistically significant. Results are depicted as tables.

RESULTS:

The demographic characteristics of all 90 patients with VAP and non-VAP group included in the study are illustrated in the form of table and the incidence of VAP in this study was found out to be 45.55% **(Table IV).**

The clinical spectrum of cases specifies that the maximum number of cases registered in the study were of central nervous system infections (28 cases), followed by Suspected Poisoning (18 cases), Delayed recovery from anesthesia (15 cases), Neuromuscular disorders like Guillan-Barre syndrome, Myasthenia Gravis, Polymyositis and Dermatomyositis (8 cases) and Neuroparalytic snake bites (4 cases). There was no statistically significant association was found between the clinical conditions in VAP group, clinical conditions in non-VAP group, diagnosis in survivors, and diagnosis in non-survivors with “p” value = 0.08.

The mean APACHE II Score (during 24 hours of admission in Intensive Care Unit) of the patients who developed VAP was 23.37$\pm$ 9.182 **SD**, while those who did not develop VAP were 13.94$\pm$ 7.685 **SD.** The difference between the two groups was statistically significant with “P” value<0.00**.** The mean Acute Physiology Score (APS) component of APACHE II Score in VAP group was15.92$\pm$ 6.532 **SD** and was 8.10$\pm$ 5.162 **SD** in non-VAP group, the difference was statistically significant with “P” value<0.001. The mean Glasgow Coma Scale (GCS) in VAP group was 7.01$\pm$ 3.210 **SD,** while it was 5.12$\pm$ 3.126 in non-VAP group. This difference was also statistically significant with “P” value=0.043. On the other hand, no significant difference was found in the Age Score and Chronic Health Condition Score in two groups **(Table V).**

Of 41 patients diagnosed as VAP based on **CPIS** Score of more than six, 33 (80.48%) patients had mononmicrobial infection. The most common organism isolated was *Pseudomonas aeruginosa* followed by Methicillin-resistant *staphylococcus areus (MRSA), Klebsiella*, and *Acinetobacter Baumannii (A.Baumannii)*. Large amount strains of *P.aeuroginosa* were challenging to commonly used beta-lactam antibiotics known to be effective against *P.aeuroginosa*, with 5 (38.46%) isolates being resistant to ceftazidime, cefipime, cefoperazone +sulbactam. All 13 (100%) isolates being resistant to Polymyxin B and Colistin, while 9 (69.23%) isolates were sensitive to cabapenems. All 10 (100%) isolates of *S-aureus* were found to be resistant to oxacillin, showing the high prevalence of *MRSA* as a cause of VAP in our location. All 10 (100%) isolates were sensitive to Vancomycin and Linezolid. Out of 11 isolates of *Klebsiela pnemoniae*, 9 (81.81%) were found resistant to ceftriaxone, cefotaxime and ceftazidime, signifying a high prevalence of Extended- Spectrum beta-Lactamase (ESBL) producing organism as a cause of VAP in our ICU setting. Five isolates (45.45%) were sensitive to gatifloxacin and meropenem, while 6 (54.54%) were sensitive to only imipenem. All 11 (100%) isolates were sensitive to both colistin and polymyxin B. Of the 8 isolates of *Acintobacter baumannii* were sensitive to Polymyxin B and colistin, but only 3 isolates out of 8 (100%) were found sensitive to carbapenems**.**

The primary outcome measure evaluated in the study was mortality. The overall mortality was 46.66%, with death of 42 patients during the course of their ailment. Mortality in VAP group was 68.29% with death of 28 patients out of 41, who developed VAP during course of their disease process. Mortality in non-VAP group was significantly low at 44%, with death of 22 patients out of 49.The difference between the two groups was statistically significant with “P” value<0.001. On the other hand, there was no statistically significant difference noted between the mortality in late-onset VAP as compared to early-onset VAP with “P” value=0.351. The overall threat of mortality was stratified by the APACHE II Score during the 1st 24 hours of admission in ICU. The mean APACHE II score among survivors was 14.74$\pm$7.22 **SD** and among non-survivors were 24.28$\pm$ 7.94 **SD,** which is statistically significant difference (p<0.001). The mortality rates was high in patients with central nervous system infections or neuromuscular disorders (58%), suspected poisoning (46%) and in cases of delayed recovery from anesthesia (22%), but all cases with neuropralytic snake bites were stay alived. Mortality rate was greatest in infections caused by *Acintobacter baumannii*, 5 (83.33%) of 6 patients died during the course of illness. The next most deadly organism was *Klebsiela Pneumoniae*, with a mortality rate of 54.54%.

Secondary outcome measures judged were the length of mechanical ventilation and duration of hospital stay. The mean duration of mechanical ventilation in non-VAP group in days was 6.64$\pm$4.248 **SD**, and 13.48$\pm$ 6.828 **SD** in VAP group. The mean duration of stay (in days) in hospital in the non-VAP group was 10$\pm$6.128 **SD,** while 17.22$\pm$11.22 **SD** in VAP group. Both these parameters were noted to be significantly elevated in VAP group as compared to non-VAP group with “P”value <0.001.

TABLE I: THE APACHE II ("ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVALUATION II") SEVERITY OF DISEASE CLASIFICATION SYSTEM CALCULATOR
(Table taken from Wikipedia, the free encyclopedia)

Physiologic Variable	**High Abnormal Range**					**Low Abnormal Range**				
	+4	**+3**	**+2**	**+1**	**0**	**+1**	**+2**	**+3**	**+4**	**Points**
Temperature - rectal (°C)	≥41°	39 to 40.9°		38.5 to 38.9°	36 to 38.4°	34 to 35.9°	32 to 33.9°	30 to 31.9°	≤29.9°	
Mean Arterial Pressure - mm Hg	≥160	130 to 159	110 to 129		70 to 109		50 to 69		≤49	
Heart Rate (ventricular response)	≥180	140 to 179	110 to 139		70 to 109		55 to 69	40 to 54	≤39	
Respiratory Rate (non-ventilated or ventilated)	≥50	35 to 49		25 to 34	12 to 24	10 to 11	6 to 9		≤5	
Oxygenation: A-aDO_2 **or** PaO_2 (mm Hg) a. FIO_2 ≥0.5 record A-aDO2 b. FIO_2 <0.5 record PaO2	≥500	350 to 499	200 to 349		<200 PO2>70	 PO2 61 to 70		 PO2 55 to 60	 PO2<55	
Arterial pH (preferred) Serum HCO3 (venous mEq/l) (not preferred, but may use if no ABGs)	≥7.7 ≥52	7.6 to 7.69 41 to 51.9		7.5 to 7.59 32 to 40.9	7.33 to 7.49 22 to 31.9		7.25 to 7.32 18 to 21.9	7.15 to 7.24 15 to 17.9	<7.15 <15	

Serum Sodium (mEq/l)	≥180	160 to 179	155 to 159	150 to 154	130 to 149		120 to 129	111 to 119	≤110	
Serum Potassium (mEq/l)	≥7	6 to 6.9		5.5 to 5.9	3.5 to 5.4	3 to 3.4	2.5 to 2.9		<2.5	
Serum Creatinine (mg/dl) Double point score for acute renal failure	≥3.5	2 to 3.4	1.5 to 1.9		0.6 to 1.4		<0.6			
Hematocrit (%)	≥60		50 to 59.9	46 to 49.9	30 to 45.9		20 to 29.9		<20	
White Blood Count (total/mm3) (in 1000s)	≥40		20 to 39.9	15 to 19.9	3 to 14.9		1 to 2.9		<1	
Glasgow Coma Score (GCS) Score = 15 minus actual GCS										
A. Total Acute Physiology Score (sum of 12 above points)										
B. Age points (years) ≤44=0; 45 to 54=2; 55 to 64=3; 65 to 74=5; ≥75=6										
C. Chronic Health Points (see below)										
Total APACHE II Score (add together the points from A+B+C)										

Chronic Health Points: If the patient has a history of severe organ system insufficiency or is immunocompromised as defined below, assign points as follows:
5 points for non-operative or emergency postoperative patients
2 points for elective postoperative patients
Definitions: organ insufficiency or immunocompromised state must have been evident **prior** to this hospital admission and conform to the following criteria:

- **Liver** – biopsy proven cirrhosis and documented portal hypertension; episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic failure/encephalopathy/coma.
- **Cardiovascular** – New York Heart Association Class IV.
- **Respiratory** – Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction (i.e., unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40 mmHg), or respirator dependency.
- **Renal** – receiving chronic dialysis.
- **Immunocompromised** – the patient has received therapy that suppresses resistance to infection (e.g., immunosuppression, chemotherapy, radiation, long

term or recent high dose steroids, or has a disease that is sufficiently advanced to suppress resistance to infection, e.g., leukemia, lymphoma, AIDS).

INTERPRETATION OF SCORE:

SCORE	DEATH RATE (%)
0-4	4
5-9	8
10-14	15
15-19	25
20-24	40
25-29	55
30-34	75
>34	85

Table II: Clinical Pulmonary Infection Score ® Calculator
(Table taken from Wikipedia, the free encyclopedia in the internet)

Parameter	**Score** (check all that apply)
Temperature (Celsius)	○ ≥36.5 and ≤38.4 ○ ≥38.5 and ≤38.9

	○ ≥39.0 or ≤36.5
White Blood Cell Count	○ ≥4,000 and ≤11,000 ○ <4,000 or >11,000 ○ <4,000 or >11,000 AND band forms ≥50%
Tracheal Secretions	○ None or scant ○ Non-purulent ○ Purulent
PaO_2/FiO_2 (*ARDS is defined as a PaO_2/FiO_2 ≤200, PAOP ≤18 mmHg, and acute bilateral infiltrates)	○ >240, ARDS* or pulmonary contusion ○ ≤240 and no ARDS*
Chest Radiograph	○ No infiltrate ○ Diffuse (or patchy) infiltrate ○ Localized infiltrate

TABLE III: CLINICAL PULMONARY INFECTION SCORE CALCULATION

PARAMETER	POINTS
TEMPERATURE (^0C)	
36.5-38.4	**0**
38.5-38.9	**1**
≥ 39.0 and ≥ 36.0	**2**
BLOOD LEUKOCYTE LEVEL, LEUKOCYTE/mm^{-3}	
4000-11000	**0**
<4000 or >11000	**1**
Plus band forms ≥ 500	**2**
TRACHEAL SECRETIONS	
< 14+	**0**
≥ 14+	**1**
Plus purulence	**2**

OXYGENATION, PO_2:FiO_2, mmHg	
> 240 or ARDS * Pulmonary Contusion	**2**
≤ 240 and no ARDS	**0**
PULMONARY RADIOGRAPH FINDING	
No infiltrate	**0**
Diffuse or Patchy infiltrate	**1**
Localized infiltrate	**2**
CULTURE OF TRACHEAL ASPIRATE SPECIMEN (SEMIQUANTITATIVE:0-1,-2, OR 3+)	
Pathogenic bacteria cultured ≤ 1 or No Growth	**0**
Pathogenic bacteria cultured > 1+	**1**
Plus same pathogenic bacteria on Gram's Stain > 1+	**2**

ARDS: ACUTE RESPIRATORY DISTRESS SYNDROME.
PO_2:FiO_2: RATIO OF PARTIAL PRESSURE OF ARTERIAL OXYGEN TO THE FRACTION OF INSPIRED OXYGEN.

TABLE IV: AGE AND SEX DISTRIBUTION OF VAP AND NON-VAP GROUP OF PATIENTS (n=90).

AGE GROUP	**NON-VAP GROUP (n=49)**		**VAP GROUP (n=41)**	
YEARS	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**
15-20	11	22.44	09	21.95
21-30	15	30.61	10	24.39
31-40	08	16.32	06	14.63
41-50	08	16.32	05	12.19
51-60	05	10.20	05	12.19
60-70	02	04.08	06	14.63
SEX				
FEMALE	19	38.77	19	56.35
MALE	30	61.22	22	53.65

TABLE V:COMPARISON OF INDIVIDUAL SCORES AND TOTAL APACHE II SCORE (n=90).

SCALE	**NON-VAP GROUP (n=49)**		**VAP GROUP (n=41)**		**SIGNIFICANCE OF DIFFERENCE**
	MEAN	**SD** (standard deviation)	**MEAN**	**SD** (standard deviation)	**P-VALUE**

Acute Physiology Score	7.92	6.021	14.45	7.43	<0.001
Glasgow Coma Scale	5.72	3.456	8.01	4.461	0.043
Age Score	1.79	1.823	1.85	1.762	0.162
Chronic Health Condition	0.72	1.631	0.89	1.920	0.565
Total APACHE II Score	24.12	8.89	13.94	7.680	<0.001

DISCUSSION:

APACHE II score was significant parameter to stratify risk of developing VAP. A significantly elevated value was observed in VAP group. In a similar study done by Panwar et al [14], it was accomplished that the patients who develop VAP had a significantly higher APACHE II score within the first 24 hours of admission. Furthermore, statistically significant dissimilarity was observed between VAP and non-VAP group with respect to the mean of Acute Physiology Score (APS) component and Glasgow Coma Score (GCS) of APACHE II score, but no significant difference was observed in the Age Score and Chronic Health Condition score in the two groups. The mean APACHE II score was significantly higher in non-survivors than survivors in this study. Moreover, the derangements in Acute Physiology Score and the severity of the underlying ailment of the patient at the time of admittance are more responsible for the mortality than underlying chronic health condition. A similar association of mortality with high means APACHE II score was also noted in a study by Panwar et al [14].

The results of our study are comparable to the local study done by Kidwai et al[16]. Study carried out by Kidwai et al. has evidently shown that higher incidence of infection with Gram Negative Organisms are causing VAP. They have demonstrated that Ceftazidime, imipenem, ciprofloxacin and amikacin resistance rates were higher against *Acinetobacter baumanni*, which showed moderate resistance against cefoperazone/sulbactum. Furthermore, they have also demonstrated that Ciprofloxacin and ceftazidime resistance rates were also elevated against *Pseudomonas aeruginosa*, *Enterobacter spp.* and *E. coli* [16]. In contrast to the results of the study by Kidwai et al, our study did not reveal polymicrobial pathogens in any of isolate taken for the diagnoses of VAP, and E. coli was also not seen in even a single case. Furthermore, he had not applied **APACHE II** scoring system on any patient.

The incidence of VAP in this study was 45.55%, which correlates well with other similar study done by Panwar et al, in which the incidence of VAP was 47%, depending upon the diagnostic criteria used [14]. Incidence of VAP was 28.04% in the study done by Gupta et al [18], which is quite low as compared to our study. This difference is because of the exclusion of the patients with cerebrovascular diseases and sepsis with or without septic shock from our study. There was no statistically significant association found between

the age of the patients, and gender distribution. Also both males and females are equally predisposed to develop VAP [18].

Kollef and coworkers demonstrated the patients with VAP due to high risk pathogens (*Pseudomonas aueroginosa, Acinobacter baumannii and stenotrophomonas Maltophilia*) had significantly higher hospital mortality rate (65%) than patients with late- onset VAP due to other microbes (31%) or patients without late-onset pneumonia [19]. Concerning gram-positive pathogens, in a study comparing VAP due to *MRSA or MSSA* (*Methicillin-sensitive staphylococcus aureus*), mortality was found to be directly attributable to pneumonia for 86% of the former cases versus 12% of the later, with a relative risk of death equal to 20.7 for *MRSA* Pneumonia [20]. The overall depiction of antibiotic sensitivity pattern of the pathogens isolated from patients in our study recommends that a large number of these are highly resistant to the frequently used drugs and is main cause of VAP in our set up. Mortality was also predisposed by the type of organism isolated. It is peak for infections caused by *Acinetobacter bauamannii* (83.33%) and *Klebsiella pneumoniae* (54.54%).

Though it was not the objective of our study. An incidental finding was noted in this study, that the risk of VAP was increased to a great extent in patients who underwent re-intubation. A similar high incidence of VAP was found to be associated with re-intubation in other studies [21]. This might be because, that the patient who required re-intubation would have been susceptible to the aspiration in the interval between extubation and re-intubation. This underlies the significance of proper weaning practices in the prevention of VAP and associated mortality.

The only limitation in our study is that, we had excluded the patients $\leq$15 years of age, but this is because of the reason that a good limit is to use **APACHE II** only for patients aged 15 or older. This might play a role as a confounding variable to increase the chances of bias in the results.

CONCLUSION:

APACHE II score is a good parameter to signify the risk of death as well as the risk of developing VAP. The results this type of local studies should be collected at all centers, as such information can facilitate in guiding the early empirical antibiotic treatment, which would help us in preventing the development of additional resistant strains like *LRSA*, *Burkholderia Cepacia complex* and *Stenotrophomonas Maltophilia* etc.

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