

# Multi Drug Resistant Organism (MDRO) in Ventilator Associated Pneumonia (VAP) as a Cause of Morbidity and Mortality in Patients Post Obstetric Procedure: A Case Report

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**Abstract:** Ventilator Associated Pneumonia (VAP) is the most common form of nosocomial infection in intensive care units (ICU), especially in patients who use mechanical ventilation. The presence of VAP will increase mortality rate if pneumonia is caused by certain pathogens such as Multi Drug Resistant Organism (MDRO). This article reviews the case report of a 32-year-old woman with a diagnosis post-cesarean section day 4 and Suspected VAP with MDR risk. The patient was then treated in the ICU using a ventilator support because the patient had type I respiratory failure. There were three signs of systemic infection in patients, namely fever, tachycardia and leukocytosis. Aside of that, chest radiograph examination revealed infiltrates in the lung field. From the sputum culture results, there was growth of *Acinetobacter Baumannii* which is MDRO. In patients with MDRO or suspected MDRO, the recommended use of antibiotics is combination antibiotic regiments. Early recognition of MDRO in VAP can provide better management and prognosis, so that it can reduce morbidity and mortality in patients post obstetric procedure.

**Keywords:** Ventilator associated pneumonia, multi drug resistant organism

## 1. Introduction

Ventilator Associated Pneumonia (VAP) is the most common form of nosocomial infection in intensive care units (ICU), especially in patients who use mechanical ventilation. According to the American Thoracic Society in 2005, VAP is a lung infection that occurs after 48–72 hours of mechanical ventilator use. Ventilator Associated Pneumonia (VAP) is the second most common nosocomial infection at ICU with an incidence of 11.7 per 1000 treatments using a mechanical ventilator. The estimation of nosocomial pneumonia prevalence in ICU vary between 10-50%. According to the American Thoracic Society, the incidence of VAP in patients using mechanical ventilators ranges from 8 - 28%, but this figure can vary even up to 50%. The incidence rate of VAP itself will increase along with the use of mechanical ventilators' duration. It is estimated that the incidence rate will increase around 3% per day for the first 5 days, 2% during 6-10 days of use and 1% per day after day 10. VAP can increase mortality rates 2-10 times higher than patients without pneumonia. In Indonesia, deaths due to VAP in ICU at Cipto Mangunkusumo Hospital were reported as much as 57.2%. Based on research by Brahmani, et al the mortality rate in postoperative patients with mechanical ventilators at Sanglah Hospital Denpasar in 2015 had reached 71.5%.<sup>1,2,3</sup>

The presence of VAP will increase mortality rate if pneumonia is caused by certain pathogens such as Multi Drug Resistant Organism (MDRO). MDRO is a microorganism, especially bacteria, that are resistant to one or more classes of antimicrobial agents. MDRO can be caused by several things, including improper dosage of antibiotics, improper diagnostic, and improper causative bacteria. Examples of pathogenic germs are *A. baumannii*,

*Pseudomonas aeruginosa* and MRSA or in cases with secondary bacteremia. The MDRO incidence rate in VAP itself reaches 30-50% of all VAP incidents.<sup>1,3,4</sup>

In patients with MDRO or suspected MDRO, the recommended use of antibiotics is combination antibiotic regiments. In MDR pathogens such as *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and *Acinetobacter sp*, the preferred antibiotic regimen is Cephalosporin or Carbapenem or Beta-lactamase groups adjusted for the sensitivity results and combined with Fluoroquinolones. Whereas in MDR pathogens such as Methicillin Resistant *Staphylococcus Aureus* (MRSA), Aminoglycoside is the choice combined with Linesolid or Vancomysin.<sup>1,3,4</sup>

The involvement of MDR pathogens in VAP events will increase both morbidity and mortality in VAP patients. The mortality of VAP patients ranges from 24-50% but in patients with MDRO the mortality rate can reach 76%.<sup>5</sup>

## 2. Case Report

32-year-old woman referred from a private hospital in Denpasar with a diagnosis of post-cesarean section day 4 + post Hysterectomy due to placenta accreta + post urinary bladder rupture repair (21/04/20) + AKI prerenal dd/ renal phase polyuria + hypokalemia + Suspected VAP with MDR risk + Pulmonary edema due to AKI related. When the cesarean section was done, the patient experienced bleeding due to placenta accreta at the private hospital, thereafter during surgery was consulted to the Gynecologic Oncology division and a total abdominal hysterectomy was performed. During the operation, a urinary bladder was ruptured and repair was made. The patient was intensively treated at the ICU in the private hospital and underwent improved

conditions. Because the patient's condition had improved, the patient was finally allowed to be treated in non intensive ward. But during treated in non intensive ward, the patient experienced food aspirations, as evidenced by the existence of leftovers food during intubation, then the patient's consciousness was decreased and her condition worsened. The patient was then decided to be referred to Sanglah General Hospital in Denpasar.

A history of the previous three pregnancies took place without complications, there was no spontaneous bleeding, and the patient's family denied any history of suffering from other diseases. Upon arrival at Sanglah Hospital, the patient's consciousness was under the drug influence and experienced fever. From laboratory examination, it was found leukocyte level was 27,790/mm<sup>3</sup>, hemoglobin level was 9.09 g/dl, and albumin level was 2.10.

The patient was then treated in the ICU using a ventilator support because the patient had type I respiratory failure. The patient was also diagnosed with septic shock due to Ventilator Associated Pneumonia, and given two antibiotic regimens namely cefepime and levofloxacin, and intravenous paracetamol administration. Patient was treated together with Internal Medicine, Pulmonology, Urology and Anesthesiology departments. Furthermore, patients also got inotropic drugs such as Vascon and Dobutamin as a hemodynamic support. Patients also got intravenous tranexamic acid as an anti-fibrinolytic therapy.

From the sputum culture results, there was growth of *Acinetobacter Baumannii* which is MDRO and sensitive to the antibiotics Amikacin and Trimetoprim Sulfametoxazole. From further evaluation, it was decided to change the antibiotic regimen to Meropenem and Amikacin. Aside from that, the patient has been given PRC transfusion and underwent Hemodialysis 2 times a week. Patients were consulted to the plastic surgery department because of the appearance of a stress ulcer on the buttocks since 2 weeks of treatment. Wounds were treated with burnazin, sterile gauze every was changed every 3 days, and right and left tilt mobilization was done every 2 hours.

On the 46<sup>th</sup> day of treatment, the patient's clinical condition was worsened and was declared dead in front of family and paramedics with the cause of death was multiple organ failure due to septic shock and ARDS

### 3. Discussion

Ventilator Associated Pneumonia (VAP) ventilator is the most common form of nosocomial infection found in intensive care units (ICU), especially in patients who use mechanical ventilation. According to the American Thoracic Society in 2005, VAP is a lung infection that occurs after 48–72 hours of mechanical ventilator use.<sup>6,7,8</sup>

The incidence rate of VAP will increase along with the duration of the usage of mechanical ventilators. It is estimated that the incidence rate will increase around 3% per day during the first 5 days, 2% during 6-10 days of usage

and 1% per day after day 10. VAP can increase mortality rates 2-10 times higher than patients without pneumonia.<sup>9,10</sup> In a study on VAP in ICU conducted by Ranjan for 1 year, the prevalence of VAP patients who died was 48.3%.<sup>11</sup> In Indonesia, deaths due to VAP in ICU at Cipto Mangunkusumo Hospital were reported as much as 57.2%.<sup>7</sup> Based on research by Brahmani, et al the mortality rate in patients after surgery with a mechanical ventilator at Sanglah Hospital Denpasar in 2015 had reached 71.5%.<sup>6,7</sup>

Multi Drug Resistant Organism (MDRO) is defined as a microorganism especially bacteria that are resistant to one or more classes of antimicrobial agents. The presence of VAP will increase mortality rates if pneumonia is caused by MDRO pathogens. Of all VAP incidents, the MDRO incidence rate in VAP itself reaches 30-50%.<sup>6,8,9</sup>

Based on the incident VAP is divided by 2, early onset VAP occurs 48-72 hours, while late onset VAP, occurs after 96 hours. Early onset VAP commonly has a better prognosis since it is caused by germs that are still sensitive to antibiotics. Late onset VAP that occurs after 5 days or more has a worse prognosis since it is caused by MDR pathogens such as MRSA, *A. Baumannii*, *P. Aeruginosa*, *K. Pneumoniae*, *E. Coli* with ESBL (+). In this case, VAP that occurs is classified as a late onset VAP with the causative pathogen was the MDR pathogen in form of *Acinetobacter Baumannii*.<sup>7,8</sup>

VAP causative bacteria can be classified into 3 groups; in group I are gram-negative bacteria (*Enterobacter* spp, *Escherichia coli*, *Klebsiella* spp., *Proteus* spp, *Serratia marcescens*), *Haemophilus influenzae*, *Streptococcus pneumoniae* and Methicillin sensitive *Staphylococcus aureus* (MSSA). The causative bacteria of group II are the causative bacteria of group I plus anaerobic bacteria, *Legionella pneumophila* and Methicillin resistant *Staphylococcus aureus* (MRSA). The causative bacteria of group III are *Pseudomonas aeruginosa*, *Acinetobacter* spp and MRSA.<sup>13,14</sup> In this case, the etiological cause was *Acinetobacter Baumannii* which is class III bacteria.

The pathogenesis of VAP is very complex, Kollef stated that the incidence of VAP depends on the length of exposure to the environmental health supervisor, and other risk factors. These risk factors increase the likelihood of VAP by increasing the colonization of the aerodigestive tract by pathogenic microorganisms and increasing the aspiration of contaminated secretions into the lower respiratory tract. Germs in the aspirate will produce biofilms in lower respiratory tract and lung parenchyma. The biofilm will facilitate germs to further invade the lung parenchyma until an inflammatory reaction occurs in the lung parenchyma.<sup>13</sup>

The diagnosis of VAP is based on history taking, symptoms and clinical signs (non-specific), physical examination, radiological examination, laboratory examination and particularly, microbiological examination. Clinical manifestations include fever, chills, sweating, cough (productive, or non-productive, or mucous and purulent sputum production), chest pain due to pleurisy and spasms. Three components of systemic signs of infection found are

fever, tachycardia, and leukocytosis accompanied by a picture of new infiltrates or worsening in chest X-ray and the discovery of bacteria that cause lung infections. Several studies have shown that repeated chest radiograph examinations have a diagnostic accuracy of more than 68%, which is generally accompanied by a water bronchogram. There were three signs of systemic infection in patients, namely fever, tachycardia and leukocytosis. Aside of that, chest radiograph examination revealed infiltrates in the lung field.<sup>10,12</sup>

The high morbidity and mortality of VAP requires appropriate and fast antibiotic therapy, so information on the causes of VAP and its resistance is needed with the right sampling technique. Sampling can be done by non-invasive and invasive methods. The most common non-invasive method is endotracheal aspiration, while the invasive method is protected specimen brush (PSB) and bronchoalveolar lavage (BAL). Sampling in these patients was carried out non-invasively by endotracheal aspiration.<sup>6,8,13</sup>

From the sputum culture results, there was growth of *Acinetobacter Baumannii* which is MDRO. In conditions where culture results have not yet come out, the use of antibiotics according to the germ pattern often found in hospitals is a wise choice. Initial selection of antimicrobials is almost always on an empirical basis and is based on factors such as: severity of infection, patient-specific risk factors, and total number of days in hospital before onset.<sup>7,10</sup>

Close supervision of disease progression, patient's clinical status, changes in mechanical ventilation modes, improvement of chest x-ray, and several other biomarkers will help optimize the usage of antibiotic therapy.<sup>6,8,9</sup>

Various studies have shown that patients treated with antipseudomonas penicillin treatment plus lactamase inhibitors and aminoglycosides have lower mortality rates. Piperacillin-tazobactam is the most widely used antibiotic (63%) followed by Fluoroquinolone (57%), Vancomycin (47%), Cephalosporin (28%) and Aminoglycosides (25%). Singh, et al stated that Ciprofloxacin was very effective in most of Enterobacteriaceae bacteria, *Haemophilus influenza* and *Staphylococcus aureus*.<sup>15</sup>

In patients with MDRO or suspected MDRO, the recommended use of antibiotics is combination antibiotic regimens. In MDR pathogens such as *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and *Acinetobacter sp*, the preferred antibiotic regimen is Cephalosporin or Carbapenem or Beta-lactamase groups adjusted for the sensitivity results and combined with Fluoroquinolones. Whereas in MDR pathogens such as Methicillin Resistant *Staphylococcus aureus* (MRSA), Aminoglycoside is the choice combined with Lineolid or Vancomycin.<sup>6,8,9</sup>

In this case, based on patient's sputum culture result, MDR pathogen was *Acinetobacter Baumannii*. The administration of antibiotics was adjusted to the results of sensitivity tests which are Amikacin and Trimethoprim Sulfamethoxazole. However, because it did not provide an optimal response, it

was decided to replace the antibiotic regimen with a combination of Meropenem and Amikacin.

#### 4. Conclusion

A comprehensive preoperative evaluation is needed in patients with previous cesarean section that suspects there is a possibility of morbidly adherent placenta. Thus, the management of a multidisciplinary team can be planned to reduce morality and mortality.

The involvement of MDR pathogens in VAP will increase both morbidity and mortality in VAP patients. Proper diagnosis and monitoring, and also multidisciplinary management play an important role. The combination of antibiotics' administration, especially those in accordance with MDRO pathogens, will help reduce morbidity and mortality. The transfer of patients from the intensive room also needs to be considered to first step down to the semi-intensive room so that strict and comprehensive postoperative monitoring can be done.

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