MICROBIAL PROFILE AND ANTIBIOTIC SUSCEPTIBILITY PATTERNS OF PATHOGENS CAUSING VENTILATOR-ASSOCIATED PNEUMONIA AT INTENSIVE CARE UNIT, SESTRE MILOSRDNICE UNIVERSITY HOSPITAL CENTER, ZAGREB, CROATIA

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SUMMARY – Ventilator-associated pneumonia (VAP) is very common in many intensive care Units, but there are still many uncertainties about VAP, especially about the choice of initial empiric antibiotics. The incidence of specific pathogens with different susceptibility patterns causing VAP varies from hospital to hospital. This is the reason why empiric initial antibiotic treatment for VAP should be based not only on general guidelines (that recommend therapy according to the presence of risk factors for multidrug-resistant bacteria), but also on up-to-date information on local epidemiology. The aim of this study was to determine the microbial profile of pathogens causing VAP and their antibiotic susceptibility patterns. The study was conducted in the 15-bed surgical and neurosurgical Intensive Care Unit, Department of Anesthesiology and Intensive Care, Sestre milosrdnice University Hospital Center, Zagreb, Croatia. Retrospective data were collected from September 2009 to March 2013. All patients that developed VAP during the study period were eligible for the study. According to study results, the incidence of VAP was 29.4%. The most commonly isolated bacterium was *Staphylococcus aureus* (21.1%), followed by *Pseudomonas aeruginosa* (19.0%) and *Acinetobacter* species (13.6%). All *Staphylococcus aureus* isolates were susceptible to vancomycin and linezolid. *Pseudomonas aeruginosa* showed 100% susceptibility to cefepime and very high susceptibility to piperacillin-tazobactam (96%), ceftazidime (93%) and ciprofloxacin (89%). Ampicillin-sulbactam was highly effective for *Acinetobacter* species, showing resistance in only 8% of isolates. In conclusion, according to study data, appropriate empiric antibiotic therapy for patients with VAP without risk factors for multidrug-resistant bacteria is ceftriaxone and for patients with risk factors for multidrug-resistant bacteria ampicillin-sulbactam plus cefepime plus vancomycin or linezolid.

Key words: *Pneumonia, ventilator-associated – etiology; Drug resistance, microbial; Intensive care units; Croatia*

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Introduction

Ventilator-associated pneumonia (VAP) is defined as a type of nosocomial pneumonia occurring more than 48 hours after initiation of endotracheal intubation and mechanical ventilation[1]. The incidence of VAP ranges from 9% to 27%, so VAP is a very common problem in intensive care units (ICU), but there

are still many uncertainties about VAP, especially about the choice of initial empiric antibiotics[2,3]. An inappropriate empiric antibiotic treatment is associated with increased mortality, prolonged duration of mechanical ventilation, prolonged length of ICU stay, and increased treatment costs. Empiric antibiotic therapy should be properly selected according to current guidelines, but also adjusted to specific local pathogens[4]. The incidence of specific pathogens with different susceptibility patterns causing VAP may not only vary from hospital to hospital, but also within the same hospital or ICU over time[5]. This is the reason why empiric initial antibiotic treatment for VAP should be based on general guidelines, but also on up-to-date information on local epidemiology. There is a lack of published data from Croatian ICUs regarding local microbiological profile of pathogens causing VAP, as well as on their antibiotic susceptibility and resistance patterns.

The aim of this study was to determine microbial profile of pathogens causing VAP and their antibiotic susceptibility patterns. This information will help us in selection of appropriate empiric antibiotic therapy.

Patients and Methods

The study was conducted in a 15-bed surgical and neurosurgical Intensive Care Unit of the Department of Anesthesiology and Intensive Care, Sestre milosrdnice University Hospital Center, Zagreb, Croatia. This study was approved by the Hospital Ethics Committee (E.P. number: 35-1/09). Retrospective data were collected from September 2009 to March 2013. Because of the retrospective and observational nature of the study, an informed consent was unnecessary.

All patients that developed VAP during the study period were eligible for the study. As for clinical diagnosis, VAP was established on the Modified Clinical Pulmonary Infection Score (CPIS) (Table 1)[6]. CPIS is based on six clinical assessments, each scored zero to two points. A score of more than six was considered suggestive of VAP. The CPIS score was calculated only when there was clinical suspicion of VAP (presence of new or progressive infiltration on chest radiography and presence of at least two of the following criteria: fever, leukocytosis and purulent tracheal secretion). Also, when there was clinical suspicion of VAP, quantitative culture of endotracheal aspirate (ETA) was performed to identify VAP pathogens. Only pathogen isolated at a concentration of more than 10^5 CFU/mL was considered causative of VAP. Growth of any organism below the concentration of 10^5 CFU/mL was assumed to be due to colonization. ETA sample with more than 10 squamous epithelial cells *per* visual field represents an invalid sample[7]. Purulent sputum is defined as secretions from the lungs that contain more than 25 neutrophils *per* visual field. Only the first VAP episode was evaluated.

Patient age, gender, smoking habit, Simplified Acute Physiology Score II (SAPS II), Acute Physiology and Chronic Health Evaluation II (APACHE II), comorbidities and main reason for ICU admission were recorded.

Early-onset VAP was defined as that occurring within the first 4 days of mechanical ventilation (MV) and was more likely to be caused by antibiotic susceptible bacteria. Late-onset VAP (after 4 days of MV)

Table 1. The Modified Clinical Pulmonary Infection Score (CPIS)

Points	0	1	2
Tracheal secretion	Rare	Abundant	Abundant + purulent
Chest x-ray infiltrates	No infiltrate	Diffuse infiltrate	Localized infiltrate
Temperature (°C)	36.5-38.4	38.5-38.9	<36 or >39
Leukocyte count (/mm^3)	4000-11000	<4000 or >11000	<4000 or >11000 + band forms >500
PaO2/FiO2 (mm Hg)	>240 or ARDS		<240 and no evidence of ARDS
Microbiology	Negative		Positive

ARDS = acute respiratory distress syndrome

was more likely to be caused by multidrug-resistant (MDR) bacteria. Multidrug resistance is defined as non-susceptibility to at least one agent from three or more antimicrobial categories[8].

Antibiotic susceptibility patterns were determined using disc diffusion method and, if required, E-test, according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) standards. The antibiotic sensitivity and resistance pattern is shown only for the bacteria isolated in more than 9 (10%) ETA samples.

Statistical analysis

Data entry and analysis were performed using MedCalc. The results were expressed as number (%) for categorical variables and as median (25^{th}-75^{th} interquartile range) for non-categorical variables.

Table 2. Characteristics of VAP patients at ICU admission

Number of patients	113
Men	72 (63.7)
Age (years)	68 (56-77)
Smokers	23 (20.4)
SAPS II	37 (27-48)
APACHE II	15 (10-18)
Comorbidities:	
Diabetes mellitus	19 (16.8)
Malignant disease	15 (13.3)
COPD	16 14.2)
Chronic cardiac disease	28 (24.8)
Kidney failure	8 (7.1)
Hypertension	52 (46)
Alcoholism	15 (13.3)
Main reason for ICU admission:	
Medical*	3 (2.7)
Trauma without surgery	5 (4.4)
Surgery	105 (92.9)
Head	45 (39.8)
Neck and thorax	3 (2.7)
Abdominal	45 (39.8)
Trauma	12 (10.6)

Results are presented as median (25th-75th interquartile range), or as number (%); VAP = ventilator-associated pneumonia; ICU = intensive care unit; SAPS II = Simplified Acute Physiology Score II; APACHE II = Acute Physiology and Chronic Health Evaluation II; COPD = chronic obstructive pulmonary disease; *acute respiratory failure, sepsis, state post-resuscitation

Results

During the study period, 5071 adult patients were admitted to our ICU. Four hundred and fifty three (8.9%) of these patients were intubated and mechanically ventilated for more than 48 hours. VAP developed in 113 out of 453 (24.9%) patients during the ICU stay and all these patients were eligible for the study. Clinical characteristics of patients at ICU admission are shown in Table 2. Twenty patients were excluded from the analysis (seven patients had invalid sample, six patients had growth of bacteria below the concentration of 10^5 CFU/mL, five patients had sterile ETA sample, and in two patients ETA sample was not collected). So, the final analysis of bacterial etiology included 93 patients/ETA samples with 147 bacterial species isolated. For five bacteria isolated in three ETA (*Haemophilus influenzae, Acinetobacter* species, methicillin sensitive *Staphylococcus aureus,* unspecified gram-negative bacteria, unspecified gram-positive bacteria), susceptibility profile was not reported, so final analysis of antibiotic susceptibility and resistance patterns included 90 patients with 142 isolated bacteria.

Among 147 isolated bacteria, 110 (74.8%) were gram-negative bacteria (Table 3). *Pseudomonas aeruginosa* was the most common isolated gram-negative bacterium, accounting for 28 of 147 (19.0%) isolates. The next most commonly isolated bacteria were *Acinetobacter* species, accounting for another 20 (13.6%) isolates, followed by *Escherichia coli* (10.9%), *Haemophilus influenzae* (8.7%), *Enterobacter* species (8.1%) and *Klebsiella* species (6.2%). The overall proportion of gram-positive bacterial species was 37 (25.2%). Table 3 shows that *Staphylococcus aureus* was the most commonly isolated gram-positive bacterium. Among all *Staphylococcus aureus* isolates, 15 (48.4%) isolates were methicillin resistant *S. aureus* (MRSA). *Staphylococcus aureus* was the most common cause of VAP, accounting for 31 (21.1%) of total isolated bacteria. In 20 ETA samples, mixed bacterial and fungal species were isolated. Twenty-one fungal isolates included yeasts and moulds. There were 18 *Candida* species and 3 *Aspergillus* species isolated.

Out of 93 patients that developed VAP, 41 (44.1%) died. Sixty-six bacteria were isolated in ETA sam-

Table 3. Bacterial species isolated from ETA samples in VAP patients

			Early-onset VAP (≤4 days of MV)	Late-onset VAP (>4 days of MV)
	Total number of isolated bacteria	147	93 (63.3)	54 (36.7)
	Gram-negative bacteria:	110 (74.8)	73 (66.3)	37 (33.7)
	Moraxella catarrhalis	2 (1.4)	2 (100)	0
	Haemophilus influenzae	13 (8.7)	9 (69.2)	4 (30.8)
	Pseudomonas aeruginosa	28 (19)	14 (50)	14 (50)
	Acinetobacter species	20 (13.6)	14 (70)	6 (30)
	Stenotrophomonas maltophilia	2 (1.4)	1 (50)	1 (50)
Enterobacteriaceae	*Escherichia coli*	16 (10.9)	13 (81.2)	3 (18.8)
	Klebsiella species	9 (6.2)	9 (100)	0
	Enterobacter species	12 (8.1)	8 (66.7)	4 (33.3)
	Proteus mirabilis	2 (1.4)	0	2 (100)
	Serratia species	3 (2.1)	2 (66.7)	1 (33.3)
	Citrobacter species	2 (1.4)	1 (50)	1 (50)
	Unspecified gram-negative bacteria	1 (0.7)	0	1 (100)
	Gram-positive bacteria:	37 (25.2)	20 (54.1)	17 (45.9)
	Staphylococcus aureus	31 (21.1)	17 (54.8)	14 (45.2)
	Streptococcus pneumoniae	4 (2.7)	2 (50)	2 (50)
	β-hemolytic *Streptococcus* group B	1 (6.8)	1 (100)	0
	Unspecified gram-positive bacteria	1 (0.7)	0	1 (100)
	Fungi	21	16	5
	Aspergillus	3	2	1
	Candida	18	14	4

Results are presented as number of bacterial species isolates (% of the number of total isolated bacteria); VAP = ventilator-associated pneumonia; MV = mechanical ventilation; ETA = endotracheal aspirate

ples of these patients. Gram-negative bacteria were the cause of death in 72.7% of all bacteria isolated in deceased patients. The highest mortality rate was recorded in patients infected with *Klebsiella* species, i.e. six of nine (66.7%), followed by MRSA (60.0%) and *Pseudomonas aeruginosa* (53.6%) (Table 4).

Out of 147 isolated bacteria, 93 (63.3%) were categorized under early-onset VAP and 54 (36.7%) under late-onset VAP. *Staphylococcus aureus, Pseudomonas aeruginosa*, and *Acinetobacter* species were the most common isolates in the early-onset and late-onset VAP. *Staphylococcus aureus* and *Pseudomonas aeruginosa* were more frequently isolated in ETA from patients with late-onset VAP as compared to those with early-onset VAP (26.0% *vs*. 18.2% and 26.0% *vs*. 15.0%). *Acinetobacter* species was more frequently isolated from patients with early-onset VAP compared to patients with late-onset VAP (15.1% *vs*. 11.1%) (Table 3).

Monomicrobial infection occurred in 54 of 93 (58.1%) patients, and polymicrobial infection in 39 (41.9%) patients, 27 of which were infected with two pathogens, ten with three pathogens, and two with four pathogens.

Figure 1 shows antimicrobial susceptibility and resistance patterns of the most commonly isolated bacteria. Among *Staphylococcus aureus* isolates, 15 (50%) were susceptible and 15 (50%) resistant to cloxacillin. All *S. aureus* isolates were susceptible to vancomycin and linezolid. All *Haemophilus influenzae* isolates were susceptible to 2nd and 3rd generation cephalosporins. Antibiotic susceptibility and resistance patterns of *Enterobacter* species, *Klebsiella* species and *Escherichia coli* are shown together under *Enterobacteriaceae*. *En-*

Table 4. Mortality associated with most commonly isolated bacteria

Bacteria	Mortality due to specific bacteria n (%)
Pseudomonas aeruginosa	15 (53.6)
Acinetobacter species	10 (52.6)
Escherichia coli	6 (37.5)
Haemophilus influenzae	3 (25)
Enterobacter species	4 (33.3)
Klebsiella species	6 (66.7)
MSSA	6 (37.5)
MRSA	9 (60)

Results are presented as number of bacterial species isolates in patients died (% of total number of each isolated bacterium); MSSA = methicillin sensitive *Staphylococcus aureus;* MRSA = methicillin resistant *Staphylococcus aureus*

terobacter species isolates were in more than 65% of cases susceptible to sulfamethoxazole-trimethoprim and ciprofloxacin and in more than 80% of all isolates were susceptible to cefepime. Among *Klebsiella* species isolates, 3 (33.3%) were extended spectrum beta-lactamase (ESBL) producers and were resistant to 2nd and 3rd generation cephalosporins. All *Escherichia coli* isolates were susceptible to 2nd and 3rd generation cephalosporins. *Pseudomonas aeruginosa* showed 100% susceptibility to cefepime and very high susceptibility to piperacillin-tazobactam (96%), ceftazidime (93%) and ciprofloxacin (89%). Among *Acinetobacter* species, 63% of isolates had decreased susceptibility to meropenem, and 58% decreased susceptibility to imipenem. Ampicillin-sulbactam was highly effective for *Acinetobacter* species, showing resistance in only 8% of isolates.

Table 5. Antibiotic resistance of the most commonly isolated bacteria

Bacteria	Total number of each isolated bacterium/Number of resistant bacteria/Number of MDR bacteria
Pseudomonas aeruginosa	28/13/1
Acinetobacter species	19/19/19
Escherichia coli	16/10/1
Haemophilus influenza	12/5/0
Enterobacter species	12/12/2
Klebsiella species	9/9/4
MSSA	16/9/0
MRSA	15/15/15

MDR = multidrug resistant; MSSA = methicillin sensitive *Staphylococcus aureus;* MRSA = methicillin resistant *Staphylococcus aureus*

Among 142 isolated bacteria with susceptibility and resistance pattern, 102 (71.8%) were resistant bacteria, 42 (41.7%) of which were MDR bacteria (Table 5). The most common resistant bacteria were *Acinetobacter* species (100%), *Klebsiella* species (100%) and MRSA (100%). *Acinetobacter* species and MRSA were MDR bacteria in all ETA samples. *Klebsiella* species were MDR in 44.4%, followed by *Enterobacter* species that were MDR in 16.7% of cases and *Escherichia coli* that were MDR in 6.3% of all isolates. *Pseudomonas aeruginosa* was MDR in only 3.6% of cases.

Discussion

Through this research, we determined the antibiotic susceptibility patterns of gram-positive and gram-negative bacteria causing VAP, as well as the

Table 6. Initial empiric therapy for VAP according to the American Thoracic Society[12]

VAP with no risk factors for MDR pathogens	VAP with risk factors for MDR pathogens
Ceftriaxone or Levofloxacin, moxifloxacin or ciprofloxacin or Ampicillin + sulbactam or ertapenem	Antipseudomonal cephalosporin (cefepime or ceftazidime) or Antipseudomonal carbapenem (imipenem or meropenem) or β-lactam/β-lactamase inhibitor (piperacillin + tazobactam) + antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin) or Aminoglycoside (amikacin, gentamicin or tobramycin) + Linezolid or vancomycin (if risk factors for MRSA are present)

VAP = ventilator-associated pneumonia; MDR = multidrug resistant; MRSA = methicillin resistant *Staphylococcus aureus*

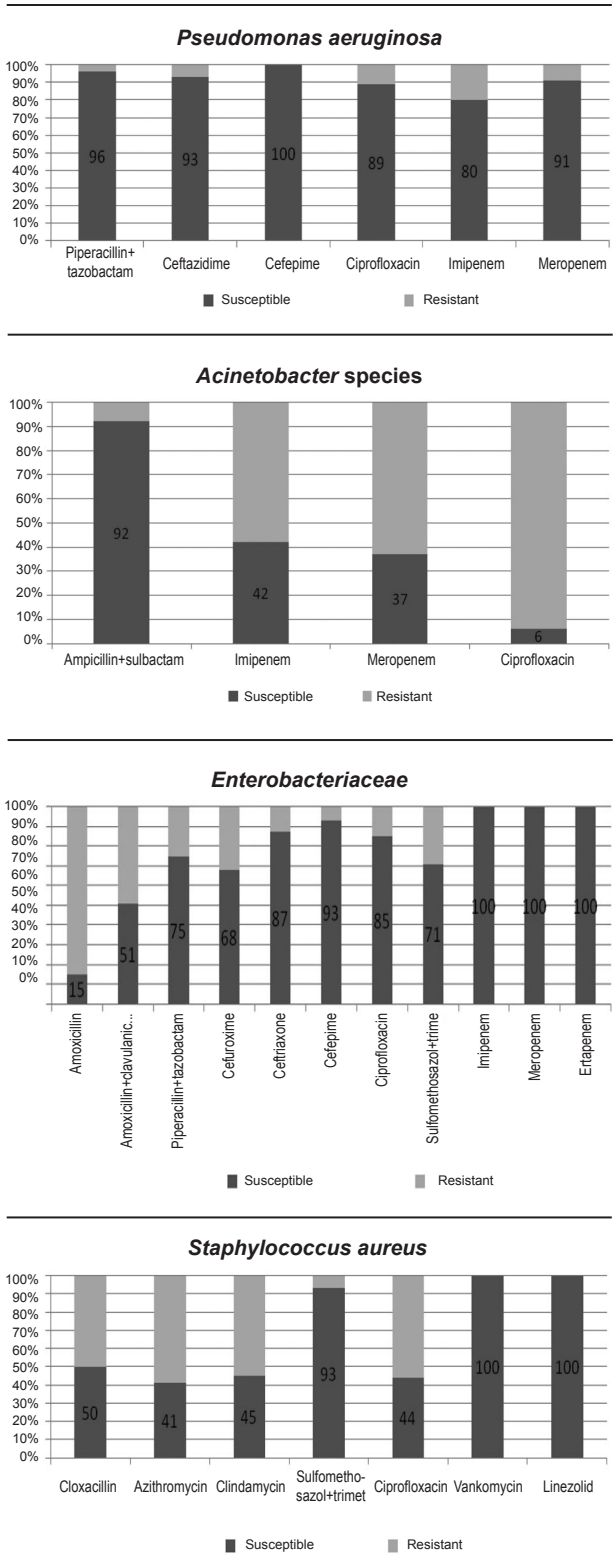

Fig. 1. Antibiotic susceptibility and resistance of the most commonly isolated bacteria (%).

frequent causative microorganisms of early- and late-onset VAP in our ICU. The microbial profile of pathogens causing VAP may differ between hospitals and ICU settings, even within the same institution between different ICUs. Therefore, surveillance of bacterial susceptibility should be conducted and local epidemiological data should be provided for every ICU[4]. This information can help in guiding the initial empiric antibiotic therapy, which would be helpful in decreasing mortality and preventing development of MDR bacteria[9-11]. Antibiotic choices based on published guidelines may be ineffective if local microbial flora shows different susceptibility patterns.

According to the American Thoracic Society, empiric antibiotic selection for VAP should be based on the time of VAP onset and on the presence of risk factors for MDR bacteria[12]. Whereas early-onset VAP is more likely to be caused by antibiotic-sensitive bacteria, late-onset VAP is more likely to be caused by MDR pathogens. The most common MDR bacteria are *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, resistant *Enterobacteriaceae* species and MRSA. Risk factors for acquiring MDR bacteria are antibiotics and hospitalization in the preceding 90 days, current hospitalization longer than 5 days, duration of mechanical ventilation longer than 7 days, immunosuppressive therapy or disease, high frequency of antibiotic resistance in the ICU, home infusion therapy or wound care, chronic dialysis within 30 days, and family member with MDR pathogen or residence in a nursing home or extended-care facility. Patients with early-onset VAP who have risk factors for MDR bacteria are at a greater risk of colonization and infection with MDR pathogens and should be treated similar to patients with late-onset VAP. The American Thoracic Society guidelines shown in Table 6 suggest that patients who do not have risk factors for MDR bacteria should be treated with ceftriaxone or fluoroquinolone or ampicillin + sulbactam or ertapenem. When patients are at risk of the occurrence of MDR bacteria, initial empiric therapy should be broad-spectrum and effective against MDR pathogens. A recommended empiric regimen for patients with risk factors for MDR bacteria is an antipseudomonal cephalosporin (cefepime, ceftazidime) or an antipseudomonal carbapenem (imipenem, meropenem) or beta-lactam/beta-lactamase inhibitor (piperacillin-tazobactam)

plus an antipseudomonal fluoroquinolone (ciprofloxacin, levofloxacin) or an aminoglycoside (amikacin, gentamicin, tobramycin) plus either linezolid or vancomycin.

Although empiric antibiotic therapy selection can be guided by Gram stain and preliminary bacterial culture results of ETA samples, most important guidance in selection of appropriate antibiotic therapy is the presence or absence of risk factors for MDR pathogens.

It has been assumed that early-onset VAP is caused by antibiotic susceptible, community acquired, microbial pathogens colonizing oro- and nasopharyngeal secretions, such as *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis* and *Staphylococcus aureus*. Late-onset VAP is often associated with resistant causative microorganisms since patient colonization with MDRs is expected during prolonged ICU stay. However, paradigms have changed.

Most cases of VAP in our setting are those of early-onset VAP (63.3%). According to many studies, early-onset VAP is more likely to be caused by antibiotic-sensitive bacteria, while late-onset VAP is more likely to be caused by MDR bacteria. Microbial flora present in oral cavity of intubated patients changes during hospitalization because protective mechanisms decline in critically ill patients due to the reduction of salivary secretion, lower levels of salivary local immunity factors, and absence of self-cleaning by chewing. In such conditions, dental plaque and oral mucosa in hospitalized patients become colonized by more pathogenic and often resistant microbial species[13].

Our data revealed that MDR pathogens, such as *Acinetobacter* species and MRSA, are present at almost the same frequency in early- and late-onset VAP. For example, *Acinetobacter* species were numerically higher among early-onset VAP subjects as compared to late-onset VAP subjects, although many studies have shown that *Acinetobacter* species are a major causative agent of late-onset VAP[14]. Similar results have been reported by Restrepo *et al.* and Ibrahim *et al*., who demonstrated that there were no differences in the rate of potential MDR bacteria between early-onset and late-onset VAP[15,16]. These results are expected since many patients admitted to ICU have numerous risk factors predisposing previous colonization with MDR bacteria[17,18]. Our finding also indicated that the causative pathogens varied in different setups and depended not only on the time of VAP onset, but also on the characteristics and diagnoses of patients admitted to ICU, as well as on the presence of risk factors for MDR bacteria.

Earlier reports have shown that different gram-negative bacteria are the most common causative agent of VAP. In our study, 74.8% of VAP cases were caused by gram-negative bacteria, which is consistent with similar studies where approximately 60% of bacteria were found to be gram-negative bacteria[19]. Among gram-positive bacteria, the most common bacterial species isolated in the study period was *Staphylococcus aureus*, with a high resistance rate. MRSA was isolated in 15 (48.4%) cases. All MRSA isolates were susceptible to vancomycin and linezolid, making these antimicrobials drugs of choice for empiric antibiotic therapy for VAP caused by gram-positive bacteria. As demonstrated by the ZEPHyR study results, linezolid has superiority over vancomycin in clinical outcome of MRSA pneumonia, due to its pharmacokinetic and pharmacodynamic properties. Hence, it should be considered as the antibiotic of choice. Also, in our study, *Staphylococcus aureus* was the most frequently isolated species, accounting for 54.1% of isolates in early-onset VAP and 45.9% of isolates in late-onset VAP. According to Park *et al*., one of the risk factors for VAP caused by *Staphylococcus aureus* is neurosurgical procedure as the reason for ICU admission, and our patient cohort included almost 40% of neurosurgical patients[20].

According to our data, appropriate empiric antibiotic therapy for patients with VAP without risk factors for MDR bacteria is ceftriaxone since non-MDR bacteria isolated in our patients were susceptible to ceftriaxone. Appropriate empiric antibiotic therapy for patients with risk factors for MDR bacteria, according to present data, is ampicillin-sulbactam plus cefepime plus vancomycin or linezolid. Ampicillin-sulbactam should be part of empiric regimen for *Acinetobacter* species. Cefepime should be added due to the high frequency of VAP caused by *Pseudomonas aeruginosa*. *Enterobacteriaceae* species also showed high susceptibility to cefepime. Vancomycin or linezolid should be part of regimen because *Staphylococcus aureus* is the most frequent isolate with high methicillin resistance rates.

The most common VAP pathogen associated with mortality was *Klebsiella* species, accounting for 66.7% of overall mortality. Although the overall number of patients with VAP caused by *Klebsiella* species was small, the reasons for such outcome may be numerous virulence factors expressed in this bacterial species.

Yeasts and moulds isolated in our patients that developed VAP (n=21) were considered as colonization of tracheal secretions and were not counted in the VAP causative microorganism analysis.

The significance of fungal isolates in tracheobronchial secretions in patients with VAP is unclear and is a subject of numerous studies. Although fungal species are not common causative agents of VAP in non-neutropenic critically ill patients, and usually are considered as colonization, there are reports of *Candida* species impact on innate immune response, immunosuppression, and subsequent worse clinical outcomes in patients with VAP caused by MDR bacteria due to the *Candida* immunomodulatory mechanisms[21,22].

Our study had a few limitations. One was the length of study period during which susceptibility patterns of *Acinetobacter* species had shifted towards resistance patterns. According to the national antibiotic resistance data provided by the Committee for Antibiotic Resistance Surveillance in Croatia, ampicillin-sulbactam resistance in *Acinetobacter* species was 13% in 2009, while resistance rates increased to 19% in 2012. This trend shows that local epidemiology data should be updated. Another limitation was the lack of correlation between specific risk factors and early- or late-onset VAP and MDR causative microorganisms.

This study has set up new research goals. Further surveillance of microbial profile and susceptibility patterns in our ICU should be conducted regularly in order to detect potential alterations, especially since new resistant bacterial strains are emerging throughout south-east Europe. Other research goals should be determination of characteristics and diagnoses of patients developing VAP, presence of risk factors for MDR bacteria infection, and correlation of specific MDR bacteria with mortality.

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Sažetak

MIKROBIOLOŠKI PROFIL I ANTIBIOTSKA OSJETLJIVOST UZROČNIKA VENTILACIJSKE PNEUMONIJE U JEDINICI INTENZIVNOG LIJEČENJA KLINIČKOG BOLNIČKOG CENTRA SESTRE MILOSRDNICE, ZAGREB, HRVATSKA

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Ventilacijska pneumonija (VAP) je vrlo česta u jedinicama intenzivnog liječenja, ali još uvijek postoje mnoge nedoumice vezane uz VAP, osobito što se tiče početnog empirijskog odabira antibiotika za liječenja VAP-a. Učestalost pojedinih patogena s različitom osjetljivošću na antibiotike razlikuje se od bolnice do bolnice. To je razlog zbog kojeg bi se empirijska antibiotska terapija trebala temeljiti ne samo na općim smjernicama (koje preporučuju terapiju na temelju prisutnosti rizičnih čimbenika za bakterije rezistentne na više lijekova), nego i na podacima o lokalnoj epidemiologiji. Cilj ovoga istraživanja je bio utvrditi mikrobiološki profil patogena koji uzrokuju VAP i njihovu osjetljivost na antibiotike. Istraživanje je provedeno u 15-krevetnoj Jedinici intenzivnog liječenja Odjela za anesteziologiju, reanimatologiju i intenzivno liječenje Kliničkog bolničkog centra "Sestre milosrdnice", Zagreb, Hrvatska. Podaci su skupljani retrospektivno od rujna 2009. do ožujka 2013. godine. Svi bolesnici kod kojih se razvila VAP tijekom navedenog razdoblja su uključeni u istraživanje. Prema našim rezultatima, incidencija VAP-a bila je 29,4%. Najčešće izolirana bakterija je bila *Staphylococcus aureus* (21,1%), iza koje slijede *Pseudomonas aeruginosa* (19,0%) i *Acinetobacter* sp. (13,6%). Svi izolati bakterije *Staphylococcus aureus* su bili osjetljivi na vankomicin i linezolid. *Pseudomonas aeruginosa* je u 100% izolata bio osjetljiv na cefepim te visoko osjetljiv na piperacilin-tazobaktam (96%), ceftazidim (93%) i ciprofloksacin (89%). Ampicilin-sulbaktam se pokazao vrlo učinkovitim za *Acinetobacter* sp. s rezistencijom u samo 8% izolata. U zaključku, prema našim rezultatima, empirijska antibiotska terapija za bolesnike s VAP-om bez rizika za bakterije rezistentne na više lijekova je ceftriakson, a za bolesnike s rizičnim čimbenicima za bakterije rezistentne na više lijekova je ampicilin-sulbaktam plus cefepim plus vankomicin ili linezolid.

Ključne riječi: *Pneumonija, izazvana ventilacijom – etiologija; Lijekovi, rezistencija, bakterijska; Jedinice za intenzivnu skrb; Hrvatska*