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Minor Diagnostic Factors in Ventilator Associated Pneumonia in Children

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Abstract

Background: Ventilator-associated pneumonia (VAP) is nosocomial pneumonia. Minor diagnostic criteria in children are poorly understood. Present study aimed to determine the new diagnostic factors for VAP in children admitted in the intensive care unit according to clinical, laboratory, and radiological assessments.

Materials and Methods

One hundred thirty pediatric intensive care unit (PICU) admitted patients were selected and classified as VAP (29 patients), and non-VAP (101 patients), prospectively. Clinical parameters, laboratory and radiological findings were followed in patients with and without VAP.

Results

Among the patients, 60% (78 cases) were male. The median age was one month. All of the VAP patients were neonates with the average age of 10.7±25.29 months. There was no significant difference in age and gender. Duration of mechanical ventilation and ICU admission had significant difference between groups (29.31±20.5 versus 8.45±8.76, and 32.62±21.15 versus 12.88±12.16 days, respectively, $p<0.001$). Tachycardia was detected in 27 (93.1%), and 51(50.5%) patients in VAP and non-VAP, respectively ($p<0.001$). Respiratory secretion was detected in 8(27.6%) and 9(8.9%) in VAP, and non-VAP, respectively ($p=0.009$). Crackles was detected in 9(31%) and 15(14.9%) in VAP and non-VAP, respectively ($p=0.04$). Blood and bronchoalveolar lavage (BAL) culture, need to change device setting, O2 desaturation, WBC count and chest X- ray showed significant difference between groups ($p<0.05$).

Conclusion

According to the results, some clinical and laboratory factors including WBC count, blood culture, crackles and need to change settings should be considered as minor but new diagnostic criteria for VAP.

Key Words: Children, Intensive Care Unit, Ventilator associated pneumonia.

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1- INTRODUCTION

Hospital-acquired pneumonia (HAP) is the second most common nosocomial infection in the Intensive Care Unit (ICU) (1). HAP is a major threat to the health of admitted children in neonatal intensive care unit (NICU). It leads to mortality, prolongation of hospital stay and cost treatment increment. Eighty-six percent of HAP is associated with mechanical ventilation (MV) which leads to ventilator-associated pneumonia (VAP) (2). The incidence rate of VAP varies from 1.7 to 8.9 per 1,000 ventilator/days (3). VAP occurs in 5% of young children admitted in ICU. About one-fifth of children with VAP will expire (4). International Nosocomial Infection Control Consortium (INICC) reported that the incidence rate of VAP was 13.6 per 1,000 ventilators/days in Asia, Latin America, Africa and Europe from 2003 to 2008 (5). VAP is a common cause of HAP among newborns (6.8 to 32.2%) (8). Gram-negative bacteria aspiration by endotracheal tube and spread of upper respiratory tract bacteria to lower respiratory tract to lower are the main causes of VAP (9). Therefore, the risk of VAP in patients with MV is very high (1). VAP leads to antibiotic use increment and antibiotic-resistance (10). According to Centers for Disease Control (CDC), aspiration reduction and colonization prevention decreased the incidence rate of VAP (11). Because VAP leads to increased hospitalization, prevention is a priority (12). Determination of actual rate of VAP in children is difficult since the difference between children and adults diagnostic procedures as well as identifying radiological pneumonia could be quite problematic (13). VAP risk factors in children include low birth-weight, Mechanical Ventilation (MV) duration, tracheal intubation, suction and treatment with opioid (14-16). The diagnostic criteria for VAP are overlapped with other similar syndromes such as visceral adipose tissue (VAT). Therefore, the diagnosis of VAP might be complicated in critically ill patients. Chest radiograph and bacterial culture of endotracheal aspirate or bronchoalveolar lavage (BAL) specimen are required for an accurate diagnosis of respiratory tract infections. In respiratory tract infections, in-time treatment with antibiotics for multidrug-resistant pathogens is suggested. Using serial surveillance of endotracheal aspirate specimens is an efficient method to identify multidrug-resistant pathogens and their antibiotic susceptibilities (17). Present cross sectional study was carried out evaluating the minor but new effective factors on diagnosis of VAP in ICU admitted children based on clinical, laboratory and imaging evidence.

2- MATERIALS AND METHODS

2-1. Method

Present cross sectional descriptive study was performed in Pediatric Intensive Care Unit (PICU) of Dr. Sheikh Hospital, Mashhad University of Medical Sciences, Mashhad- Iran, from 2014 to 2015. The study participants included 130 children admitted in ICU, mechanically ventilated for over 48 hours, aged less than 16 years. Parental informed consent was obtained prior to the study. The patients were divided into two groups as with VAP (29 patients), and without VAP (101 patients). This study was approved by Mashhad University Medical Ethics Committee.

Patients were excluded if they were diagnosed with VAP less than 72 hours after birth. VAP was defined according to CDC criteria which is presented in **Table.1** (18). Primary outcome was the development of VAP. The secondary outcomes included the length of MV, duration of hospitalization, biochemical changes, C-reactive protein (CRP), new radiological findings as well as mortality and morbidity.

Table-1: CDC diagnostic criteria for VAP in children (18).

Age range	Criteria
Neonates	Onset >72 h after birth and one of the following radiologic criteria: −new or progressive infiltrates −consolidations −adhesions or fluid in lobar fissures/pleura and Worsening gas exchange (SaO2 ↓; O2 requirement ↑; Ventilation parameters ↑) and Four of the following signs and symptoms: −fever (>38.0°C), hypothermia (<36.5°C), or temperature instability −new onset or increasing bradycardia (<80/min) or tachycardia (>200/min) −new onset or increasing tachypnea (>60/min) or apnea (>20 seconds) −new onset or increasing signs of dyspnea (retractions, nasal flaring, grunting) −increasing production of respiratory secretions and need for suctioning −purulent tracheal secretion −isolation of a pathogen in respiratory secretions −elevated C-reactive protein (>20 mg/L) I/T-ratio >0.2
2-11 months	One of the following radiologic criteria: −new or progressive infiltrate −consolidations −cavitations −pneumatoceles And Worsening gas exchange (SaO2 ↓; O2 requirement ↑; Ventilation parameters ↑) And Three of the following signs and symptoms: −fever (>38.0°C), hypothermia (<36.5°C), or temperature instability −leucopenia (<4000 WBC/mm3) or yspneaosis (≥15,000 WBC/mm3) with left shift (≥10% band forms) −new onset of purulent sputum, or change in character of sputum, or increased respiratory secretions, or increased suctioning requirements −apnea or yspnea (yspneao, nasal flaring, retraction of chest wall, grunting) −wheezing, rales, or rhonchi −cough −bradycardia (<100/min) or tachycardia (>170/min).

1-16 years	One of the following radiologic criteria: −new or progressive and persistent infiltrate −consolidation −cavitation and Three of the following signs and symptoms: −fever (>38.4°C) or hypothermia (<36.5°C) −leukopenia (<4000 WBC/mm3) or yspneaosis (≥15,000 WBC/mm3) −new onset of purulent sputum or change in character of sputum or increased respiratory secretions or increased suctioning requirements −new onset or worsening cough or yspnea, apnoea, or tachypnea −rales or bronchial breath sounds −worsening gas exchange (SaO2 ↓; O2 requirement ↑;Ventilation parameters ↑)

SaO2: Oxygen saturation; WBC: White blood cells; VAP: Ventilator-associated pneumonia.

2-2. Statistical analysis

A sample size study population of 130 patients was considered appropriate to achieve a reasonable statistical analysis. Statistical analysis was performed using SPSS software version 16.0 (SPSS Institute, Inc., Chicago, IL, USA). All experimental values are presented as mean ± standard deviation (SD) or frequency. The comparison between groups was done by independent t- test. The relationship between qualitative variables was evaluated by Chi-square test. P -value less than 0.05 was considered significant.

3- RESULTS

3-1. Baseline Characteristics

Among the 130 patients, 60% (78 cases) were male; 29 patients were in VAP group, and 101 patients were in non-VAP group. The median of age was one month. The average age of patients in VAP and non-VAP groups was 10.7±25.29 and 19.7±41.37 months, respectively. There was not any significant difference in baseline characteristics including gender and age between VAP and non-VAP group (p>0.05). The duration of MV was 29.31±20.50 and 8.45±8.76 days in the VAP and non-VAP group with a significant difference (p<0.001). Both groups were ventilated via orotracheal method (89% in case versus 96% in control). Mean duration of ICU admission was 32.62±21.15 and 12.88±12.16 days in VAP and non-VAP group, respectively with a significant difference (p<0.001).

3-2. Clinical characteristics

There was not any relationship between type of ICU including general and surgical and VAP. 41.4% (n= 12) and 58.4% (n= 59) of the patients in VAP and non-VAP group were admitted in general ICU. The difference was not significant (p>0.05). 38.5% (n= 10) and 22.1% (n= 21) of the patients were preterm infants in the VAP and non-VAP groups, respectively (p>0.05). The rate of caesarean delivery among the patient's mothers in VAP group was 62.5% (n= 15) versus 43.3% (n= 39) in control (p>0.05). The causes of the patients' referral to the ICU were different. Tracheoesophageal fistula was the most common cause in both groups with no significant difference (p>0.05). Nutritional status was also evaluated for its probable effect in the diagnosis of VAP. 51.7%

(n=15) in VAP group, and 64.4% (n=65) in non-VAP group had total parenteral nutrition (TPN). There was no significant difference between groups (p>0.5).

3-3. Clinical symptoms

The body temperature, respiratory status (tachypnea, apnea, dyspnea), purulent tracheal secretions, and bandemia more than 10%, did not show significant difference between VAP and non-VAP group (p>0.05). In contrast, the heart rate (tachycardia) showed significant difference between VAP and non-VAP group (p<0.001). Respiratory secretion was observed more among patients with VAP (27.6%, n=8) in comparison with non-VAP patients (8.9%, n= 9) (p<0.05). The patients with VAP had greater frequency of positive crackles in comparison with non-VAP patients (p=0.04). Also, the need for device change setting was observed more among the VAP-patients (p=0.002). O_2 desaturation was reported in 93.1% (n= 27) of VAP patients versus 5.9% (n= 6) in non-VAP patients (p =0.001).

3-4. Laboratory tests

The level of C-reactive protein (CRP) was positive in some patients in both groups in different times of measurement. The difference was not significant (p>0.05). The white blood cells (WBCs) showed significant difference between VAP and non-VAP group (p<0.001). The rate of leucopenia was similar in groups, while the incidence of leukocytosis in VAP-patients was considerably higher than the subjects without VAP. The cerebrospinal fluid (CSF) culture was negative in both groups. 93.1% (n= 27), and 94.1% (n= 95) of patients in VAP and non-VAP groups respectively, had negative results in urine culture. The BAL culture was performed for 24.1% (n=7) of the VAP-patients and 3.4% (n=1) of them had a positive result, versus 1% (n=1) in non-VAP patients. The difference between groups was significant (p<0.05). The blood culture was conducted for all the patients in the VAP group and 95% (n= 96) of the non-VAP patients. There was a significant difference between both groups (p<0.001).

3-5. Chest radiography

The chest X-ray results were abnormal in all patients in the VAP group, while there was normal result in 93.1% (n= 94) of non-VAP group. There was significant difference between VAP and non-VAP group in consolidation, new infiltration, progressive infiltration and pleural effusion (p<0.05). Consolidation was the main lesion in 58.6% (n= 17) of VAP patients. Significant differences between VAP and non-VAP groups were presented in **Table.2**.

3-6. Recovery and mortality rates

57.4% (n= 13) of the patients without VAP and 44.8% (n= 58) of VAP-patients made a complete recovery; 6.9% (n= 2) and 11.9% (n= 12) of the patients with and without VAP made a partial recovery, respectively. Also, 48.3% (n= 14) of VAP-patients and 30.7% (n= 31) of non-VAP patients expired (p=0.203).

Table-2: The comparison of clinical and laboratory data between VAP and non-VAP groups.

Clinical /laboratory characteristics	VAP group :29 patients Mean ±SD Or frequency (%)	Non-VAP:101 patients Mean ±SD Or frequency (%)	P-value
Duration of MV (day)	29.31±20.50	8.45±8.76	<0.001*
Duration of ICU (day)	32.62±21.15	12.88±12.16	<0.001*
Heart rate (bit/minute) Bradycardia Tachycardia Normal	 1(3.4%) 27(93.1%) 1(3.4%)	 3(3%) 51(50.5%) 47(46.5%)	<0.001#
Respiratory secretion (positive)	8(27.6%)	9(8.9%)	0.009#
Positive crackles	9(31%)	15(14.9%)	0.04#
Need for device change setting	8(27.6%)	7(6.9%)	0.002#
O_2 desaturation	27 (93.1%)	6 (5.94%)	<0.001#
Count of white blood (cell/ml) Leucopenia Leukocytosis Normal	 3 (10.3%) 23(79.3%) 3 (10.3%)	 10 (9.9%) 46(45.5%) 45(44.5%)	<0.001#
Positive BAL culture	1 (3.4%)	1(1%)	0.009#
Positive blood culture	8(27.6%)	6 (5.9%)	<0.001#
Abnormal CXR results	29(100%)	7(6.9%)	<0.001#

VAP: Ventilator-associated pneumonia; MV: Mechanical ventilation; ICU: Intensive care unit; BAL: Bronchoalveolar lavage; CXR: Chest X- ray. * Independent t test, # Chi-square.

4- DISCUSSION

Present study was carried out evaluating the minor but new effective factors on diagnosis of VAP in ICU admitted children based on clinical, laboratory and imaging evidences. One hundred thirty patients aged less than 16 years old with or without VAP were studied. Results showed that some of the clinical symptoms, radiological and laboratory findings could be involved in VAP diagnosis in ICU admitted children. According to present study, WBC count, BAL culture, the setting changes and crackles are effective factors for VAP diagnosis. The rate of VAP incidence is different in all countries. Afjeh et al. in a study on the newborns connected to the ventilator for over 48 hours reported that VAP occurred in 17.3% of the patients, which was equivalent to 11.6 per 1000 days (19). According to Elward et al., the VAP rate was 11.6 per 1,000 ventilators/days (4). The rate of VAP was 26.7% in present study which was higher than Afjeh et al.'s and Edward et al.'s studies. This can be due to type of sampling, because present study was done in a referral pediatric surgery center. Therefore, the number of surgical patients and patients with transcription elongation factor (TEF) was significant. A study by Patria et al. in Italy claimed that the incidence rate of VAP was 6.6% in children (20). According to another study in Australia, the VAP rate was 7.07 per 1,000 days of MV. In a research, the re-intubation, absence of a feeding tube as well as the absence of stress ulcer prophylaxis are the risk factors to VAP (21). A study in Egypt reported that the rate of VAP was 31.8 per 1,000 days of MV (22). An Indian study explained that MV for more than 4 days was a risk factor for VAP. The VAP rate reported 36.2% in another study (23). The incidence rate of VAP was lower in Gautam et al.'s studies (21) comparing with Rasslan and Awasthi et al.'s report. This might be due to the differences in MV duration, sampling and geographical diversities. Consistent with present study, Patria's study claimed that the length of MV and ICU stay are

associated with VAP. Furthermore, morality was higher in VAP children comparing with non-VAP (20). The study of Srinivasan et al. aimed to determine the risk factors of VAP. According to Srinivasan, VAP-children had a prolonged MV and ICU admission as well as higher mortality rate. Srinivasan reported that the development of VAP is correlated with post-surgical diagnosis as well as using narcotics (9). Inconsistent with present study, the study of Srinivasan et al. acknowledged that there was a significant difference in the gender of patients with VAP (9). This might be due to different sampling, since MV for more than 48 hours was an inclusion criteria in Srinivasan's experiment. The studies of Apisarnthanarak et al. and Almuneef et al. were conducted to determine the rate, characteristics, risk factors and outcomes of VAP in extremely preterm neonates in NICU. The findings indicated that the rate of VAP and mortality were very high in extremely preterm neonates (14, 24).

Additionally, according to Bigham et al.'s study, VAP is associated with prolonged PICU admission (25). It was also in close relation with longer MV duration and increased mortality rate. VAP was correlated with subglottic stenosis, trauma and tracheostomy as well (25). According to present study, the blood and BAL cultures were two contributing factors in the diagnosis of VAP. Diagnostic value of blood culture was higher than BAL culture, while according to Luna et al. the sensitivity of blood culture was low in comparison to the BAL culture in detection of same pathogenic microorganisms (26). Also, Kotgire's study indicated the limited value of blood culture in microbiological diagnosis of VAP (27). Regarding the diagnostic effect of BAL culture, it has been stated that its invasive testing increases the accuracy and specificity of VAP diagnosis (10). The study of Sachdev et al. compared available methods to diagnose VAP in intubated patients. According to their findings, BAL was the most effective method of diagnosis for VAP (28). Consistent with present study, the changes on chest X- ray were observed in all patients who participated in Afjeh et al.'s study (19). Present research revealed that consolidation was the most common lesion observed in VAP-patients. In Afjeh et al.'s study, radiograph changes were found in only 50% of the patients. In present study, there were no significant radiographic changes in 93.1% of the non-VAP patients. Therefore, expertise is very importance and absolutely essential to the correct interpretation of X-rays (19). In spite of factors such as need to change the setting and crackles which were not included in the CDC diagnostic criteria, current study showed that these symptoms should be taken seriously as contributing factors in diagnosis of VAP. According to present study, WBC count was a diagnostic criterion for VAP patients which was not considered in CDC criteria. The study of Feldman et al. on bacterial colonization of the endotracheal tube revealed that the colonies were formed within 12 hours after endotracheal tube placement and reached maximum after 96 hours. Because the high incidence of VAP in intubated patients, finding new approaches to prevent VAP seems extremely necessary (30). A few other studies concluded that the subglottic secretion suction, directly affects the prevention of VAP.

5- CONCLUSION

Minor factors for diagnosis of VAP need to more attention and evolution. Some clinical and laboratory factors including WBC count, blood culture, crackles and need to change settings should be considered as minor but new diagnostic criteria for VAP. Multi center studies with larger sample size is recommended to confirm the results of present study.

6- CONFLICT OF INTEREST: None.

7- AUTHORSHIP STATEMENT

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