Original Article

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Comparison between the Clinical Pulmonary Infection Score and Modified Centre for Disease Control Criteria for Diagnosis of Ventilator-associated Pneumonia: A Cross-sectional Study

Internal Medicine Section

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ABSTRACT

Introduction: Ventilator-Associated Pneumonia (VAP) is a frequent complication of Mechanical Ventilation (MV). The incidence of VAP is not precisely known and ranges from 13 to 51 per 1,000 ventilator days. A uniform surveillance definition for VAP is not available. The Centre for Disease Control (CDC)/ National Healthcare Safety Network (NHSN) and the Clinical Pulmonary Infection Score (CPIS) algorithms are widely used.

Aim: To compare the modified CDC criteria and the CPIS algorithm for VAP.

Materials and Methods: A cross-sectional study was conducted at the respiratory care unit of the Department of Respiratory Medicine at RG Kar Medical College and Hospital in Kolkata, West Bengal, India, over a period of 18 months, from January 2021 to June 2022. A total of 60 adult patients on MV for more than 48 hours, with a high index of suspicion for VAP, clinically and radiologically, were included in this study. The microbiological (bacteriological quantitative culture) and radiological profiles {CXR parenchymal opacities, Ultrasonography (USG) and Contrast-Enhanced Computed Tomography (CECT) thorax} of VAP infections were assessed and compared. Statistical analysis was conducted after entering the data into a Microsoft Excel spreadsheet.

Results: Among the 60 patients, most were male (76.67%) and aged between 51 and 60 years (40%). A total of 48 (80%) patients had a positive CPIS score, while 42 (70%) had positive modified CDC criteria. A fair degree of concordance was found between the two algorithms. *Pseudomonas* was the most common organism identified in both early and late-onset VAP. Among all antibiotics, Polymyxin B was found to be sensitive to all the organisms.

Conclusion: The VAP is the most frequent infection associated with Intensive Care Unit (ICU) admissions. Polymicrobial aetiology and MDR strains were found in a significant number of cases. In the present study, the CPIS criteria demonstrated a fair concordance with the modified CDC criteria and slightly better sensitivity than the modified CDC criteria in diagnosing VAP.

Keywords: Intensive care unit infection, Lung infection score, *Pseudomonas*

INTRODUCTION

The VAP impacts 10-20% of patients requiring MV and nearly doubles the risk of mortality in critically ill patients [1]. Consequently, the prevention and early diagnosis of VAP have emerged as high priorities. However, the prevention of VAP is hindered by challenges related to its definitions and diagnosis. In particular, surveillance definitions for VAP pose significant problems due to interobserver variability and a lack of specificity and sensitivity [2]. There is no gold standard for the surveillance of VAP, but the most widely used method is the CDC/NHSN algorithm, which facilitates clinical and microbiological diagnosis of VAP [3]. However, this algorithm is also prone to interobserver variability.

The CPIS is another useful tool with an easy scoring system but requires microbiological data that may not be immediately available [4]. There is a lack of sufficient data comparing the CDC and CPIS algorithms, particularly from India. This absence of updated national studies is creating a knowledge gap in the prevention and treatment of VAP. The present study aimed to evaluate the degree of agreement between the modified CDC criteria and the CPIS criteria. Additionally, the microbiological (bacteriological quantitative culture) and radiological profiles (CXR parenchymal opacities, USG and CECT thorax) of VAP infections were assessed and compared.

MATERIALS AND METHODS

A cross-sectional study was conducted in the respiratory care unit of the Department of Respiratory Medicine at RG Kar Medical College and Hospital in Kolkata, West Bengal, India, over a period of 18 months, from January 2021 to June 2022. After obtaining approval from the review committee and the Institutional Ethics Committee (IEC No. RKC/344, Date: 15.02.2021), patients admitted to the respiratory care unit who fulfilled the inclusion criteria were considered for the study.

Sample size calculation: The sample size was calculated to be 60, based on a prevalence of VAP of 25% [5]. The sample size calculation was carried out with the assistance of a statistician.

Inclusion criteria: All patients who had been mechanically ventilated for more than 48 hours and those in whom VAP was clinically suspected were included.

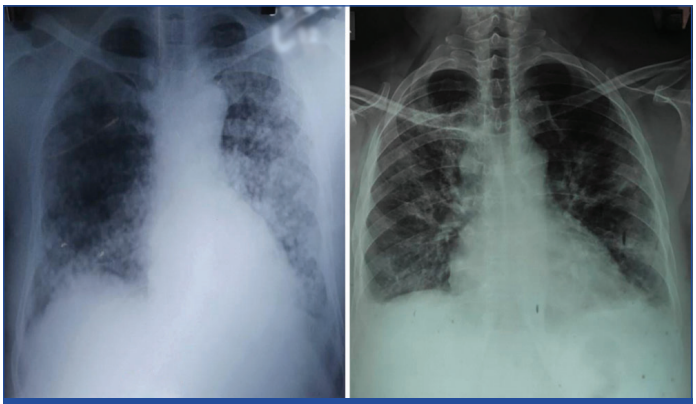
Exclusion criteria: Patients who had pneumonia before or within 48 hours of intubation, patients below 18 years of age and patients unwilling to provide consent were excluded.

Study Procedure

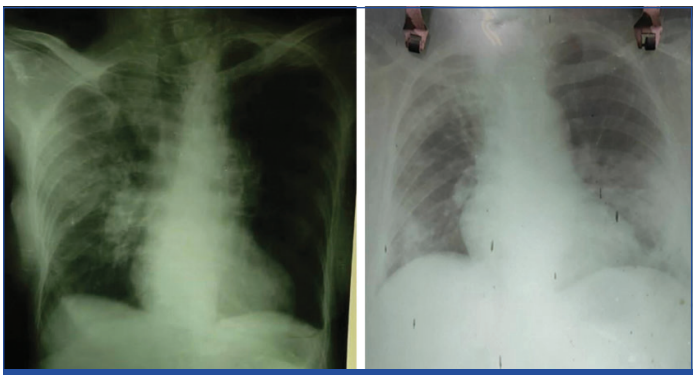
Early VAP is defined as an infection occurring within four days of hospitalisation and MV, while late VAP is designated for infections that occur five days or more post-admission [6]. Respiratory failure

is conventionally defined by an arterial oxygen tension (PaO_2) of <8.0 kPa (60 mmHg), an arterial carbon dioxide tension ($PaCO_2$) of >6.0 kPa (45 mmHg), or both. Additionally, failure of oxygenation is classified as hypoxaemic (Type 1) and failure of ventilation is defined as hypercapnic (Type 2) [7].

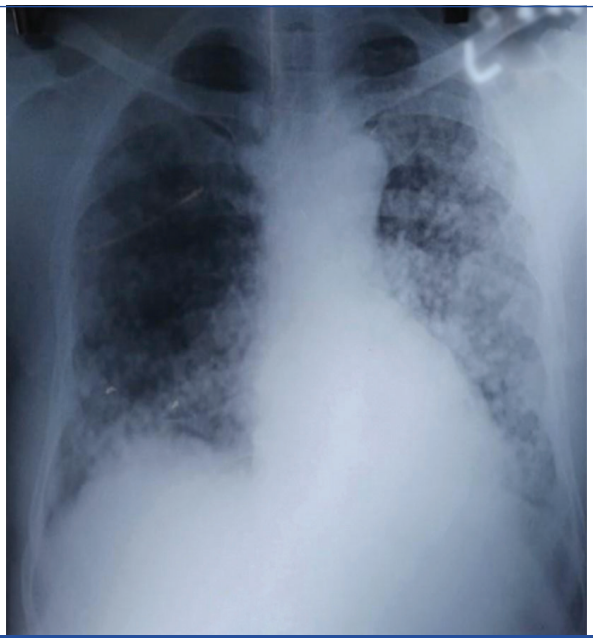
History taking and clinical examinations were performed, followed by laboratory investigations including chest X-ray [Table/Fig-1-5], Arterial Blood Gas (ABG) analysis, thoracic USG, contrast-enhanced CT scan of the thorax, endotracheal aspirates and fibreoptic bronchoscopy with bronchoalveolar lavage as required. Culture sensitivity tests of the collected specimens were conducted.



[Table/Fig-1]: Multilobar infection with mild effusion.
[Table/Fig-2]: Patchy pneumonitis in both lungs. (Images from left to right)



[Table/Fig-3]: Extensive consolidation of the right lung.
[Table/Fig-4]: Bilateral pneumonitis. (Images from left to right)



[Table/Fig-5]: Bilateral pneumonia with multilobar distribution.

Evaluation was carried out using the modified CDC criteria [8,9], which include assessments like chest X-ray results, total leucocyte count, fever and clinical parameters like mental status, respiratory secretions, oxygenation status, respiratory rate and the presence of rhonchi and crepitations. The CPIS criteria [6], which encompass temperature, chest X-ray, total leucocyte count, respiratory secretion (including quantity, nature and bacteriology) and oxygenation, were applied in all cases. The concordance between the two criteria was then estimated.

STATISTICAL ANALYSIS

Statistical analysis was conducted after entering the data into a Microsoft Excel spreadsheet. Quantitative variables were expressed as mean±SD. A p-value of <0.05 was considered statistically significant. Confounding factors were addressed using appropriate methods of adjustment. The correlation between the CDC and CPIS algorithms was measured using Cohen's Kappa statistic (κ). κ is a robust tool for measuring observational correlation, accounting for variation due to chance. The standard error for κ was calculated using the original equation developed by Cohen [10]. A κ value of <0.20 indicates poor agreement, 0.21-0.40 indicates fair agreement, 0.41-0.60 indicates moderate agreement and values of 0.61-0.80 and 0.81-1.00 indicate very good agreement [11].

RESULTS

A total of 60 patients were included in the study, with a predominance of males and the most common age group was 51-60 years. Regarding co-morbidities, the majority of patients had chronic Obstructive Airway Disease (OAD) (68%), while 45% had Diabetes Mellitus (DM) and hypertension [Table/Fig-6].

Parameters	Category	n (%)
Age group (in years)	< 40	2 (3.33%)
	41-50	7 (11.67%)
	51-60	24 (40%)
	61-70	19 (31.67%)
	>70	8 (13.33%)
Gender	Female	14 (23.33%)
	Male	46 (76.67%)
Co-morbidities	Hypertension	27 (45%)
	Diabetes mellitus	27 (45%)
	Obstructive airway disease	41 (68%)

[Table/Fig-6]: Patients' demography profiles and co-morbidities.

Most patients experienced early onset VAP and leucocytosis was most common in those with late onset VAP [Table/Fig-7]. Type 2 respiratory failure was observed in 51.7% of patients, with mean ages of >60 for both females (60.3%) and males (62%) [Table/Fig-8].

	White Blood Cells (WBC) count		
	4000-12000	>12000	Total
Onset of VAP	n (%)	n (%)	n (%)
Early	17 (62.96)	14 (42.42)	31 (100)
Late	10 (37.04)	19 (57.58)	29 (100)

[Table/Fig-7]: Onset of Ventilator-Associated Pneumonia (VAP) vs. WBC count (µL).

Oxygenation status	n (%)
No respiratory failure	8 (13.3)
Type 1 respiratory failure (failure of oxygenation)	21 (35)
Type 2 respiratory failure (failure of ventilation)	31(51.7)
Total	60 (100)

[Table/Fig-8]: Oxygenation status and respiratory failure in the patients.

Among the 60 patients, 51 had chest X-ray infiltrates, of which 42 exhibited new purulent sputum or a change in sputum character, along with worsening symptoms. Consequently, 42 patients (70%) had positive modified CDC criteria [Table/Fig-9]. Elderly patients

CDC criteria	n (%)	Female Mean age (in years)	Male Mean age (in years)
Chest infiltrates	51 (85)	59.5	60.7
Fever	37 (61.67)	58.2	61.3
Abnormal WBC	33 (55)	60.6	62
Altered mental status	18 (30)	52.8	65.4
New purulent/change in character of sputum	42 (70)	57	61.9
Worsening of gas exchange	40 (66.67)	58.3	61.1
Worsening of symptoms	42 (70)	57	61.2
Rales or Bronchial BS	34 (56.67)	58.8	59.9

[Table/Fig-9]: Characteristics of CDC criteria.
BS: Breath sounds

predominated according to the modified CDC criteria, accounting for 71.5% of the age group 51-70 years [Table/Fig-10].

Age group (in years)	CDC	
	No n (%)	Yes n (%)
<41	0	2 (4.8)
41-50	3 (16.7)	4 (9.5)
51-60	7 (38.9)	17 (40.5)
61-70	6 (33.3)	13 (31)
>70	2 (11.1)	6 (6)
Total	18 (100)	42 (100)

[Table/Fig-10]: Age group vs Modified CDC criteria.

According to the CPIS, most patients were male (72.9%) [Table/Fig-11]. Late onset VAP was more common according to both the CDC and CPIS algorithms, with patients exceeding 50%. The CPIS demonstrated better sensitivity compared to the modified CDC criteria, at 80% versus 70%. There was a fair degree of agreement between the CPIS and modified CDC criteria, with Cohen's κ 0.34 [Table/Fig-12].

Gender	CPIS	
	Negative (≤6) n (%)	Positive (>6) n (%)
Female	1 (8.3)	13 (27.1)
Male	11 (91.7)	35 (72.9)
Total	12 (100)	48 (100)

[Table/Fig-11]: Clinical Pulmonary Infection Scores (CPISs) with gender.

Onset of VAP	Parameters	
	CDC=Y n (%)	CPIS >6 n (%)
Early	18 (42.9)	23 (47.9)
Late	24 (57.1)	25 (52.1)
Total	42 (70)	48 (80)

[Table/Fig-12]: Onset of VAP vs. clinical parameters.

The most commonly identified organisms were *Pseudomonas* i.e., 16 (26.6%) isolates, closely followed by *Acinetobacter* and *Klebsiella*, with a similar distribution in both early and late onset VAP cases [Table/Fig-13].

Regarding antibiotic susceptibility, *Pseudomonas aeruginosa* exhibited 100% resistance to amoxiclav, ceftazidime and vancomycin but showed significant sensitivity to Polymyxin B (93.8%) [12], piperacillin-tazobactam (87.5%) [13] and meropenem (81.3%) [14]. *Acinetobacter baumannii* was also 100% resistant to amoxiclav, ceftazidime, vancomycin and cotrimoxazole, but demonstrated sensitivity to Polymyxin B (91.7%) [11], amikacin (83.3%) [10] and imipenem (75%) [6]. Among all antibiotics tested, Polymyxin B was found to be effective against all the organisms [Table/Fig-14].

Organism	Onset of VAP		Total n (%)
	Late (≥5 days) n (%)	Early (<5 days) n (%)	
P. aeruginosa	7 (24.14)	9 (29.03)	16 (26.66%)
A. baumanii	4 (13.79)	8 (25.81)	12 (20%)
K. pneumoniae	6 (20.69)	4 (12.9)	10 (16.7%)
E. coli	5 (17.24)	3 (9.68)	8 (13.3%)
S. pneumoniae	2 (6.9)	4 (12.9)	6 (10%)
S. aureus	2 (6.9)	2 (6.45)	4 (6.7%)
Proteus	2 (6.9)	0 (0)	2 (3.3%)
H. influenzae	1 (3.45)	0 (0)	1 (1.7%)
Moraxella	0 (0)	1 (3.23)	1 (1.7%)

[Table/Fig-13]: Microbial organisms vs. the onset of VAP.

DISCUSSION

Suspicion and clinical criteria continue to serve as the foundation for VAP diagnosis, however, the criteria used for diagnosis vary widely [15]. Historically, the diagnosis of VAP has relied on two or three components: 1) systemic signs of infection; 2) new or worsening infiltrates observed on chest imaging; and 3) microbiological evidence of pulmonary parenchymal infection when available [11]. Various diagnostic algorithms have been proposed to standardise the diagnosis, but discrepancies remain regarding which one is the most effective.

In the present study, the most common age group was 51-60 years (40%), with a predominant male gender (76.67%). In the study conducted by Dey A and Indira B the most affected age group for VAP was found to be 46-60 years [14]. Similarly, in the study by Apostolopoulou E et al., 71% of patients were male and 29% were female [13].

Risk factors like diabetes mellitus and oxygenation status were studied. In the present study, 45% of patients had diabetes, with a higher proportion of male patients. Martins M et al., found the burden of diabetes to be around 35.5% [12]. Additionally, 68% of patients in our study had a history of obstructive airway disease and Type 2 respiratory failure was more prevalent (51.7%). The mean age for males with Type 2 failure was 62 years, while for females it was 60.3 years. Thus, elderly patients with a history of obstructive airway disease predominated, with a significant number of them being diabetic. In this study, 51.66% (n=31) experienced early onset VAP, whereas 48.33% (n=29) had late onset VAP. Golia S et al., reported that out of 52 VAP cases in a tertiary care hospital in India, 23 (44.23%) were early onset and 29 (55.77%) were late onset [16].

Regarding organisms identified in the present study, the most common were *Pseudomonas aeruginosa* and *Acinetobacter baumannii* (both 25.81%) in cases of early onset VAP. For late onset VAP, the predominant organisms were *Pseudomonas aeruginosa* (24.14%) and *Klebsiella pneumoniae* (20.69%). Similar results were noted in a study by Dey A and Indira B conducted in Manipal, where the most common organism causing both early and late onset VAP was *Acinetobacter* (48.94%), followed by *Pseudomonas aeruginosa* (25.53%) [14]. ESKAPE organisms (*Enterococcus*, *Staphylococcus aureus*, *Klebsiella*, *Acinetobacter*, *Pseudomonas* and *Enterobacter* spp.) accounted for 80% of VAP episodes, according to a study conducted by Joseph NM et al., in a tertiary care hospital in India [17].

In the present study, 48 (80%) of patients were positive for VAP according to CPIS criteria, compared to 42 (70%) as per the modified CDC criteria [17]. In a study by Safdar N et al., in the USA, out of 73 ventilated patients, 36 (49.31%) met CDC

Antibiotics	*A. baumanii*	*E. coli*	*H. influenzae*	*K. pneumoniae*	*Moraxella*	*P. aeruginosa*	*Proteus*	*S. aureus*	*S. pneumoniae*
Amoxyclav	0	0	0	0	0	0	33.3%	25%	0
Ceftriaxone	0	12.5%	0	11.1%	0	0	33.3%	25%	0
Levofloxacin	33.3%	62.5%	100%	11.1%	0	62.5%	33.3%	25%	50%
Tigecycline	58.3%	25%	0	44.4%	100%	31.3%	33.3%	75%	83.3%
Cefo-Sulbactum	50%	50%	0	0	0	31.3%	33.3%	25%	66.7%
Polymyxin B	91.7%	100%	100%	66.7%	100%	93.8%	33.3%	25%	100%
Pip-Tazo	41.7%	50%	0	44.4%	0	87.5%	0	50%	100%
Meropenem	75%	100%	0	77.8%	0	81.3%	66.7%	25%	83.3%
Imipenem	33.3%	50%	0	11.1%	0	31.3%	33.3%	25%	50%
Amikacin	83.3%	87.5%	100%	55.6%	100%	31.3%	0	0	33.3%
Linezolid	16.7%	0	0	0	0	6.3%	0	75%	16.7%
Vancomycin	0	12.5%	0	11.1%	0	0	0	100%	0
Teicoplanin	16.7%	50%	0	33.3%	0	18.8%	0	75%	0
Cotrimoxazole	0	25%	0	44.4%	0	6.3%	33.3%	0	0

[Table/Fig-14]: Pattern of antibiotic susceptibility of different organisms.

criteria for VAP; 35 (47.94%) were classified as high likelihood for the original CPIS, while 14 (19.17%) were high likelihood for the modified CPIS [11]. A study from JIPMER, Puducherry, India, conducted by Gunalan A et al., showed that 93 (34.1%) of patients had VAP according to CPIS criteria, compared to 33 (12.1%) as per NHSN/CDC criteria [18]. Safdar N et al., found that the original CPIS exhibited a high degree of concordance with CDC criteria, with Cohen's kappa statistic of 0.81 [11]. The modified CPIS showed a fair to moderate concordance with κ of 0.39. Patients who met CDC criteria had a mean CPIS score of 7.9 and a mean modified CPIS score of 6.3. Rahimbashar F et al., from Iran showed that using Hospital in Europe Link for Infection Control through Surveillance (HELICS) as the reference standard, the sensitivity and specificity for each of the assessed diagnostic algorithms were as follows: CDC/NHSN (sensitivity 54.2%; specificity 100%) and CPIS (sensitivity 68.75%; specificity 95.23%) [15]. The present study indicated a fair degree of agreement between the CPIS and modified CDC criteria, with Cohen's kappa value of 0.34. The CPIS criteria showed a sensitivity of 80%, while the modified CDC had a sensitivity of 70%. The mean CPIS score in patients diagnosed according to the CDC criteria was 7.7.

In the present study, the production of Extended-Spectrum Beta-Lactamases (ESBL) and Metallo-Beta-Lactamases (MBL) was observed quite commonly in infections caused by *Pseudomonas*, *Acinetobacter* and *Klebsiella*. Ahmed W et al., from Pakistan elucidated that *Klebsiella pneumoniae* was 100% resistant to piperacillin, vancomycin and meropenem [19]. A study by Sarkar MD et al., from Bangladesh revealed that *Acinetobacter baumannii* was 30% sensitive to tigecycline [20].

Limitation(s)

The present study employed a cross-sectional design and there was no provision for blinding. The study was conducted during the Coronavirus Disease 2019 (COVID-19) pandemic, which posed certain limitations.

CONCLUSION(S)

Polymicrobial aetiology and MDR strains were found in a significant number of cases. Late onset VAP was more common according to both the CDC and CPIS. ESBL producing MDR organisms, such as *Pseudomonas aeruginosa* and *Acinetobacter*, were the most prevalent. The CPIS criteria demonstrated good concordance with the modified CDC criteria and slightly better sensitivity than the modified CDC criteria in diagnosing VAP.

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