Evaluation of treatment protocol of ventilator-associated pneumonia in pediatric intensive care unit of Assiut University Children Hospital (clinical audit)

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Background

Ventilator-associated pneumonia (VAP) is a hospital-acquired pneumonia that occurs in patients who have been linked to mechanical ventilation for more than or equal to 48 h without symptoms or signs of infection of the lower respiratory tract before connection to mechanical ventilation.

Aim

(a) To assess the degree of adherence of pediatricians in pediatric intensive care unit (PICU) at Assiut University Children Hospital to the American protocol of management of VAP.
(b) To assess the demographic and clinical characteristics of admitted children.

Results

The study included 50 cases admitted in PICU at Assiut University Children Hospital who developed VAP. There were 32 males and 18 females with age ranging from 1 month to 17 years. VAP was detected more commonly among age group 1 month to less than 5 years (76%) followed by age group 5 to less than 10 years (16%) followed by age group 10 to 17 years (8%). Late-onset VAP was observed in 86% of cases, while early-onset VAP was observed in 14% of cases. VAP with risk factors for resistant organisms was observed in 94% of cases, while VAP without risk for resistant organisms was observed in 6% of cases. In our study, the treatment that was given for the studied cases was in the form of empirical therapy. According to the American Protocol of Management, VAP in PICU was given in 86% of cases. Changing antimicrobial therapy after 48–72 h according to culture results and clinical response was done in 78% of cases. Proper broad-spectrum empirical therapy and de-escalation of antibiotics according to culture results and clinical response was done in 76% of cases.

Conclusion

The PICU team of Assiut University Children Hospital follows the American guidelines of treatment of VAP in 76% of cases that were admitted during the period of the study.

Keywords:
pediatric intensive care units, treatment, ventilator-associated pneumonia

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Introduction

Ventilator-associated pneumonia (VAP) is the second most common nosocomial infection in pediatric intensive care unit (PICU) [1,2]. The following factors were statistically significant risk factors for VAP: previous antibiotics administration, previous noninvasive ventilation, reintubation, prolonged stay on mechanical ventilation and PICUs, inadequate infection-control measures, inadequate suctioning technique, supine position, sedatives, coma, absence of routine oral care, inadequate nasogastric tube-feeding technique, presence of nasogastric tube, and oral route of endotracheal intubation [3,4]. There are no widely recognized, gold standards for VAP diagnosis at the present time. Several clinical techniques have been recommended, but none have the sensitivity or specificity required to accurately diagnose VAP [5]. To date, the Centers for Disease Control and Prevention protocol for VAP diagnosis has been widely accepted and used in PICU for surveillance [6,7]. Early and successful treatment of VAP reduces mortality [8].

Patients and methods

Type of the study

Clinical audit, observational prospective study. The study was carried out at Assiut University Hospital after taking approval from Medical Ethics Committee of Faculty of Medicine with no: 17100344. Identifiable data were kept securely.

Site of the study

PICU at Assiut University Children Hospital.

Duration of the study

Six months from February 1, 2019 to July 30, 2019.

Patients' ages: 1 month–18 years.

Inclusion criteria:

(1) Children of both sexes.
(2) Aged from 1 month to 18 years.
(3) The patients are fulfilling the diagnostic criteria for VAP, which were mentioned before in the review [Table 1].

Exclusion criteria:

(1) Patient aged less than 1 month.
(2) Patients developed symptoms and signs of pneumonia within the first 48 h after connection to mechanical ventilation.

Methods and patients

The study included 50 cases admitted in PICU in Assiut University Children Hospital who developed VAP during the period from February 1, 2019 to July 30, 2019. They consisted of 32 males and 18 females with age ranging from 1 month to 17 years.

Data collection

In the present study, we aimed to evaluate the performance of the pediatricians as regards sticking to the American protocol of treatment of VAP in PICU that was mentioned before in the review (Table 2).

Reviewing sheets of patients with VAP who were admitted in PICU at Assiut University Children Hospital during the study duration.

The following data were collected and recorded for each patient in a master sheet for patients with VAP in PICU:

(1) For each patient, we looked for name, age, diagnosis, date of PICU admission, date of connection to mechanical ventilation, and onset of VAP.
(2) Symptoms and signs of VAP, for example, new onset or progressive dyspnea or apnea or tachypnea, new onset or worsening cough, fever or hypothermia, worsening gas exchange, oxygen desaturation or increased oxygen requirement, crackles or bronchial breath sounds or wheezes, tachycardia or bradycardia, and change in sputum character or volume.
(3) The investigations done in the studied cases were blood culture, bronchoalveolar lavage (BAL), urine culture, peritoneal culture, cerebrospinal fluid culture, C-reactive protein, complete blood count, erythrocyte sedimentation rate, and chest radiograph.
(4) The treatment that was given for the studied cases.

Table 1 The CDC PNU-1 criteria for diagnosis of ventilator-associated pneumonia[9]

Radiological	Clinical/laboratory
At least one of the following on two or more serial chest radiograph	For any patient, at least 1of the following
	Body temperature >38.0°C
	WBC $\leq$4000/mm^3 or WBC >12 000/mm^3
New or progressive infiltration	And at least 2 of the following
Consolidations	New onset of purulent sputum or change in character or volume of sputum
Cavitations	Cough or dyspnea
Pneumatoceles, in infants $\leq$1 year old age	Crackles or bronchial breathing
	Worsening gas exchange after stabilization or improvement on mechanical ventilation
Note: in patients without underlying chest or cardiac disease, one radiological criteria is acceptable	For children (>1 y to$\leq$12 y), at least 3 of the following:
	Body temperature >38.0°C or<36.0°C
	WBC $\leq$4000/mm^3 or WBC $\geq$15 000/mm^3
	New onset of purulent sputum or change in character or volume of sputum
	Cough or dyspnea, apnea
	Crackles or bronchial breathing
	Worsening gas exchange after stabilization or improvement on mechanical ventilation
	For infants <1 year
	Worsening gas exchange after stabilization or improvement on mechanical ventilation
	And at least 3 of the following
	Hypothermia or hyperthermia
	WBC <4000/mm^3 or WBC >15 000/mm^3 and band forms >10%
	New onset of purulent sputum or change in character or volume of sputum
	Apnea, increased respiratory effort
	Wheezes, crackles, or rhonchi
	Cough
	Heart rate <100 beats/min or heart rate >170 beats/min

Results

Tables 3–8.

Table 2 The American protocol of management of ventilator-associated pneumonia in pediatric intensive care unit

Initiate proper broad-spectrum empiric antibiotic treatment urgently once suspected VAP [10,11]
The American Thoracic Society recommends considering multidrug-resistant microbes in patients with antibiotic therapy in the previous 3 months, current hospital admission of ≥5 days, a high prevalence of multidrug-resistant bacteria in PICU or community, immunosuppressive disease or drugs, home infusion therapy, chronic dialysis within 1 month, home wound care or chronic neurological disease [10]
For early-onset VAP, initial empirical therapy with ceftriaxone, ampicillin/sulbactam, cefotaxime, cefuroxime or ertapenem is suggested by the American Thoracic Society [10]. Piperacillin/tazobactam should be used in severe early-onset VAP [12]. In cases of methicillin resistant *Staphylococcus aureus*, linezolid should be added [13]. Vancomycin is known as an effective solution to methicillin resistant *Staphylococcus aureus* pneumonia [8,13]
For late-onset VAP or in VAP with risk factors for resistant microbes such as *P. aeruginosa*, *Klebsiella* spp., ceftazidime, cefepime, meropenem, imipenem, and piperacillin/tazobactam with or without fluoroquinolone (ciprofloxacin) or aminoglycoside (gentamicin, amikacin, or tobramycin) should be used. If MRSA is prevalent in PICU add linezolid or vancomycin to the regimen [10,11]
Change antimicrobial therapy on day 2 or 3 according to culture results and clinical response. This is focused on the overuse of broad-spectrum antibiotics in PICU results in an increase in antibiotic resistance [14]
Consider the clinical course of the patient on therapy; most findings should be resolving within the first 6 days of treatment after start of antibiotics, this suggests that a short course of treatment is adequate
If the clinical course does not fit, consider other sites of infection, other reasons for lung infiltrates, and resistant bacteria [10]

PICU, pediatric intensive care unit; VAP, ventilator-associated pneumonia.

Table 3 Criteria of the studied cases diagnosed to have ventilator-associated pneumonia

	n (%) (*N*=50)	*P*
Risk for resistant organisms		
VAP with risk for resistant organisms	47 (94)	<0.001**
VAP without risk for resistant organisms	3 (6)	
Onset of VAP		
Early	7 (14)	<0.001**
Late	43 (86)	

VAP, ventilator-associated pneumonia.

Statistical analysis

Categorical variables were described by number and percent, χ^2 test and Fisher exact test were used to compare between categorical. A two-tailed *P* value less than 0.05 was considered statistically significant. All analyses were performed with the IBM SPSS 20.0 software (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY).

Discussion

VAP is a common nosocomial infection in PICU. In the present study, we tried to highlight on management of VAP in PICU.

Table 4 The presenting complaint in the studied patients

	n (%) (*N*=50)	*P*
Fever	38 (76)	<0.001**
Hypothermia	8 (16)	<0.001**
New onset or worsening cough	43 (86)	<0.001**
New onset or progressive dyspnea or apnea	47 (94)	<0.001**

Table 5 Clinical findings in the studied patients

	n (%) (*N*=50)	*P*
Bradycardia	6 (12)	<0.001**
Tachycardia	29 (58)	0.258
Worsening gas exchange	48 (96)	<0.001**
Crackles or bronchial breathing or wheezes	46 (92)	<0.001**
Change in sputum character or volume	48 (96)	<0.001**

VAP was more common in males (64%) in comparison with females (36%). This result is in keeping with Khattab *et al.*[15] who found that approximately three-quarters of VAP cases were males.

VAP was detected more commonly among age group 1 month– less than 5 years (76%) followed by age group 5 years–less than 10 years (16%) followed by age group 10 years–17 years (8%). These results are in accordance with Galal *et al.*[16] who found that the children who developed VAP were significantly younger compared with other ages because of their immature immune system and smaller airways.

Early-onset VAP was observed in 14% of cases in comparison with late-onset VAP that was observed in 86% of cases. This result is in keeping with Golia *et al.*[17] who found that late-onset VAP cases were significantly higher than early-onset ones among PICU patients.

VAP with risk for resistant organisms was observed in 94% of cases, while VAP without risk for resistant organisms was observed in 6% of cases. This is in keeping with Angaali *et al.*[18] who found that late-onset VAP is often caused with multidrug-resistant organisms.

We must consider risk factors for multidrug-resistant pathogens causing VAP that were mentioned by Rotstein *et al.*[11] who reported that resistant pathogens are prevalent in children receiving antibiotics in the previous 3 months, current hospital admission of more than or equal to 5 days, a high level of antimicrobial resistance in the population or in the PICU, immunosuppressive drugs and diseases, hospital admission for more than or equal to 2 days in the previous 3 months, dialysis in the previous 1 month, and chronic neurological disease.

The investigations that were done for the studied cases were in the form of:

Table 6 Cultures done in the studied patients

	n (%) (*N*=50)
Cultures	
Blood culture	
Done	49 (98)
Not done	1 (2)
Result of blood culture	
No growth	16 (32.6)
Klebsiella	8 (16.3)
Pseudomonas aeruginosa	5 (10.2)
Staphylococcus aureus	4 (8.2)
Nonpathogenic *Staphylococcus aureus*	4 (8.2)
Escherichia coli	4 (8.2)
Fungi	3 (6.1)
Gram negative bacilli	2 (4.1)
Gram positive cocci	2 (4.1)
Morganella morganii	1 (2)
BAL	
Done	47 (94)
Not done	3 (6)
Result of BAL	
Klebsiella	16 (43)
Pseudomonas aeruginosa	8 (17)
No growth	6 (12.8)
Acintobacter	4 (8.5)
Fungi	3 (6.4)
Streptococcus pneumoniae	2 (4.3)
Escherichia coli	3 (6.4)
Gram positive cocci	2 (4.3)
Gram negative bacilli	1 (2.1)
TB	1 (2.1)
Nonpathogenic *Staphylococcus aureus*	1 (2.1)
Urine culture	
Done	7 (14)
Not done	43 (86)
Result of urine culture	
No growth	5 (71.4)
Fungi	2 (28.6)
Peritoneal aspirate culture	
Done	1 (2)
Not done	49 (98)
Result of peritoneal aspirate culture	
No growth	1 (100)
CSF culture	
Done	3 (6)
Not done	47 (94)
Result of CSF culture	
No growth	3 (100)

BAL, bronchoalveolar lavage; CSF, cerebrospinal fluid.

Table 7 Laboratory and radiological investigations done in the studied patients

	N=50	*n* (%)
CBC		
Done	50	100
Not done	0	0
Result of CBC		
Leukocytosis	46	92
Leukopenia	4	8
CRP		
Done	48	96
Not done	2	4
Result of CRP		
Increased	48	100
Normal	0	0
ESR		
Done	30	60
Not done	20	40
Result of ESR		
Increased	30	100
Normal	0	0
CXR		
Done	50	100
Not done	0	0
Result of CXR		
New or progressive infiltrates	31	62
Consolidation	13	26
Cavitation	3	6
Pneumatocele	3	6

CBC, complete blood count; CRP, C-reactive protein; CXR, chest radiograph; ESR, erythrocyte sedimentation rate.

Blood culture was done in 98% of patients, of those 32.6% showed no growth, 16.3% were *Klebsiella*, and 10.2% were *Pseudomonas aeruginosa*. BAL was done in 94% of patients, of those 43% were *Klebsiella*, 17% were *P. aeruginosa*, 12.8% showed no growth, and 8.5% were Acinetobacter. Urine culture was done in 14% of patients, of those 71.4% were no growth and 28.6% were fungi. Peritoneal culture was done in 2% of cases, of those 100% were no growth. Cerebrospinal fluid culture was done in 6% of cases, of those 100% were no growth.

Complete blood count was done in 100% of cases and it showed leukocytosis in 92% of cases and leukopenia in 8% of cases. C-reactive protein was done in 96% of cases and it was increased in 100% of cases. Erythrocyte sedimentation rate was done in 60% of patients and it was increased in 100% of patients. Chest radiograph was done in 100% of cases and showed new or progressive infiltrates in 62% of cases, consolidation in 26% of cases, cavitation in 6% of cases, and pneumatocele in 6% of cases.

Regarding cultures that were done for the studied cases, we noticed that *Klebsiella* is the most common organism in blood culture (16.3% of cases) and BAL (43% of cases) followed by *P. aeruginosa* that was detected in 8.2% of blood culture results and 17% of BAL results. This is in keeping with Chaudhury *et al.*[19] who reported that the most frequent microorganisms isolated from VAP patients were, in order: *Klebsiella* spp. and *P. aeruginosa*. Additionally, Mansour and Albendary[20] reported *Klebsiella* spp. as the most frequent causative organism like ours.

In the present study, the treatment that was given for the studied cases was in the form of empirical therapy.

Table 8 Types of antimicrobial therapy in the studied patients

Treatment of VAP	*n* (%) (*N* = 50)	*P*
Empirical therapy according to the American protocol of management of VAP	43 (86)	<0.001**
Changing antimicrobial therapy after 48–72 h according to culture results and clinical response	39 (78)	<0.001**
Proper empirical therapy and de-escalation of antibiotic therapy	38 (76)	<0.001**

VAP, ventilator-associated pneumonia.

According to the American Protocol of Management, VAP in PICU was given in 86% of cases. Changing antimicrobial therapy after 48–72 h according to culture results and clinical response was done in 78% of cases. Proper broad-spectrum empirical therapy and de-escalation of antibiotics according to culture results and clinical response was done in 76% of cases.

We must keep in mind that starting proper broad-spectrum antibiotics urgently once suspected VAP to cover all likely microbes as delay of antibiotic therapy and inappropriate empirical therapy result in increased mortality [6].

The empirical antibiotics should be changed or stopped after assessing culture results and clinical response, these should be evaluated at 48–72 h in order to prevent the development of resistance [7].

Conclusion

The PICU team of Assiut University Children Hospital follows the American Protocol of Management of VAP in 76% cases that were admitted during the period of the study. Infants are at greater risk than older children for development of VAP. Late-onset VAP cases were significantly higher than early-onset ones in PICU. VAP is often associated with risk for resistant organism. Early successful management of VAP reduces mortality rates.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

None.

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