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Bacterial Identification And Antibiotics Sensitivity Of Ventilator-Associated Pneumonia (VAP) Patients At RSD Dr. Soebandi Jember

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A B S T R A C T

Ventilator-Associated Pneumonia (VAP) is pneumonia in patients with a mechanical ventilator. The use of empirical antibiotics therapy to VAP patients based on bacterial identification and its antibiotics sensitivity. This study aims to determine bacterial identification and antibiotics sensitivity of VAP patients at RSD dr. Soebandi Jember. A descriptive observational study was conducted with a retrospective approach. The data were collected from the medical record of VAP patients from September to October 2019. All samples meet the inclusion and exclusion criteria. Data analysis utilized Microsoft Excel 2010. This paper had 15 VAP patients who conducted bacterial identification and its sensitivity to antibiotics. The most frequent bacteria that cause VAP was Acinetobacter baumannii. Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterobacter aerogenes, Burkholderia cepacia, Pseudomonas fluorescens, Salmonella arizonae, and Escherichia coli also cause VAP. Antibiotics with the highest sensitivity to VAP-causing bacteria were amikacin, meropenem, and piperacillin-tazobactam. Meanwhile, the antibiotics that bacterial resistant were cefixime, cefotaxime, and ceftriaxone.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is pneumonia in a ventilated patient on a ventilator for at least 48 hours (Dahlan, 2014). Its symptoms are fever, tachypnea, increased respiratory secretions, leukocytosis. Other than that, its symptom also includes lung consolidation accompanied by new or changes in infiltrates on radiological examination (Hunter, 2006; (Mandell and Wunderink, 2015). Gadani's research showed that 37% of patients hospitalized in the Intensive Care Unit (ICU) became VAP (Gadani et al., 2010). Prolonged use of a ventilator leads to VAP risk, thereby increasing mortality from 5% to 65% (Schweiger et al., 2013) Several factors that influence VAP include the patient's age, length of use of a ventilator, patient consciousness level, comorbid disease, and antibiotic treatment (Wu et al., 2019)

Several studies have reported bacterial resistance to antibiotics in humans, animals, and the environment García et al.,2020; Hoque et al., 2020). The negative impact of bacterial resistance in humans is that the infection does not recover by antibiotic therapy, more complication, a longer length of stay, higher cost of care, and increased patient mortality rate (Collignon, 2012; (Friedman et al., 2016). To avoid the negative impact of bacterial resistance to antibiotics, the treatment of bacterial infectious diseases in humans, including VAP, should be given according to bacterial culture and antibiotics sensitivity test results. Unfortunately, it needed several days for the results. Before there are results, antibiotics therapy

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was given empirically based on the hospital antibiogram.

Every hospital should have an antibiogram regularly as a reference for empiric antibiotics therapy. Previously RSD Dr. Soebandi did not have bacterial mapping and antibiogram of VAP patients. This study aims to determine the bacterial species and its antibiotics sensitivity of VAP patients at RSD. Dr. Soebandi Jember, so that it can be as a practical guide for antibiotics therapy.

METHOD

This research was a descriptive study. Data were obtained retrospectively from VAP patients' medical records hospitalized at RSD Dr. Soebandi from September to October 2019. The inclusion criteria were VAP patients who used ventilator > 48 hours, that had bacterial culture and antibiotics sensitivity test in their medical records. The exclusion criteria were VAP patients who had HIV or tuberculosis comorbid. This research utilized total sampling.

VAP patients' sputum was collected from the endotracheal tube, carried by transport media, and then cultivated in blood agar and Mac Conkey media. Growth continued to be planted on Muller Hinton agar to identify the bacteria and antibiotics sensitivity test (Soleha, 2015). Identification of bacteria used Analytical Profile Index (API), API Strep, and API 20E (O'Hara, 2005). Antibiotic sensitivity test utilized agar diffusion method with various antibiotic discs (Soleha, 2015).

Data analysis applied with Microsoft Excel 2010. This study was approved by The Health Research Ethics Committee, Faculty of Medicine, University of Jember, number 1.347/H25.1.11/KE/2019

RESULT

15 sputum of VAP patients had bacterial identification and antibiotics test sensitivity. The gender distribution was 11 male and four female. Based on the age group, four patients aged < 17 years, one patient aged 17-25 years, three patients aged 25-45, 4 patients aged 45-65, and 3 patients aged > 65 years old. The bacterial culture results showed that 14 samples had bacterial growth and 1 sample had no bacterial growth (see table 1).

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Table 1. The samples' characteristics.

Characteristic	Amount (n)	%
Gender		
Men	11	73,3
Women	4	26,6
Age		
< 17 years	4	26,6
17-25 years	1	6,6
25-45 years	3	20
45-65 years	4	26,6
> 65 years	3	20
Bacterial culture results		
Bacterial growth	14	93,3
No bacterial growth	1	6,7

In bacterial growth from 14 sputum of VAP patients, there were Acinetobacter baumannii in 4 samples (29%). Klebsiella pneumonia, Enterobacter aerogenes, and Pseudomonas aeruginosa each bacteria were two samples (14%). Burkholderia cepacia, Pseudomonas fluorescens, Salmonella arizonae, and Escherichia coli each bacteria were 1 sample (7%) (see table 2).

Table 2. Species of bacteria from the sputum of VAP patients.

Species	Amount (n)	%
Acinetobacter baumannii	4	29
Klebsiella pneumoniae	2	14
Enterobacter aerogenes	2	14
Pseudomonas aeruginosa	2	14
Burkholderia cepacia	1	7
Pseudomonas fluorescens	1	7
Salmonella arizonae	1	7
Escherichia coli	1	7
Total	14	100

Furthermore, samples with bacterial growth were analyzed for the antibiotics sensitivity test. The results showed that nine out of 11 bacterial isolates (81.8%) were sensitive to amikacin. Meanwhile, six out of eight (75%) were sensitive to meropenem, five out of seven (71.4%) were sensitive to piperacillin-tazobactam. Antibiotics resistance had occurred. Six out of seven bacterial isolates (85.7%) were resistant to cefixime. Meanwhile, five out of six (83.3%) were resistant to ceftriaxone, seven out of ten (70%) were resistant to cefotaxime (See table 3).

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Table 3. Results of antibiotics sensitivity test

Antibiotics	Bacterial isolate number													
	1	2	3	4	5	6	7	8	9	10	11	12	13	14
	Antibiotics sensitivity													
Amikacin	R	S	-	R	-	-	S	S	S	S	S	S	S	S
Ampicillin	-	R	-	-	-	-	S	I	-	-	S	I	S	-
Ampicillin-sulbactam	R	-	-	-	R	R	-	-	-	-	S	I	I	S
Aztreonam	-	R	-	-	-	-	R	R	S	S	S	R	R	-
Cefuroxime	-	R	-	-	-	-	R	-	-	-	S	R	R	-
Chloramphenicol	-	-	R	-	S	S	R	S	-	-	S	R	S	R
Ciprofloxacin	R	-	-	R	I	R	R	R	S	S	S	S	R	R
Cephalexin	R	-	-	R	S	R	S	-	S	S	-	R	S	S
Cefixime	-	-	-	-	-	-	-	R	R	R	S	R	R	R
Cefotaxime	R	R	-	R	-	-	R	-	S	S	S	R	R	R
Ceftazidime	R	I	R	R	-	-	R	I	S	S	S	I	R	R
Ceftriaxone	-	-	-	-	-	-	R	R	-	-	S	R	R	R
Gentamicin	-	R	-	-	S	R	S	S	-	-	S	-	-	-
Levofloxacin	R	I	-	-	-	-	S	I	S	S	S	S	R	R
Meropenem	-	-	-	-	S	R	-	-	S	I	S	S	S	S
Cotrimoxazole	R	R	-	R	-	-	I	R	-	-	S	S	R	R
Tobramicin	R	-	R	S	S	R	R	R	S	S	S	R	R	S
Tetracycline	R	S	-	R	-	-	S	R	-	-	S	R	R	R
Ticarcillin	-	S	-	R	S	R	R	S	I	S	-	-	-	-
Piperacillin-tazobactam	R	-	-	-	-	-	-	-	S	S	S	S	S	I

Abbreviation: R= resistant; I= Intermediate; S= sensitive, and (-)= untested antibiotics.

Bacterial species according to the bacterial isolate number: 1. Acinetobacter baumannii; 2. Klebsiella pneumoniae; 3. Burkholderia cepacia; 4. Acinetobacter baumannii; 5. Pseudomonas flurescens; 6. Acinetobacter baumannii;7. Salmonella arizonae; 8. Enterobacter aerogenes; 9. Pseudomonas aeruginosa; 10. Pseudomonas aeruginosa; 11. Klebsiella pneumoniae; 12. Enterobacter aerogenes; 13. Escherichia coli; 14. Acinetobacter baumannii.

DISCUSSION

The results of this study showed that VAP was more frequent in men than in women. This result is in line with Gadani et al., which reported that VAP was more frequent in men than women (Gadani et al., 2010). The smoking habits in most men can cause damage to the epithelium lining in the airway, thus interfering with the clearance of the pathogen (Falaga et al., 2007). Based on the age group, patients who had VAP mainly occurred in the elderly (45-65 years old) and (> 65 years old), sequentially obtained 4 and 3 samples. The elderly group has an increased risk of infection due to decreased immune system and physiological change that affects the organ system, increasing the risk of respiratory tract infection (El Chakhtoura et al., 2017)

The presence of bacterial growth in 14 sputa of VAP patients showed that most VAP patients at RSD dr. Soebandi was caused by bacteria. Only 1 sample did not have bacteria growth. It is because that the

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sputum was collected after antibiotics treatment (Kalil *et al.*, 2016; Harris et al., 2017). In this study, eight Gram-negative bacteria species grew on bacterial culture. A study found Gram-negative bacteria caused 45-70% of VAP (Barbier et al., 2013). This paper showed that the most common bacteria that cause VAP was Acinetobacter baumannii (29%). Research reported that Acinetobacter baumannii was the cause of VAP in the ICU by 7.9% (Kalanuria et al., 2014). Acinetobacter baumannii is Gram negative, rod-shaped, and non-motile aerobic bacteria. It is often found in nosocomial pneumonia and immunosuppressed patients (Cilloniz, 2014). This bacteria has a particular target of moist tissue such as mucous membranes (Howard et al., 2012).

Klebsiella pneumonia, Enterobacter aerogenes, and Pseudomonas aeruginosa each bacteria were two samples (14%). Klebsiella pneumoniae and Enterobacter aerogenes are in the Enterobacteriaceae family that cause nosocomial pneumonia (Amer et al., 2018). Enterobacter aerogenes cause various nosocomial infections; one of them is VAP (Donenberg et al., 2015). Pseudomonas aeruginosa, in the form of rods and Gram-negative, can infect immune-compromised humans and become one of the pathogens that cause pneumonia in the ICU setting (Zander and Farver, 2018).

Pseudomonas fluorescens causes diseases in the respiratory tract and bacteremia in immune-compromised humans (Scales et al., 2014). In this paper, there were Escherichia coli and Salmonella arizonae; each bacteria were as many as two samples. They are Gram-negative, rod bacteria, and members of the Enterobacteriaceae family. Salmonella arizonae infection can occur in immune-compromised patients (Lee et al., 2016). Also, there was Burkholderia cepacia in one sample. However, these Gram-negative bacteria were reported to cause community-acquired pneumonia (Bayram et al., 2011).

Antibiotics therapy empirically on VAP with the suspected cause of Gram-negative bacteria can use beta-lactam and non-beta-lactam antibiotics. Its antibiotics such as Fluoroquinolone, aminoglycosides, and polymixine (Kalil et al., 2016). The bacterial isolates were most sensitive to amikacin, meropenem, and piperacillin-tazobactam. 81% of the tested isolates were sensitive to amikacin, which is included in the aminoglycoside group. Aminoglycosides are therapy for infections caused by Gram-negative bacteria. It has a mechanism by inhibiting bacterial protein synthesis (Brunton et al., 2008). Some isolates were resistant to aminoglycoside. Aminoglycoside works through aminoglycoside modifying enzymes (AMEs) and ribosome target mutations (Garneau, 2016).

Meropenem and piperacillin-tazobactam are often used as empirical therapy for VAP – administered intravenously. In this study, meropenem had a high level of sensitivity. Meropenem is a beta-lactam antibiotic in the carbapenem class and has a broader spectrum of activity than most other beta-lactam

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antibiotics (Hardman and Limbird, 2012). Piperacillin-tazobactam is stable against beta-lactamase and effective against Gram-positive and Gram-negative bacteria (Ito et al., 2010).

There were many bacteria from the Enterobacteriaceae family in this study. Most Enterobacteriaceae families are sensitive to cephalosporine and fluoroquinolone. Less than one percent of these bacteria had Extended-Spectrum Beta-Lactamase (ESBL) (Shindo et al., 2013). ESBL is an enzyme that can hydrolyze most of the penicillin class antibiotics. This paper showed that bacteria were resistant to the cephalosporin class, especially the third generation. The third generation of cephalosporin consists of cefixime, ceftriaxone, cefotaxime, and ceftazidime. The most common resistance mechanism to cephalosporins is the destruction of antibiotics through hydrolysis of the beta-lactam ring. The level of resistance to third-generation cephalosporin in Enterobacteriaceae currently reached 10-70% (Ruppé et al., 2015). The production of beta-lactamase usually causes the resistance of Enterobacteriaceae to antibiotics. ESBL arises when there are mutations in genes encoding TEM-1, TEM-2, or SHV-1. Its mutations are new beta-lactamase capable of hydrolyzing third-generation cephalosporin and aztreonam (Paterson, 2006).

CONCLUSION

Acinetobacter baumannii is the most frequent VAP-causing bacteria at dr. Soebandi Hospital, Jember. Klebsiella pneumoniae, Pseudomonas aeruginosa, Enterobacter aerogenes, Burkholderia cepacia, Pseudomonas fluorescens, Salmonella arizonae, and Escherichia coli also cause VAP. Amikacin, meropenem, and piperacillin-tazobactam are antibiotics with the highest sensitivity to VAP-causing bacteria. Meanwhile, the antibiotics that bacterial resistant are cefixime, cefotaxime, and ceftriaxone.

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