A descriptive study on the diagnosis and treatment of ventilator-associated pneumonia in the neonatal intensive care unit of Assiut University Children's Hospital

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Background
Neonatal ventilator-associated pneumonia (VAP) is a common nosocomial infection and a frequent reason for empirical antibiotic therapy in neonatal intensive care units.
Patients and methods
Reviewing data of diagnosis and management of neonates with VAP admitted to Assiut University Neonatal Intensive Care Unit was carried out during a period of 1 year.
Results
The current study was carried out at Assiut Children University Hospital during the period spanning between October 2016 and November 2017 to audit the clinical practice towards management of neonates with mechanical VAP. It included 50 neonates who were diagnosed to have mechanical VAP.
Conclusion
The incidence of suspected VAP and concomitant antibiotic use is much higher than for confirmed VAP; therefore, inclusion of suspected episodes should be considered for accurate evaluation. There is a high diagnostic inconsistency and a low reliability of interpretation of chest radiographs with regard to VAP. Implementation of combined antimicrobial stewardship and infection control measures may lead to an effective decrease in VAP incidence and antibiotic use.

Keywords:
antibiotic stewardship, diagnostic criteria, infection control, neonatal ventilator-associated pneumonia, risk factors

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Introduction

Neonates have unique characteristics predisposing them to nosocomial infections. The skin and mucous membranes are more permeable and less effective as barriers to infection. In addition, there is an immature immune system [1]. Newborns who are admitted to neonatal intensive care units (NICU) are at a high risk for developing nosocomial infections, because of the severity of their illness and exposure to invasive medical devices (e.g. mechanical ventilator, central venous catheter, and resistant microorganisms) [2]. Nosocomial infections cause significant morbidity and mortality and have a considerable impact on healthcare costs [3]. Ventilator-associated pneumonia (VAP) is the second most common nosocomial infection in the NICU, and it develops in mechanically ventilated patients 48 h or more after the patient is put on mechanical ventilation (MV) [4]. VAP occurs in 6.8–32.3% of the neonates in NICUs. The incidence of VAP in neonates varies according to birth weight and gestational age, especially when under 28 weeks [5].

Aim of the work

The aim of this work was to assess the degree of adherence of the medical staff team in the NICU at Assiut University Children Hospital to the introduced protocol for the diagnosis and management of VAP in neonates according to Centers for Disease Control and Prevention guidelines during a period of 1 year.

Patients and methods

Reviewing data of diagnosis and treatment of neonates with VAP admitted to Assiut University NICU was carried out during a period of 1 year. Ethical Review Board in Assiut Faculty of Medicine approved the study, and a consent was taken from the parents of the included children The present study included 50 patients of ages ranging from 1 to 28 days who were admitted to the NICU of the Children's Hospital, Assiut University, during the period spanning from October 2016 to November 2017. They were connected to MV for more than 48 h and were free from infection at the start of MV by clinical assessment and by laboratory investigations.

Inclusion and exclusion criteria

The patients included in this study fulfilled the following criteria:
Inclusion criteria: all neonates diagnosed to have VAP in Assiut University (NICU) during the period of the study were included.

Exclusion criteria: neonates suggested to have neonatal sepsis or community-acquired pneumonia or congenital pneumonia were excluded from the study.

Duration of the study: 1 year.

All neonates included in the research were subjected to the following (and they are):
(1) Data of history taking.

For every neonate, personal data were taken, including sex, gestational age, and birth weight.
(2) Data of clinical examination
   (a) Apnea, tachypnea, and nasal flaring with retraction of chest wall or grunting.
   (b) Worsening of gas exchange, oxygen desaturations, increased oxygen requirements, or increased ventilation demand.
   (c) Temperature instability with no other recognized cause.
   (d) New onset of purulent sputum, or change in the character of sputum, or increase in respiratory secretions, or increased suctioning requirements.
   (e) Apnea, tachypnea, and nasal flaring with retraction of chest wall or grunting.
   (f) Wheezing, crepitation, or both signs.
   (g) Cough.
   (h) Bradycardia (<100 beats/min) or tachycardia (>170 beats/min).
(3) Essential investigations
   (a) Total white blood cells: it may be normal or leucopenia if count is less than 4000 or leukocytosis if count is more than 15 000.
   (b) Chest radiography usually shows new or progressive persistent infiltration.
   (c) Cultures: all cultures should be obtained before antibiotic therapy.
      (i) Blood culture: use two culture bottles, one aerobic and the other anaerobic. Obtaining more than one blood culture may improve the results and can be helpful in distinguishing blood culture contaminants from true pathogens. It may be positive growth in blood culture not related to another source of infection or negative growth.
      (ii) Tracheal aspirate culture in intubated infants with a clinical picture suggestive of VAP: It may be positive growth in bronchoalveolar lavage (BAL) not related to another source of infection or negative growth.
(4) Lines of treatment:
   (a) Initial (empirical) therapy is most often begun before a definite causative agent is identified.
   (b) Continuing therapy is based on culture and sensitivity results and on clinical course.
   (c) Selection of the appropriate antimicrobial therapy:
      (i) Recommended first-line antibiotics: ampicillin and gentamicin.
      (ii) Third-generation cephalosporin (cefotaxime or ceftazidime) may be added to gentamicin.

Later, staphylococcal coverage with vancomycin and aminoglycoside or third-generation cephalosporin is given.
      (iii) Anaerobic infection: clindamycin is administered.
      (iv) Fungal infection: fluconazole or amphotericin is administered.

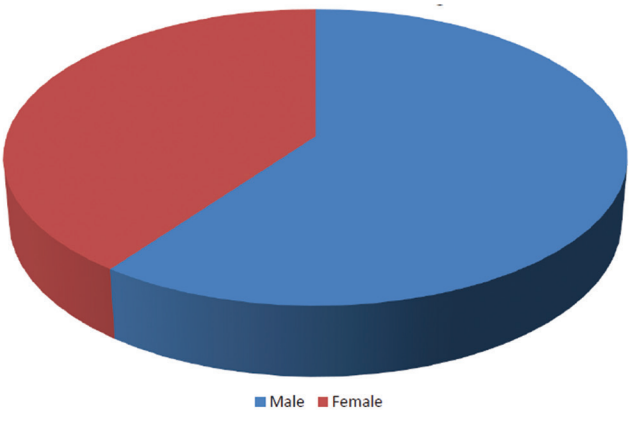
Results

The current study was conducted at Assiut Children's University Hospital in the period spanning between October 2016 and November 2017 to audit the clinical practice towards management of neonates with mechanical VAP. It included 50 neonates who were diagnosed to have mechanical VAP.

Fig. 1 shows recorded data about sex distribution among the studied cases. Fig. 2 shows recorded data about gestational age among the studied cases. Fig. 3 shows recorded data about birth weight among the studied cases.

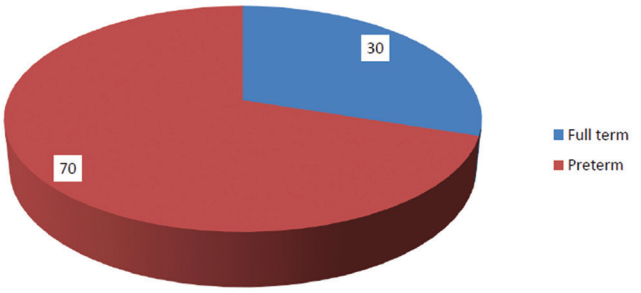
Table 1 shows leukocytic count among the studied cases. Table 2 shows radiographic findings among

Figure 1



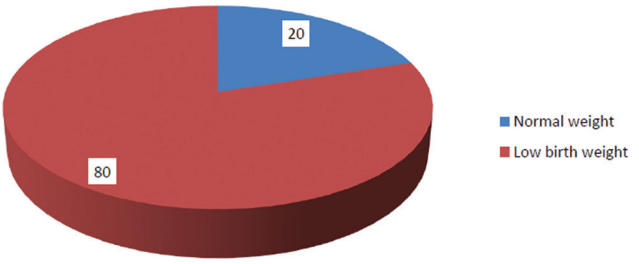
Recorded data about sex distribution among the studied cases.

Figure 2



Recorded data about gestational age among the studied case.

Figure 3



Recorded data about birth weight among the studied cases.

Table 1 Leukocytic count among the studied cases

	Performed			Not performed
	Normal	Increase	Decrease	
Leukocytic count	6/50	32/50	12/50	0/50
	12%	64%	24%	0%

Table 2 Radiographic findings among the studied cases

	Performed		Not performed
	Yes	No	
New or progressive persistent infiltration	32/50	18/50	0/50
	64%	36%	0%
Consolidation	18/50	32/50	0/50
	36%	64%	0%

Table 3 Microorganisms isolated from neonates with positive blood cultures

Causative organism	*n* (%)
No growth	14 (28)
Klebsiella sp.	10 (20)
Escherichia coli	5 (10)
Staphylococcus epidermidis	4 (8)
Fungi	3 (6)
Others	4 (8)
Total	40 (100.00)

the studied cases. Table 3 shows microorganisms isolated from neonates with positive blood cultures. Table 4 shows microorganisms isolated from BAL of the studied cases. Table 5 shows empirical antibiotic therapy used in the current study. Table 6 shows change to second-line antibiotic used in the current study.

Discussion

Nosocomial infections, particularly in NICUs, are recognized as one of the most important causes of morbidity and mortality in hospitalized neonates. These are major public health problems worldwide, particularly in developing countries [6]. A constant and active surveillance system is necessary to control the factors that cause and aggravate the risk of these infections [7]. MV is an essential feature of modern NICU care. Unfortunately, MV is associated with a substantial risk of VAP [8].

The present study included 50 neonates who were diagnosed to have mechanical VAP. Preterm neonates represented a large percentage of cases (70%).

Low birth weight (LBW) is an important risk factor in the development of nosocomial infection. In our study, the majority of studied neonates (80%) were LBW. This finding was also reported by Ahmed *et al.* [9].

In this study, the most common findings in patients with VAP were increased suction requirement and increased respiratory secretion (100%), whereas new-onset purulent sputum was found in only 64% of cases.

In the present study, all patients were evaluated for temperature and heart rate. The temperature was normal in 76% of cases, whereas it was increased in 24% of cases. Normal heart rate was found in 58%, while tachycardia was found in 30% and bradycardia was found in 12% of cases.

In the present study, auscultation of the chest was carried out for all cases wherein crepitation was present (76%), while wheezing was found in 24% of cases.

In the present study, the majority of the studied neonates (64%) had leucocytosis; this is in agreement with Chirico and Loda [10] who found leucocytosis in most cases of VAP.

In the present study, radiography was performed in all patients, new or progressive persistent infiltration was found in 64% of patients, while consolidation was present in 36% of patients.

In the present study, blood culture was performed in 80% of neonates, with no growth being found in 28% of these cultures. The false-negative blood cultures may be due to many factors, such as concurrent use of antibiotics, suboptimal sample volumes, and anaerobic infections. A negative blood culture does not exclude

Table 4 Microorganisms isolated from bronchoalveolar lavage of studied cases

Causative organism	*n* (%)
No growth	12 (40)
Klebsiella sp.	8 (26.67)
Escherichia coli	6 (20)
Others	4 (13.33)
Total	30 (100)

Table 5 Empirical antibiotics used in the current study

Antibiotics	n (%)
Combination (against Gram-negative and positive bacteria)	50 (100)
Antibiotic against Gram positive only	0 (0)
Antibiotic against Gram negative only	0 (0)

Table 6 Change to second-line antibiotics used in the current study

State	*n* (%)
No change in empirical therapy	8 (16)
Changed to second line	
Based on culture and sensitivity	26 (52)
Empirical change	16 (32)

sepsis, as about 26% of all neonatal sepsis could be due to anaerobes [11].

In our study, we found that *Klebsiella* sp. were the most frequently isolated organisms from blood cultures, which is consistent with the results of previous Egyptian studies by Brady [2] and Abdel-Wahab *et al.* [12], who found that the most frequently isolated organisms were *Klebsiella* sp. (24%) followed by *Escherichia coli* (12%) of cases.

As regards BAL, it was carried out in 60% of cases. In our study, the microorganisms most commonly isolated from tracheal aspirate cultures were *Klebsiella* sp. and *E. coli*.

Understanding the microbiology of VAP is critical for choosing empirical broad-spectrum antibiotic therapy followed by de-escalation to specific antimicrobial therapy once cultures are known or for discontinuation of antibiotics if VAP is no longer suspicious. However, there are no consensus guidelines for antibiotic treatment either in neonates or in children, and empirical treatment should be selected according to the nosocomial flora and resistance patterns of pneumonia, which, in turn, leads to an increase in the mortality rate [13].

In our study, it was noticed that a combination of more than one antibiotic to cover both Gram-negative and positive bacteria was used in 100% of studied neonates.

As regards second-line antibiotics used in the current study, 20% of neonates had a change in empirical therapy. In 52% of neonates, the first antibiotic was changed to another agent on the basis of the results of culture and sensitivity, whereas, in 28% of neonates, the first agent was changed without waiting for the results of culture and sensitivity. This may be attributed to the associated clinical deterioration.

Median hospital stay was 18 days, with a range between 2 and 34 days. As regards the outcome of the current study, 28 (56%) neonates died, and only 22 (44%) neonates survived. The mortality rate was high in the present study; this may be explained by the commonest organisms for nosocomial infection in this study, Gram-negative rods, which are often associated with antibiotic resistance, rapid clinical deterioration, and are commonly associated with shock and cardiovascular collapse.

Conclusion

In conclusion, this study revealed that:

(1) The most important risk factors for VAP in this study included prematurity and low birth weight.
(2) Gram-negative organisms comprised the majority of organisms obtained, wherein *Klebsiella* sp. and *E. coli* were the most common identified organism.
(3) The combination of more than one antibiotic to cover both Gram-negative and positive bacteria was used.
(4) Pneumonia among mechanically ventilated newborns in our NICU was associated with a relatively high mortality rate.

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Conflicts of interest
There are no conflicts of interest.

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