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Is methicillin-resistant *Staphylococcus aureus* a common pathogen in ventilation-associated pneumonia?

The experience of a tertiary teaching hospital in Jordan

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Abstract

Ventilator-associated pneumonia is a life threatening device related infection in intensive care units. Methicillin-resistant *Staphylococcus aureus* is considered a common contagious pathogen causing pneumonia and sepsis.

To assess the prevalence of *S aureus* in comparison to other pathogens, and their antibacterial sensitivity profile in ventilator-associated pneumonia.

Data regarding ventilator-associated pneumonia of adults admitted to the intensive care unit, at the Jordan University of Science and Technology Hospital, between 2012 and 2018 were extracted from the computerized system. Microorganisms and their susceptibility profiles were identified according to the Clinical and Laboratory Standards Institute.

There were 547 isolates, of which 35 (6.4%) were Gram positive, 59% were methicillin resistant. Gram-negative isolates were present in 507 (92.6%) isolates, of which 82% were multidrug resistant, and 1% were *Candida* species.

Gram-negative bacterial infections were significantly associated with ventilation usage. *S aureus* was not the predominant pathogen.

Abbreviations: A baumannii = Acinetobacter baumannii, ICU = intensive care unit, K pneumoniae = Klebsiella pneumoniae, MDR = multidrug resistance, MRSA = methicillin-resistant Staphylococcus aureus, P aeruginosa = Pseudomonas aeruginosa, S aureus = Staphylococcus aureus, VAP = ventilator-associated pneumonia, XDR = extensively drug resistance.

Keywords: extensively drug resistance, methicillin resistance, multidrug resistance, *Staphylococcus aureus*, ventilator-associated pneumonia

1. Introduction

Staphylococcus aureus (*S aureus*) is a common pathogen in humans.[1,2] This gram-positive organism, mainly found in elderly patients, is often virulent and resistant to therapy, resulting in an increased risk of co-morbidities.[2,3]

From hundreds of its various strains, Methicillin-resistant *S aureus* (MRSA) was defined in 1961,[4] it is considered a severe contagious pathogen causing skin infections, pneumonia, bacteremia, and other pathologies at healthcare facilities.[5,6] Patients with poor glucose control are quite susceptible to MRSA infection, being an independent risk factor for mortality.[7]

Approximately 10% of ventilation cases are associated with *S aureus* infection, with a death rate of around 50%. Device-associated infections in intensive care units (ICUs) are reported to increase the risk to health worldwide.[8]

According to a study by the World Health Organization covering low and middle income countries, the rate of ventilator-associated pneumonia (VAP) was 23.9 per 1000 ventilator days.[9] Globally, the resistance phenomenon for both MRSA and gram-negative bacteria has been noted to be on the rise.[10,11]

The objectives of this study were to estimate the rate of MRSA and other pathogens in relation to mechanical ventilation, antimicrobial resistance, length of hospital stay, and mortality at the ICU of the Jordan University of Science and Technology Hospital.

Editor: Kuang-Ming Liao.

This work was supported by the Jordan University of Science and Technology [grant numbers 20200239].

The authors have no conflicts of interest to disclose.

The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

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How to cite this article: Elnasser ZA, Obeidat HM, Bani-Salem ME, Amarin ZO, Banni-Issa AF, Kaplan NM. Is methicillin-resistant Staphylococcus aureus a common pathogen in ventilation-associated pneumonia? The experience of a tertiary teaching hospital in Jordan. Medicine 2021;100:20(e26069).

Received: 19 December 2020 / Received in final form: 22 April 2021 / Accepted: 27 April 2021

http://dx.doi.org/10.1097/MD.0000000000026069

2. Methods

This study was conducted at a tertiary-care referral hospital that is affiliated to the Jordan University of Science and Technology, and serves 1.2 million people. The ICU consists of 6 units, each with its designated beds. A medical unit with 16 beds, a surgical unit with 12 beds, a coronary care unit with 12 beds, a cardiac unit with 6 beds, a neurological surgery unit with 6 beds, and a burns unit with 2 beds. Data were obtained from the electronic database system.

This retrospective study included all patients admitted to ICU with VAP between January 2012 and December 2018. The isolates were obtained from sputum, bronco-alveolar lavage, and bronchial washings associated with ventilator usage.

In addition to age and gender, patients' details included the co-morbidities of diabetes mellitus, hypertension, chronic obstructive pulmonary disease, chronic heart failure, chronic renal failure, different malignancies, respiratory distress syndrome, antimicrobial susceptibility, length of hospital, and ICU stay and outcome.

Specimens were cultured on chocolate, blood, and MacConkey agar according to the Clinical and Laboratory Standards Institute and the European Committee on Antimicrobial Susceptibility Testing guidelines.[12]

For the purposes of this study, MRSA implied resistance against oxacillin. Multidrug resistance (MDR) was defined as antimicrobial resistance shown by a species of microorganism to at least 1 antimicrobial drug in 3 or more antimicrobial categories. Extensively drug resistance (XDR) implied that isolates were susceptible to 1 or 2 antimicrobial categories, and pan drug resistance implied that isolates were resistant to all antimicrobial categories.[13] Ventilator utilization ratio referred to the number of ventilation days per number of patient days, and VAP related to 1000 ventilation days.

The study was approved by the Institutional Research Board of the Jordan University of Science and Technology.

Statistical analysis was performed using the Statistical Package for Social Sciences (Windows 22.0, SPSS Inc.). Quantitative data were expressed as means and standard deviations. Two tail independent samples were used for comparisons, and qualitative data as percentiles. Chi-squared test was used for comparison at 95% confidence interval. The *P*-value of $<.05$ was considered statistically significant.

3. Results

During the study period, 11,850 patients were admitted to the ICU for a cumulative number of 46,865 days, and 19,724 intubation device days. A total of 346 patients developed VAP. The mean age was 56.7 ± 20 years, and 63.6% were male. *S aureus* was reported in 20 (5.8%) patients. The total hospital length of stay including ICU was 49.3 days. Co-morbidities of diabetes were present in 38.7%, hypertension in 51.4%, and cardiac disease in 29.8%.

By comparing risk factors for VAP between the MRSA group and the non-MRSA group, there was no statistically significant difference in relation to age and co-morbidities. On the other hand, gender, length of hospital stay, mortality rate, and super-infections were significantly different, where the number of males was higher in MRSA group (*P* .011). The mortality rate and super infections were higher in the non-MRSA group (*P* .007 and .003, respectively) (Table 1).

Table 1

General characteristics of patients with ventilator associated pneumonia and methicillin resistant *Staphylococcus aureus* (MRSA) status.

	MRSA (n = 20)	Non MRSA (n = 326)	Total (n = 346)	*P*-value
Age (yr, mean ± SD)	52.4 ± 21.9	56.9 ± 20.3	56.7 ± 20.4	.330
Gender M N (%)	18 (90)	202 (62)	220 (63.6)	.011
HLOS (d, mean ± SD)	77.5 ± 81.9	47.5 ± 49.7	49.3 ± 52.4	.013
Co-morbidities	17	294	311	.44
DM	6 (30.3)	128 (39.3)	134 (38.7)	.409
HTN	9 (45)	169 (51.8)	178 (51.4)	.552
Cardiac diseases	9 (45)	94 (28.8)	103 (29.8)	.125
Brain diseases	8 (40)	109 (33.4)	117 (33.8)	.547
Lung diseases	2 (10)	54 (16.6)	56 (16.2)	.539
Kidney diseases	2 (10)	32 (9.8)	34 (9.8)	.979
Malignancies	3 (15)	45 (13.8)	48 (13.9)	.881
Mortality (%)	11 (55.0%)	262 (80.4%)	273 (78.9%)	.007
Super infections (%)	13 (65)	295 (90.5)	308 (89)	.003

DM = diabetes mellitus, HLOS = hospital length of stay, HTN = hypertension.

Regarding the distribution of 547 cases of VAP, 254 patients were affected by 1 type of bacteria, and 92 patients were affected by more than 1 type of bacteria. Both gram-positive and gram-negative bacteria were isolated. Nonfermenting gram-negative bacteria were common. *Acinetobacter baumannii* (*A baumannii*) was the predominant agent at 59%, followed by *Pseudomonas aeruginosa* (*P aeruginosa*) at 17.9%. *S aureus* was recovered in 6.2% with a methicillin resistance rate of 58.8% (Table 2).

Regarding resistance to antibiotics, *A baumannii* isolates had the highest rates of resistance to different antibiotic classes, where 82% were XDR, while 22.4% of *P aeruginosa* was XDR, and 38.9% of *Klebsiella pneumoniae* (*K pneumoniae*) were MDR. Regarding *S aureus* isolates, 64.7% were MDR (Table 3). The incidence of VAP was 17.2/1000 ventilation days. Ventilator utilization ratio was 0.43 and the ventilator days were 2854 (Table 4).

Table 2

The isolated microorganisms from the target population.

Microorganism species	Total number of isolates (N)	Resistance prevalence (%)	Resistant codes N (%)
S aureus	34 (6.2)	58.8	MRSA
P aeruginosa	98 (17.9)	44.9	MDR
K pneumonia	54 (9.9)	42.5	MDR
E coli	15 (2.7)	86.7	MDR
A Baumannii	323 (59.0)	99.7	MDR
P mirabilis	4 (0.7)	100	MDR
S pneumonia	1 (0.2)	0	N/A
S maltophilia	3 (0.5)	100	MDR
M morganii	1 (0.2)	100	MDR
S marcescens	2 (0.4)	100	N/A
Koseri	1 (0.2)	0	N/A
E cloacae	3 (0.5)	33.3	N/A
Junii	1 (0.2)	100	MDR
H parainfluenza	1 (0.2)	0	N/A
Albicans	4 (0.7)	0	N/A
Burkholderia cepacia	1 (0.2)	100	MDR
Krusei	1 (0.2)	0	N/A

MDR = multidrug resistant, MRSA = methicillin resistant *Staphylococcus aureus*, N/A = nonapplicable.

Table 3

Antibacterial resistance in intensive care unit ventilation-associated pneumonia.

Antibiotics names (%)	A baumannii N = 323	P aeruginosa N = 98	K pneumonia N = 54	S aureus N = 34
Aminoglycosides				
Amikacin	12.7	22.4	1.9	–
Gentamycin	71.8	44.9	9.3	20.6
Tobramycin	45.8	40.8	5.6	2.9
Carbapenems				
Imipenem	66.9	31.6	27.8	–
Meropenem	59.1	56.1	16.7	–
Cephalosporins				
Ceftazidime	60.1	34.7	14.8	–
Cefepime	99.4	31.6	74.1	–
Ceftriaxone	43.3	7.1	68.5	5.9
Cefixime	36.8	5.2	66.7	–
Cefoxitin	0.6	–	1.9	55.9
Fluoroquinolones				
Ciprofloxacin	61	35.5	9.3	17.6
Levofloxacin	25.4	5.1	14.8	2.9
Penicillins				
Piperacillin	84.2	38.8	40.7	2.9
Oxacillin	15.2	14.3	–	58.8
Penicillins and B inhibitors				
Ticarcillin/clavulanic acid	7.4	23.5	3.7	–
Piperacillin/tazobactam	37.8	17.3	3.7	–
Ampicillin/sulbactam	71.1	2.2	18.5	–
Polymyxins				
Colistin	–	–	–	–
Lacosamide				
Clindamycin	–	–	–	32.4
Oxazolidinone				
Linezolid	43.3	29.6	7.4	2.9
Tetracyclines				
Doxycycline	–	–	–	0
Minocycline	41.2	30.6	40.7	0
Macrolide				
Erythromycin	–	–	–	14.7
Glycopeptide				
Vancomycin	–	–	–	0
Teicoplanin	11.1	–	3.7	14.7
Antimycin				
Rifampin	–	–	–	0
Type of resistance (%)				
MDR	17.7	22.4	38.9	64.7
XDR	82	22.4	3.7	0
PDR	0	0	0	0
MRSA	–	–	–	58.8

MDR = multidrug resistant, MRSA = methicillin resistant *Staphylococcus aureus*, PDR = pan drug resistant, XDR = extensively drug resistant, – = not tested.

4. Discussion

In this study, gram-negative bacteria were identified in more than 90% of the isolates. This may be explained by an increased resistance, or may be associated with infection prevention practices against gram-positive bacteria.[14] *A baumannii, P aeruginosa, K pneumoniae,* and *S aureus* were the dominant pathogens in patients with pneumonia. This is similar to a Polish study, where *A baumannii, P aeruginosa, S aureus*, and *K pneumonia* were the dominant pathogens, albeit at different percentages.[15]

Recently, *A baumannii* was classified as a frequent cause of nosocomial infection worldwide.[16] This is in concordance with the findings of this study, where *A baumannii* was a common causative pathogen of pneumonia in the ICU. *S aureus* was reported as the fourth most frequent pathogen at 6.2%. This is in contrast to its prevalence in the United States, at 20%,[17] and its prevalence in Asian countries where it occupies a third position.[18]

In this study, more than 50% of *S aureus* isolates were methicillin resistant. Vancomycin, teicoplanin, and linezolid were the antibiotics of choice for treating MRSA. Teicoplanin resistance was present in 20% of MRSA isolates, while vancomycin and linezolid were more effective. This is in contrast to a Chinese study, where vancomycin and teicoplanin were 100% effective in relation to MRSA strains, but there were few that were resistant to linezolid.[19] Drug resistance of gram-negative pathogens is high, and more so in relation to *A baumannii* strains, where it was 99.8% to cefepime, 71.4% to gentamycin, and 71.1% to ampicillin and sulbactam. In other Asian countries, for comparison, the resistance

Table 4

Ventilation days, utilization ratio, and associated pneumonia.

Ventilator-days	2854 (1532–4156)
Ventilator utilization ratio	0.43 (0.25–0.46)
Ventilator-associated pneumonia/1000	17.2 (12.2–43.7)

Ventilator utilization ratio calculated by dividing device days (nominator) over patient days (dominator).

rates were 80% to imipenem, 78.2% to ceftazidime, and 75.9% to ampicillin and sulbactam.[20]

Regarding *P aeruginosa*, the resistance to meropenem was 56.1%, gentamycin 44.9%, and ceftazidime 34.7%. This is in contrast to an Indian study, were the resistance to cefepime was 79.2%, ceftazidime 68.5%, and gentamycin 71.4%.[21]

In relation to *K pneumoniae*, 68.5% of strains were extended spectrum beta lactamase. This is in contrast to that reported at 35.1% and 19.5% in Europe and the United States respectively.[22]

The incidence of VAP was 17.2/1000 patient ventilation days. This is much higher than those reported by neighboring and some other far away countries in which the incidence varied between 0.9 and 13.1/1000 days.[23] In a systematic review of device-associated, hospital-acquired infections in developed versus developing countries, the incidence rates were 9.6 and 21.4, respectively.[24]

5. Conclusion

Device-associated infections in ICUs are common, with an emergence of extra resistance organisms. Gram-negative bacterial infections are significantly associated with ventilation usage. *S aureus* is not the predominant pathogen.

Acknowledgments

The authors thank the infection control unit for their contribution in data collection.

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