RESEARCH PAPER

Clinical Pulmonary Infection Score to Diagnose Ventilator-associated Pneumonia in Children

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Background: There is a need to validate and suggest easy clinical method for diagnosis of ventilator-associated pneumonia (VAP) in developing countries.

Objectives: To validate the use of simplified Clinical Pulmonary Infection Score (CPIS) for the diagnosis of VAP.

Design: Prospective study.

Setting: Pediatric intensive care unit of a tertiary care teaching hospital.

Subjects: 30 children receiving mechanical ventilation for more than 48 hours and with simplified CPIS≥6.

Methods: All patients underwent flexible bronchoscopy to obtain bronchoalveolar lavage which was analyzed quantitatively. Colony count ≥10^4cfu/mL was considered reference standard for definite VAP.

Results: Of the five variables used for simplified CPIS, only patient's temperature (*P*=0.013) and PaO_2/ FiO_2 ratio were significant (*P*<0.001) to differentiate the presence of definite VAP. Patients with definite VAP (BAL colony count ≥10^4cfu/mL) had CPIS of 8.4 while in no definite VAP group it was 6.4 (*P*= 0.007). CPIS of 8 was found to have sensitivity of 80%, specificity 80%, PPV 86.9%, NPV 70.5% and accuracy 80%. The area under Receiver operating characteristic curve of CPIS against reference standard was 0.81± 0.069 (*P*=0.001).

Conclusion: Simplified CPIS is useful in patients on mechanical ventilation to diagnose ventilator- associated pneumonia.

Key words: *Bronchoscopy, Clinical pulmonary infection score, India, Mechanical ventilation, Ventilator-associated pneumonia.*

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Ventilator-associated pneumonia (VAP) is an important problem in Pediatric intensive care units (PICU). The prevalence ranges from 3%-65% in PICUs in the USA [1]. The clinical diagnosis of VAP is usually based on the presence of fever, leukocyte counts, amount and character of tracheal secretions, and appearance of new or persistence of radiographic infiltrates. However, these parameters taken separately have limited diagnostic value [2]. The clinical criteria for the diagnosis of VAP have repeatedly been criticized as inappropriate, leading to over diagnosis or under diagnosis particularly in the setting of Adult respiratory distress syndrome (ARDS) [3-5]. Despite these limitations, the clinical criteria remain the starting point of diagnostic evaluation of suspected VAP case. Pugin, *et al*. [6] combined the above mentioned parameters with oxygenation (PaO_2/FiO_2) and formed the Clinical Pulmonary Infection Score (CPIS) as a diagnostic tool for pneumonia. The CPIS has been used in multiple studies on VAP in adults [3,7-9] but limited data is available on pediatric cases [10]. This prospective study was conducted to validate the use of CPIS to diagnose VAP in pediatric patients.

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METHODS

During the 9 months period of the study, all patients on mechanical ventilator for more than 48 hours by endotracheal tube (ETT) were evaluated daily, in the morning, with simplified CPIS (with the help of nursing charts) for the development of VAP and a

score was assigned by the designated investigator [9]. The chest *X*-ray and blood gas analysis report done in the morning were used for scoring. The senior nurses were trained to perform ETT suction. They were also instructed to make a note of the nature and the amount of secretions by using -/+, + and ++ for few, moderate and large, respectively. To further ensure the accuracy, the Critical care fellow or Senior resident on duty in the PICU supervised this observation of the nurses. Patients with a CPIS score of ≥6 were included in the study.

For all the enrolled patients, the following data were recorded: age, gender, clinical presentation and date of suspicion of VAP, and PICU admission and discharge. Time period of PICU stay prior to initiation of and the duration of mechanical ventilation and the length of PICU and hospital stays were also recorded. Chest radiographic findings at the time of admission, on initiation of ventilation and at the time of clinical suspicion of VAP were also recorded.

The enrolled patients were subjected to bedside flexible bronchoscopy to obtain bronchoalveolar lavage (BAL). As per PICU policy, all patients on ventilation receive continuous infusions of midazolam and morphine. A bolus dose of vecuronium (0.1 mg/kg) was given before starting bronchoscopy. All patients were monitored closely and continuously during and after the procedure with multi-parameter monitor and any cardio-pulmonary complications were recorded. No complications were recorded in the present study.

Bronchoscopic bronchoalveolar lavage: The Olympus BF type XP40 bronchoscope (Olympus Optical Co., Japan) with outer diameter of 2.8 mm and a suction channel of 1.2 mm size was used to obtain lavage. All patients were pre-oxygenated with 100% oxygen for 5-10 minutes. The site for BAL was chosen according to the chest *X*-ray appearance of localized infiltration or bronchoscopic appearance of inflammation or purulent secretions. In the absence of above clues, BAL was performed in the right lower or middle lobe. ETT suction was done just prior to procedure. Bronchoscope was introduced through a swivel adapter connected between ETT and ventilator circuit. In infants with 4.5 or less ETT size, an appropriate size laryngeal airway mask was used for bronchoscopic lavage [11]. Under visual control, the bronchoscope was advanced in the direction of the chosen segment until a wedged position was achieved and lavage was carried out with sterile saline. We used 3 mL for babies <5 Kg, 5 mL for children between 5-10 Kg, 7.5 mL for 11- 20 Kg and 10 mL for patients >20kg. Lavage was sucked into a sterile mucus trap.

Microbiological methods: All BAL samples were transported to the laboratory within 15 minutes and cultured within an hour of collection. All samples were vortexed for a minute initially before gram staining the smears. These preparations were studied for the presence of squamous cells, polymorphonuclear cells and the type of microorganism present. Simultaneously, quantitative cultures using the calibrated loop method were performed on common media such as blood agar, chocolate agar and McKonkey's agar using standard techniques [12,13]. Organisms were identified using automated Vitek-1 system (bioMerieux, France). Microbiological examination for unusual organisms such as *Mycoplasma*, *Chlamydia*, *Pneumocystis carinii* and viruses did not form a part of this study.

The Institutional review board approval was obtained for the study and informed consent for the bronchoscopic BAL was taken from the parents. In accord with previous studies of quantitative bacteriology of BAL cultures [1,14-17], a bacterial density of $\geq 10^4$cfu /mL was considered as positive for VAP and those episodes were referred to as 'Definite VAP' episodes. The organisms isolated on blood culture were compared with the organisms isolated from the BAL. The five parameters of CPIS were compared between "Definite" and "No Definite" VAP patients using independent sample *t* test and Chi-square test. Taking BAL colony counts of $\geq 10^4$ cfu/mL as the reference standard, the sensitivity, specificity, positive and negative predictive values and accuracy were calculated at various CPIS levels. The receiver operating characteristic curve (ROC) was plotted and area under curve was also obtained. The distribution pattern of the data was tested with D'Agostino-Pearson test for normal distribution. *P* value less than 0.05 was considered significant. SPSS 15 version

statistical package was used for analysis.

RESULTS

There were a total of 267 ICU admissions during the study period and 82 of these (30.7%) required mechanical vertilation (66 ventilated for more than 72 hours). Thirty patients with CPIS ≥6 were included in the study (***Table* I**). The mean duration of ICU stay up to the initiation of mechanical ventilation was 1.4 days.

All study cases were receiving antibiotics and the mean duration of therapy prior to development of VAP was 10.1 days. The median duration of ventilation before the clinical diagnosis of VAP was 9 days (range 3-60 days).The median total duration of MV was 16 days (range 7 to 120 days) while median stay in PICU was 20 days (range 9 to 124 days). The mean duration of MV was significantly higher in children less than 1 year as compared to older children (55 *vs* 20.2 days, *P*=0.001).

TABLE I BASELINE PATIENT CHARACTERISTICS (*N*=30)

Age median (range)	6.5 years (1 mo -12 yrs)
Males	20 (66.5%)
PRISM score* (range)	13 ± 6 (0-34)
Primary system involvement	
Central nervous system	9 (30)
Respiratory system	6 (20)
Septicemia	5 (16.6)
Diabetic ketoacidosis	2 (6.6)
Postoperative status	2 (6.6)
Trauma	2 (6.6)
Miscellaneous	4 (13.3)
Multiorgan dysfunction	15 (50)
Use of steroids	4 (13.3)
Immunosuppressed state	2 (20)
Use of H_2 blockers	9 (30)
Chest *X*-ray at admission	
Normal	21 (70)
ARDS	3 (10)
Others	6 (20)
Chest *X*-ray at initiation of MV	
Normal	14 (44.6)
ARDS	9 (30)
Others	7 (23.3)

**mean ±SD; Figures in parentheses indicate percentage; ARDS: acute respiratory distress syndrome; MV: Mechanical ventilation.*

Microbiological results: Eighteen blood cultures were positive. The most common organism cultured was *Pseudomonas aeruginosa (*43.6%). Other organisms obtained were *Acinetobacter baumannii, Enterobacter sps, methicillin resistant Staphylococcus aures (MRSA) and Candida albicans.* Eleven (60%) blood culture results were concordant with the organism yielded from BAL in colony counts of $\geq 10^4$ cfu/mL. Twenty one out of 30 BAL samples yielded positive cultures. However, only 19 samples yielded organisms with a colony count of $\geq 10^4$ cfu/ mL. Micro-organisms cultured included *P.aeruginosa* (9), *A. baumannii* (5), *K. pneumoniae* (4), Methicillin resistant *S. aureus* (2), P. *mirabilis* (1), and *Enterobacter* species and *Candida* sepsis (3 each). In six samples, polymicrobial growths were obtained. In three samples, *Candida* sps grew along with *Pseudomonas aeruginosa*, *Klebsiella pneumonaie* and *Acinetobacter baumannii*.

Simplified clinical pulmonary infection scores: The individual variables of CPIS were compared between patients with definite and no definite VAP (***Table* II**). None of the patient had normal chest *X*-ray at the time of enrolment. The higher temperature of patient (39.2 ± 0.7 *vs* 38.5 ± 0.8, *P* = 0.01) and low PaO_2/FiO_2 ratio (155.5 ± 41.6 *vs* 234 ± 69, *P* < 0.001) were significant variables for the diagnosis of VAP. A value of 8 on the CPIS was found to have the best accuracy with a sensitivity and specificity of 80% each (***Table* III**). Area under the ROC curve was 0.812 (*P* < 0.001) (***Fig.* 1**).

DISCUSSION

In this study, we have evaluated the clinical diagnosis of VAP assessed by simplified CPIS using bronchoscopic BAL culture as the reference standard. In the present study, individual variables used in CPIS were also compared in patients with definite VAP and with no definite VAP. Presence of fever and PaO_2/FiO_2 ratios were significantly different in two groups.

Pugin, *et al*. [6] found significant difference of temperature in adult patients with or without pulmonary infection, while other studies found

TABLE II COMPARISON OF INDIVIDUAL VARIABLES OF SIMPLIFIED CPIS IN PATIENTS WITH DEFINITE AND NO DEFINITE VENTILATOR-ASSOCIATED PNEUMONIA.

VARIABLE	Definite VAP (*n*=19)	No Definite VAP (*n*=11)	*P* value*
Temperature°C	39.2 ± 0.72	38.5 ±0.8	0.01
TLC ($mm^{3)}$	18960±7094	16386±6296	0.2
PaO_2/ FiO_2	155±41.6	234±69	0.0
Tracheal secretions			
Scanty	0	1	
Moderate	8	3	0.3
Profuse	11	7	
Chest *X*-ray			
Collapse	8	6	
Consolidation	5	2	
ARDS	3	1	0.8
B/L haziness	2	2	
Cavitatory lesion	1	0	
CPIS	8.48± 1.2	6.8 ± 1.2	0.007

**Temperature, TLC and PaO_2/FiO_2 compared using t test and chest X-ray and tracheal secretions compared by Chi-square test; VAP ventilator- associated pneumonia; TLC- total leucocyte count;, ARDS:acute respiratory distress syndrome; CPIS" clinical pulmonary infection score.*

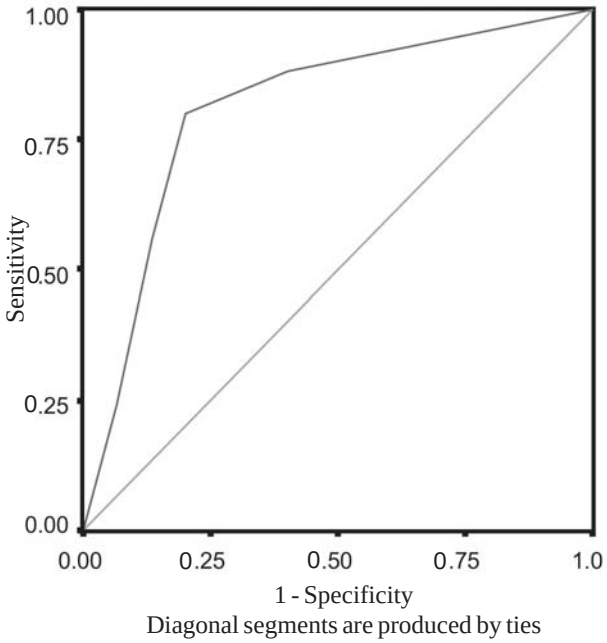

FIG. 1 *Receiver operating characteristic curve of clinical pulmonary infection score.*

TABLE III OPERATIVE INDICES OF SIMPLIFIED CLINICAL PULMONARY INFECTION SCORE FOR THE DEFINITE DIAGNOSIS OF VENTILATOR-ASSOCIATED PNEUMONIA

CPIS	Sensitivity	Specificity	PPV	NPV	Accuracy
6	100	0	62.5	0	62.5
7	88	60	78.5	75	77.5
8	80	80	87	70.5	80
9	61	87	87.5	54	67.5
10	24	93	85.7	42	50

CPIS: Clinical pulmonary infection score; PPV: Positive predictive value, NPV: Negative predictive value.

presence of fever as a poor diagnostic marker, especially in ARDS patients [3,4,7]. The presence of fever may be explained by mechanisms other than pneumonia in patients on ventilator. Meduri, *et al*. [18] found that only 42% of patients with fever and pulmonary infiltrates had pneumonia. Leucocytosis and purulent tracheal secretions had good sensitivity (77% and 69%, respectively) but poor specificity (58% and 42%, respectively) in a study by Fabergus, *et al*. [3]. It is quite obvious that leucocytosis may be induced by a variety of causes in a critically ill patient [3]. The high false positivity of purulent tracheal secretions is explained by the presence of purulent bronchitis in almost all patients particularly during prolonged MV. The negative results may be due to the peripheral location of pneumonia and impaired clearance of secretions [19] .

In the present study, chest *X*-ray was positive in all the patients at the time of enrolment. Similar observation was reported by Andrews, *et al*. [4] but only 57% had histological evidence of pneumonia. While Fabergus, *et al*. [3] found radiographic infiltrates as most sensitive (92%) clinical parameter for diagnosing VAP, the rate of false positive results was as high as 67%. This high false positivity may result from other causes mimicking VAP such as atelectasis, pulmonary infarction, alveolar hemorrhage and ARDS.

As per Pugin, *et al*. [6], a CPIS >6 was associated with high likelihood of pneumonia (sensitivity 93%, specificity 100%). The disadvantage with this score is dependence on tracheal aspirate gram stain and culture results and so the waiting period of 24 to 48 hours for the clinical diagnosis of VAP [9,20]. In the

WHAT IS ALREADY KNOWN?

- Clinical pulmonary infection score (CPIS) is an easy composite score.

WHAT THIS STUDY ADDS?

- A simplified CPIS is helpful to diagnose ventilator-associated pneumonia in children in the PICU and to initiate a definite diagnostic procedure.

present study, simplified CPIS was used [9]. This score does not include any laboratory dependent variables. The maximum possible score is 10. Based on the previous studies patients with CPIS ≥6 were enrolled in the present study [3, 6-10, 21]. Pugin, *et al*. [6] did not find any positive bronchoscopic BAL in patients with CPIS<6. The likelihood ratio of detecting pneumonia was 1.46 and 0.68 in patients with CPIS ≥6 and <6, respectively [2]. In another study, CPIS >6 virtually ruled out other causes of pulmonary infiltrates in ICU patients [22].

The mean CPIS was significantly high in patients with definite VAP (P=0.007). CPIS has been studied in many adult studies as a diagnostic tool [3,6]. Results of these studies are conflicting. High sensitivity (93%) and high specificity (100%) of CPIS >6 were reported [6]. Papazian, *et al*. [7] used CPIS for selection of cases to test the diagnostic accuracy of bronchoscopic and nonbronchoscopic techniques. CPIS at the threshold of 6 achieved an accuracy of 79%, a sensitivity of 72% and a specificity of 85%.The individual variables of CPIS were not significantly different while the composite CPIS score was significantly higher in the VAP group than in the non-VAP group. Similar results were not reported in other adult studies [2,3]. The only pediatric study evaluating CPIS had enrolled 15 mechanically ventilated children. In 14 patients CPIS was more than 6 at the time of diagnosis of VAP with positive predictive value of 93% [10].

Serial CPIS and its components have been used previously to assess the treatment response in prospective studies. Progressively falling CPIS and rising PaO_2/FiO_2 ratio distinguished survivor from nonsurvivors [9]. CPIS had also identified patients requiring antibiotic therapy and so reduced the cost of therapy [22].

There is an important limitation with the use of CPIS. All the elements of CPIS are given equal weighting. In other words, new lobar infiltration or deteriorating PaO_2/FiO_2 is of greater importance to the clinician than leukocytosis, which is non-specific. In clinical practice, CPIS has utility as a diagnostic tool to identify patients with high probability of pneumonia requiring definite diagnostic procedure and to evaluate the clinical response to therapy [23].

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REFERENCES

1. Gauvin F, Dassa C, Chaibou M, Proulx F, Farrell CA, Lacroix J. Ventilator-associated pneumonia in intubated children: Comparison of different diagnostic methods. Pediatr Crit Care Med. 2003;4:437-43.
2. Fartoukh M, Maitre B, Honore S, Cerf C, Zahar JR, Brun-Buisson C. Diagnosing pneumonia during mechanical ventilation. The clinical pulmonary infection score revisited. Am J Respir Crit Care Med. 2003;168:173-9.
3. Fabergas N, Ewig S, Torres A, El-Ebiary M, Ramirez J, Bellacasa de la JP, *et al*. Clinical diagnosis of ventilator associated pneumonia revisited: comparative validation using immediate post-mortem lung biopsies. Thorax. 1999;54:867-73.
4. Andrew CP, Coalson JJ, Smith JD, Johanson WG Jr. Diagnosis of nosocomial bacterial pneumonia in acute, diffuse lung injury. Chest. 1981;80:254-8.
5. Torres A, El-Ebiary M, Padro L, Gonzalez J, Bellacasa de la JP, Ramirez J, *et al*. Validation of different techniques for diagnosis of ventilator-associated pneumonia: Comparison with immediate postmortem pulmonary biopsy. Am J Respir Crit Care Med. 1994;149:324-31.
6. Pugin J, Auckenthaler R, Mili N, Janssens JP, Lew PD, Suter PM. Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nobronchoscopic "blind" bronchoalveolar lavage fluid. Am Respir Crit Care Med. 1991;143:1121-9.
7. Papazian L, Thomas P, Garbe L, Guignon I, Thirion X, Cherral J, *et al*. Bronchoscopic and blind sampling

techniques for the diagnosis of ventilator-associate pneumonia. Am J Respir Crit Care. 1995;152:1982-91.
8. Flanagan PG, Findlay GP, Magee JT, Ionesue AA, Barnes RA, Smithies MN. The diagnosis of ventilator-associated pneumonia using non-bronchoscopic, non-directed lung lavages. Intensive Care Med. 2000;26:20-30.
9. Luna CM, Blanzaco D, Niedermn MS, Matarucco W, Baredes NC, Desmery P, *et al*. Resolution of ventilator-associated pneumonia: Prospective evaluation of the clinical pulmonary score as an early clinical predictor of outcome. Crit Care Med. 2003;31: 676-82.
10. Grasso F, Chidini G, Napolitano L, Calderini E. Ventilator- associated pneumonia in children: evaluation of clinical pulmonary infection score in monitoring the course of illness. Crit Care. 2004;8:209.
11. Nassbaum E, Zagnoev M. Pediatric fiberoptic bronchoscopy with laryngeal mask airway. Chest. 2001;120:614- 6.
12. James L, Hoppe- Bauer JE. Processing and interpretation of lower respiratory tract specimen. *In*: Clinical Microbiological Procedures Handbook. Isenberg HD (Ed) American Society of Microbiology. Washington DC 1992. p. 1.15.1-1.15.8.
13. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing, document M 100-S16. 2006. Clinical and Laboratory Standards Institute, Wayne, PA.
14. Chastre J, Fagon JY. Ventilator associated pneumonia. Am J Respir Crit Care Med. 2002;165:867-903.
15. Elward AM. Pediatric ventilator- associated pneumonia. Pedaitr Infect Dis J. 2003; 22:445-6.
16. Pingleton S K, Fagon JY, Leeper K V Jr. Patient selection for clinical investigation of ventilator associated pneumonia. Criteria for evaluating diagnostic techniques. Chest. 1992;102:553-6.
17. Labenne M, Poyart C, Ramband C, Goldfarb B, Pron B, Jouvet P, *et al*. Blind protected specimen brush and bronchoalveolar lavage in ventilated children. Crit Care Med. 1999;27:2537- 43.
18. Meduri GU, Mauldin GL, Wunderink RG, Leeper KV, Jones CB, Tolley E, *et al*. Causes of fever and pulmonary densities in patients with clinical manifestations of ventilator- associated pneumonia. Chest. 1994;106: 221-35.
19. Rouby JJ, Martin de Lassale E, Poete P, Nicholas MH, Bodin H, Jarlier V, et al. Nosocomial bronchopneumonia in critically ill. Am Rev Respir Dis. 1992;146: 1059-66.
20. Court A, Garrard C, Crook D, Bowler I, Conolon C, Peto T, *et al*. Microbiological surveillance of the lungs using non-directed bronchial lavage. Q J Med. 1993;86:635-48.
21. Singh N, Rogers P, Atwood CW, Wegner MM, Yu VL. Short course of empiric antibiotic therapy for patients with pulmonary infiltrates in the intensive care unit. A proposed solution for indiscriminate antibiotic prescription. Am J Respir Crit Care Med. 2000;162:505-11.
22. Singh N, Falestiny MN, Rogers P, Reed MJ, Pularski J, Norris R, *et al*. Pulmonary infiltrates in the surgical ICU: Prospective assessment of predictors of aetiology and mortality. Chest. 1998;10:1129-36.
23. Hubmayr RD. Statement of the 4th International Consensus Conference in Critical Care on ICU-acquired Pneumonia- Chicago, Illinois, May 2002. Intensive Care Med. 2002;28:1521-36.