Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2022 Feb 05; 10(B):250-254.
https://doi.org/10.3889/oamjms.2022.8139
eISSN: 1857-9655
Category: *B - Clinical Sciences*
Section: *Anesthesiology*

Bacterial Patterns and Sensitivity to Antibiotics in Patients Treated with Ventilators at the Intensive Care Unit of Sanglah Hospital Denpasar, Bali, Indonesia

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Edited by: Mirko Spiroski
Citation: Devian MK, Suranadi IW, Hartawan IGA, Aryabiantara IW. Bacterial Patterns and Sensitivity to Antibiotics in Patients Treated with Ventilators at the Intensive Care Unit of Sanglah Hospital Denpasar, Bali, Indonesia. Open Access Maced J Med Sci. 2022 Feb 05; 10(B):250-254. https://doi.org/10.3889/oamjms.2022.8139
Keywords: Ventilator; Microbial Pattern; Antibiotics; Sensitivity; Resistance
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Received: 02-Dec-2021
Revised: 10-Jan-2022
Accepted: 15-Jan-2022

Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist

Abstract

BACKGROUND: Ventilator use to treat patients with respiratory failure in the intensive care unit (ICU) is crucial to prevent further organ failure caused by inadequate oxygenation. However, as an invasive procedure, the use of a ventilator could lead to nosocomial infection, such as ventilator-associated pneumonia (VAP) caused by opportunistic microorganisms in the ICU. Hence, the author is interested in finding the microbial patterns and its antibiotic sensitivity as a source of data for further researches and providing consideration on antibiotics usage for patients treated with ventilators in the ICU of Sanglah Hospital Denpasar.

AIM: This study is conducted to obtain the microbial pattern and antibiotics sensitivity on patients treated with ventilators in the ICU of Sanglah Hospital Denpasar.

MATERIALS AND METHODS: This research is based on the cross-sectional descriptive method. Research samples were chosen with consecutive sampling that is included in the research's inclusion criteria. Patient data were collected from January 1, 2021 to June 30, 2021 within the ICU of Sanglah Hospital Denpasar. Variables in this research were listed as followed: Demographic data of the patients that include age, gender, comorbid, diagnosis, ventilator usage indication, bacterial culture, and bacterial susceptibility test.

RESULTS: One hundred and eighty-five culture samples were obtained from 113 patients. Eighteen different species of bacteria were found with the three most common microorganisms being *Pseudomonas aeruginosa* (22.2%), *Acinetobacter baumanii* (20%), and *Klebsiella pneumoniae* (17.3%). Susceptibility pattern found as follows: The prevalence of *P aeruginosa* was found sensitive toward ceftazidime (68.3%), gentamicin (68.3%), and amikacin (65.9%), *A. Baumanii* are mostly sensitive to amikacin (56.8%), gentamicin (32.4%), and tigecycline (32.4%), *K. Pneumoniae* are mostly sensitive to amikacin (83.9%), meropenem (77.4%), and piperacillin/tazobactam (54.8%). Resistance pattern found as follows: The prevalence of *P aeruginosa* was found resistant toward cefixime (70.7%), cefazolin (58.5%), and cefuroxime (58.5%), *A. baumanii* are mostly resistant to cefixime (86.5%), cefoperazone (81.1%), and piperacillin/tazobactam (75.7%), *K. pneumoniae* are mostly resistant to ciprofloxacin (61.3%) and levofloxacin (48.4%).

CONCLUSION: To decrease the spreading of multidrug resistant organisms that have been found in ventilated patients, prevention strategies and rational use of antibiotics need to be performed correctly.

Introduction

The intensive care unit (ICU) is an independent part of a hospital with specialized medical staff and equipment that aims to treat patients in critical condition [1]. Critical patients' vital signs need to be monitored regularly as it has a high potential to deteriorate. In this case, one of the most common incidences is respiratory failure. To handle respiratory failure, the usage of a mechanical ventilator to maintain adequate oxygenation is crucial to prevent further organ damage [2]. However, maintaining the patient's patent airway using an endotracheal tube (ETT) is an invasive procedure, therefore, creating an entrance for microorganisms to infect and causing inflammation on the lung, this condition is called ventilator-associated pneumoniae (VAP) [3]. Research in 2018 showed that usage of the right intravenous antibiotic prophylaxis can significantly decrease the incidence of early onset VAP in comatose patients [4]. On the other hand, irrational usage of antibiotics can increase the incidence of multidrug-resistant organisms (MDRO) infection that contributes to high mortality in VAP patients [5]. Established knowledge on microbial patterns and antibiotic sensitivity found in patients treated with ventilators to provide antibiotics treatment considerations are still limited. Therefore, this study aims to obtain more data linked to the microbial pattern, its antibiotic sensitivity, and resistance in patients treated ventilators within the ICU of Sanglah Hospital Bali.

Subjects and Methods

This retrospective study is conducted based on a cross-sectional descriptive method and was ethically approved by Sanglah General Hospital's Research Ethics Committee (411/UN14.2.2.VII.14/ LT/2021). Samples for this research were chosen through consecutive sampling method using patient's medical records in Sanglah General Hospital registry from January 1, 2021 until June 30, 2021 within the ICU of Sanglah Hospital Denpasar. The sample population consists of patients that have a complete medical record, are treated with mechanical ventilation, and have a positive bacterial culture test. The subjects' bacterial culture, sensitivity, and resistance results were obtained from Sanglah General Hospital's Clinical Microbiology Department Laboratory. The data collected were analyzed univariately using Microsoft Excel. The collected variables were listed as followed: Demographic data of the patients that include age, gender, comorbid, diagnosis, ventilator usage indication, bacterial culture, and bacterial susceptibility test.

Results

A total of 113 patients' medical records were collected. The sample consists of 45 (39.8%) females and 68 (60.2%) males. The mean age for the sample was 50.2 ± 17.6. Indications of ventilator usage in the ICU are dominated by post-operative patients (55.8%). ETT sputum sample is the highest amount of bacterial culture samples type that was collected (Table 1).

Table 1: Subjects' characteristics

Characteristics	n = 113
Sex, n (%)	
Male	68 (56.6)
Female	45 (43.4)
Age (years)	
Mean ± SD	50.2 ± 17.06
Min–max	16–85
Ventilator Indication	
Respiratory failure	14 (12.4)
Pneumonia	4 (3.5)
Neuromuscular disorder	1 (0.8)
Sepsis	8 (7.1)
Decrease of consciousness	15 (13.3)
ARDS	5 (4.4)
Lung nodule	2 (1.8)
Lung edema	1 (0.6)
Post-operative respiratory insufficiency	63 (55.8)
Culture type	
Sputum	34 (18.4)
Tube Sputum	94 (50.8)
ETT Sputum	11 (5.9)
Blood	46 (24.9)

SD: Standard deviation, min–max: Minimum–maximum

Out of 113 patients, we managed to obtain 185 positive bacterial culture results. Overall, the most common microorganism found was Gram-negative bacteria with the three highest percentages that are *Pseudomonas aeruginosa* (22.2%), *Acinetobacter baumanii* (20%), and *Klebsiella pneumoniae* (17.3%) (Table 2). We also found some MDRO in the bacterial pattern with MDR-*K. pneumoniae* as the highest figure to have presented (Figure 1).

In this study, we analyzed the bacterial susceptibility using univariate analysis with samples taken from the three most common organisms found within the bacterial pattern (Table 2). Our research shows *P. aeruginosa* that has the highest bacterial percentage mostly sensitive to ceftazidime (68.3%), gentamicin (68.3%), and amikacin (65.9%), the prevalence of the two following bacteria, which are *A. baumanii* (56.8%) and *K. pneumoniae* (83.9%), shared the sensitivity toward amikacin. The resistance pattern of *P. aeruginosa* and *A. baumanii* shared similar resistance prevalence to cefixime. However, *K. pneumoniae* is mostly resistant to ciprofloxacin (61.3%) (Table 3).

Table 2: Bacterial pattern

Bacterial species	n (%)
Pseudomonas aeruginosa	41 (22.2)
Acinetobacter baumanii	37 (20)
Klebsiella pneumoniae	31 (17.3)
Eschericia coli	19 (10.3)
Staphylococcus aureus	11 (5.9)
Enterobacter cloacae	11 (5.9)
Staphylococcus hominis	6 (3.2)
Staphylococcus epidermidis	5 (2.7)
Staphylococcus maltophilia	4 (2.2)
Staphylococcus haemoliticus	3 (1.6)
Citrobacter koseri	2 (1.1)
Citrobacter freundii	1 (0.5)
Streptococcus anginosus	1 (0.5)
Streptococcus alactolyticus	1 (0.5)
Streptococcus suis I	1 (0.5)
Enterobacter faecalis	2 (1.1)
Enterococcus columbae	1 (0.5)
Acinetobacter spp.	3 (1.6)
Vibrio mimicus	1 (0.5)
Serratia marcescens	1 (0.5)
Total	185 (100)

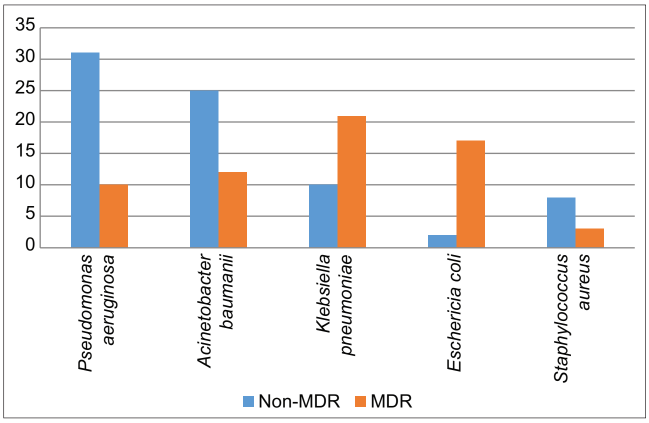

Figure 1: Prevalence of multidrug resistant organism in ventilated patient

Discussion

Ventilated subject characteristics

In this research, it is shown that males (56.6%) are more commonly treated with ventilators in the ICU and could be considered compatible with another research in Thailand [6]. The main indications of ventilator usage mentioned in Table 1, which are post-operative patients that suffer respiratory insufficiency, having a decrease of consciousness, and acute respiratory failure also shared a similar result with the indication of mechanical ventilation treatment in Poland [7]. The resulting male predominance can be supported by a study in 2018 that mentioned a higher chance of males to experience morbidities, such as cardiac and respiratory complications after receiving operative procedures [8].

Table 3: Bacterial susceptibility test result

S. No.	Antibiotics	*Pseudomonas aeruginosa* (n = 41)		*Acinetobacter baumanii* (n = 37)		*Klebsiella pneumoniae* (n = 31)	
		S (%)	R (%)	S (%)	R (%)	S (%)	R (%)
1.	Piperacillin/Tazobactam	58.5	22	13.5	75.7	54.8	6.5
2.	Ampicillin/Sulbactam	0	0	21.6	62.2	29	35.5
3.	Cefoperazone/Sulbactam	0	2.4	2.7	5.4	6.5	0
4.	Cefazolin	0	58.5	0	51.4	3.2	6.5
5.	Cefuroxime	0	58.5	2.7	43.2	3.2	0
6.	Cefoxitin	0	2.4	0	0	0	0
7.	Ceftazidime	68.3	19.5	8.1	51.4	9.7	0
8.	Ceftriaxone	0	4.9	0	67.6	29	16.1
9.	Cefotaxime	0	2.4	5.4	2.7	3.2	0
10.	Cefoperazone	2.4	0	0	81.1	0	0
11.	Cefixime	0	70.7	0	86.5	25.8	3.2
12.	Cefepime	63.4	17.1	24.3	70.3	32.3	12.9
13.	Ampicillin	0	0	2.7	0	3.2	6.5
14.	Gentamicin	68.3	19.5	32.4	62.2	51.6	35.5
15.	Amikacin	65.9	22	56.8	24.3	83.9	3.2
16.	Tigecyline	0	46.3	32.4	10.8	9.7	3.2
17.	Ciprofloxacin	63.4	26.8	18.9	73	22.6	61.3
18.	Ofloxacin	0	0	0	0	0	0
19.	Levofloxacin	36.6	34.1	24.3	24.3	16.1	48.4
20.	Meropenem	53.7	3.2	21.6	59.5	77.4	3.2
21.	Cotrimoxazole	0	35.5	59.5	27	32.3	35.5
22.	Colistin	0	2.4	2.7	0	0	0

Bacterial pattern in ventilated patients

The bacterial pattern in our study is dominated by Gram-negative bacteria (GNB), such as *P. aeruginosa* (22.2%), *A. baumanii* (20%), *K. pneumoniae* (17.3%), and *Eschericia coli* (10.3%). This finding is supported by the 2016 American Thoracic Society (ATS) guideline that mentioned similar pathogens as the cause of VAP [9]. The studies have also shown that *P. aeruginosa* infections in VAP are highly related to empirical use of antibiotics and the usage of mechanical ventilation for more than 5 days [10]. Infection of GNB is higher since they are more likely to develop into MDRO. This is caused by its ability to alter its outer layer, such as mutating the porins and hydrophobic layer, therefore, disturbing antibiotics adherence and diffusion into the microorganism [11]. Findings of MDRO in bacterial patterns need to be observed closely since it is a significant variable that contributes to patients' length of stay, cost of treatment, and mortality in the ICU [12]. In combating MDRO, ATS published a guideline that proved consistent relation of prior antibiotics treatment resulting infection of MDR pathogens in VAP. It is also mentioned that preventing the spread of MDRO in invasive ventilated patients can be achieved by considering intubation alternatives, usage of silver-coated ETT and subglottic secretion drainage ETT, and building antibiotic stewardship in the health facilities [13].

Bacterial susceptibility

This study analyzed bacterial sensitivity and resistance from the three most common bacteria that we found in our samples as shown in (Table 3). *P. aeruginosa* is mostly sensitive to ceftazidime (68.3%), gentamicin (68.3%), and amikacin (65.9%). This pattern is similar to research by Widyaningsih that found *P. aeruginosa* sensitivity toward ceftazidime, gentamicin, and netilmicin [14]. Ceftazidime high sensitivity against *P. aeruginosa* compared to the other third generation of cephalosporins is supported by research conducted in Pakistan that collect samples from hospitals isolates [15] and another research by Rhodes that shown above 60% isolates of *P. aeruginosa* to be sensitive toward ceftazidime and cefepime, therefore, supported the antibiotics recommendation in the 2016 ATS guideline [16]. We also found that *A. baumanii* isolates are mostly sensitive to amikacin (56.8%), gentamicin (32.4%), and tigecyline (32.4%). Finally, *K. pneumoniae* found to be sensitive toward amikacin (83.9%), meropenem (77.4%), piperacillin/tazobactam (54.8%), and gentamicin (51.6%). Overall, amikacin and gentamicin are still sensitive to these three bacteria; this is similar to a study in Nepal that showed amikacin sensitivity to 58% of the isolates (*K. pneumonia*, *Acinetobacter spp.,* and *P. aeruginosa*) in VAP patients [17]. A study in China has evaluated the usage of amikacin and proved even better results against GNB, such as *E. coli*, *P. aeruginosa*, and *K. pneumoniae* but in contrast, the research stated low sensitivity of amikacin against MDR-*A. baumanii* [18]. This sensitivity result may also be caused by unfavorable use of aminoglycosides monotherapy concerning the antibiotic's low lung penetration and worrying adverse effects as stated by the ATS panel. However, more studies are needed to evaluate this statement [9].

Bacterial resistance

Our research found the bacterial resistance pattern (Table 3) with *P. aeruginosa* isolates is mostly resistant toward cefixime (70.7%), cefazolin (58.5%), and cefuroxime (58.5%), *A. baumanii* isolates mostly resistant to cefixime (86.5%), cefoperazone (81.1%), and piperacillin/tazobactam (75.7%). This finding is supported by another research in Indonesia that found nearly identical bacterial patterns in VAP to be most resistant toward cephalosporins (cefixime, cefotaxime, and ceftriaxone) [19]. We also found that *K. pneumoniae* isolates to be resistant to ciprofloxacin (61.3%) and levofloxacin (48.4%). It can be concluded that extended spectrum beta-lactamases (ESBL) and AmpC-beta lactamases (AmpC) producers bacteria that are commonly developing resistance to cephalosporins and penicillins have a high contribution to this resistance pattern (Figure 1) [20], [21]. There is still a lack of study recommending treatment to fight ESBL/AmpC producers in ventilated patients. However, the use of carbapenems may be a preferable option [22], [23]. In addition, the ATS guideline recommends the use of vancomycin and linezolid for empirical treatment if the bacterial pattern indicates findings of methicillin-resistant

Staphylococcus aureus and other MDR bacteria which were also presented in this study (Figure 1).

Conclusion

Nosocomial infections associated with mechanical ventilation caused by MDRO remain a problem toward patients' outcome in the ICU. For that reason, intensivists need to adjust the right use of antibiotics and further prevention strategies for VAP according to the updated bacterial patterns and sensitivity tests results that are available.

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