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Original Article

Bacterial Spectrum and Antibiotic Susceptibility Patterns in Nosocomial Pneumonia in the Intensive Care Unit

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Abstract

Background: Nosocomial pneumonia is the most common infection acquired in the hospital with the highest prevalence in intensive care units (ICUs). Antimicrobial resistance is an important factor in predicting outcomes and resources used in ICUs. Globally ICUs are facing the emergence and spread of antibiotic-resistant pathogens, and for some pathogens there are few therapeutic options available.

Objective: To evaluate the bacterial spectrum from patients with nosocomial pneumonia in the intensive care unit of a secondary care hospital in Saudi Arabia, and their antibiotic susceptibility patterns

Methods: This prospective, descriptive study was carried out at the Department of Microbiology, King Abdullah Hospital in Bisha from June 2011 to May 2012. Lower respiratory tract samples were obtained from suspected cases of nosocomial pneumonia in the ICU. The specimens were cultured on appropriate media. The identification of bacteria and susceptibility testing were done by using BD Phoenix™ Automated Microbiology system. *In vitro* antibiotic susceptibility patterns were analyzed using WHONET software.

Results: A total of 301 clinical isolates were analyzed. The frequencies of Gram-positive and Gram-negative bacteria were 16% and 84% respectively. Among Gram-positive bacteria, Methicillin-sensitive *Staphylococcus aureus (MSSA)* and Methicillin-resistant *Staphaureus* (MRSA) were the leading pathogens, while, *Acinetobacter*, *Klebsiella* and *Pseudomonas* species were the most common Gram-negative isolates. 79% isolates of *Acinetobacter* species were resistant to carbapenem, while 3 were resistant to all the antibiotics tested including colistin and were declared as pan-drug resistant *Acinetobacter.* Extended-spectrum beta-lactamase-producing *K. pneumoniae* accounted for 28% of all *Klebsiella* species isolated and
24% of *Pseudomonas* species were resistant to ceftazidime.

Conclusion: The Gram-negative bacteria remained more prevalent in ICU patients with nosocomial pneumonia. The reduced antibiotic susceptibility among Gram-negative bacteria alerts us that more effective strategies are needed to control the spread of antibiotic resistant organisms in critical patient areas.

Keywords: Nosocomial pneumonia, Antimicrobial resistance, Enterobacteriaceae, *K. pneumoniae, Escherichia coli, Serratia marcescens*

Introduction

The intensive care units (ICUs) have the highest prevalence of infection acquired in the hospital. These infections have been associated with substantial morbidity and attributable mortality, as well as greatly increased health care costs. Crude mortality rates for non-ICU nosocomial pneumonia range from 26% to 53%.[1] It is a leading cause of infection-related deaths in hospitalized patients, with attributable mortality rates of 20% to 33% reported.

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Nosocomial pneumonia refers to pneumonia acquired while in a hospital. It is classically divided into hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP). Crude mortality rates

Although a wide spectrum of bacterial pathogens can cause nosocomial pneumonia, the most frequent causative agents are members of the Enterobacteriaceae (*K. pneumoniae, Escherichia coli, Serratia marcescens, Acinetobacter* spp., *Enterobacter* spp.) and *Pseudomonas* species as well as Gram-positive cocci like *Staphylococcus aureus.* [2,3]

The prevalence of nosocomial pneumonias attributable to resistant pathogens has risen over the

past 2 decades. Antimicrobial resistance is an important factor in predicting outcomes and resources used in ICUs. Globally ICUs are facing the emergence and spread of antibiotic-resistant pathogens, and for some pathogens there are few therapeutic options available, e.g., extended spectrum β-lactamase (ESBL)-producing gram-negative bacteria and MDR *Acinetobacter*. Awareness of these problems has been underscored with data from a number of surveillance studies aimed at improving the use of empirical therapy. In the United States, there have been several national programs, which have focused on both the etiology of infections and resistance patterns of nosocomial or ICU infections including the National Nosocomial Infections Surveillance (NNIS) [4]now known as National Healthcare Safety Network (NHSN).Risk factors for the development of nosocomial pneumonia have been categorized as patient related, infection control related, or intervention related. Patient-related risk factors include age older than 70 years, severe underlying disease, malnutrition, coma, metabolic acidosis, and the presence of comorbid illnesses. Infection control–related risk factors include a lack of hand hygiene and glove-use practices and the use of contaminated respiratory equipment. Intervention-related risk factors include surgical procedures and use of ventilator support. Risk factors for antimicrobial resistance include recent broad-spectrum antibiotics, prolonged hospitalization, poor functional status, hemodialysis, and severe illness.

Objective

The objective of this was to evaluate the bacterial spectrum from patients with nosocomial pneumonia in the intensive care unit of a secondary care hospital in Saudi Arabia, and their antibiotic susceptibility patterns

Methods

This prospective, descriptive study was carried out at the Department of Microbiology, King Abdullah Hospital in Bisha from June 2011 to May 2012. King Abdullah Hospital, Bisha, is a 400-bed referral center in Bisha region in Kingdom of Saudi Arabia. Severely ill medical and surgical patients, except for neonates are candidates for admission. The ICU has an average annual admission rate of 40 patients and an average monthly occupancy rate of 85%. Patients with road traffic accidents, sepsis, respiratory tract infections, and those undergoing surgery for complicated diseases comprise the usual patient population. The patient and nurse ratio in these units is1:1.

Lower respiratory tract samples were obtained from suspected cases of nosocomial pneumonia in the ICU. The respiratory specimens were inoculated onto 5% sheep blood agar, MacConkey agar, and Chocolate agar. Blood agar, MacConkey agar were incubated aerobically at 37^{o}C for 18 to 24 hours. Chocolate agar plates were incubated at 37^{o}C in 5% CO_2 for 18 to 24hours.Organism's identification and antibiotic susceptibility testing were done by using BD Phoenix Automated Microbiology system (Becton Dickinson, Maryland, USA).Clinical Laboratory Standards (CLSI) interpretive criteria were used for susceptibility results. Susceptibility testing was performed using the modified Kirby- Bauer disk diffusion method by using Muller Hinton Agar for antibiotics, which were not on the Phoenix panels (colistin, and tigecycline).The results were expressed as susceptible/resistant according to Clinical Laboratory Standards (CLSI) interpretive criteria.[5]

Presence of Extended-spectrum beta-lactamase (ESBL) was suggested by resistance to a third generation cephalosporins (cefotaxime, ceftriaxone or ceftezidime) in Phoenix Automated system.

Quality control was performed by using reference strains of *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 to confirm consistency of materials, methods. *In vitro* antibiotic susceptibility patterns were analyzed using WHONET software.

Results

A total of 301 clinical isolates from ICU patients admitted with nosocomial pneumonia were analyzed. The most common organisms isolated as shown in Table 1, were *Acinetobacter spp* 25.9% *(n=78), Klebsiella spp* 23.9% *(n=72), P.aeruginosa* 21.9% *(n=66), and Staph aureus including* Methicillin-resistant *Staph aureus* (MRSA)14.2%(*n= 43)*. The frequencies of Gram-positive and Gram-negative bacteria were 16% and 84% respectively. Among Gram-positive bacteria, Methicillin-sensitive *Staphylococcus aureus (MSSA)* and Methicillin-resistant *Staph aureus* (MRSA) were the leading pathogens, while, *Acinetobacter*, *Klebsiella* and *Pseudomonas* species were the most common Gram-negative isolates.

Tables 1&2 show the percentage of antibiotics resistance in Gram-positive and Gram-negative isolates resistant to the antibiotics tested. 25 % of the *Staph aureus* were methicillin resistant and declared as

MRSA. On the other hand, all staph isolates were found sensitive to vancomycin and linezolid.

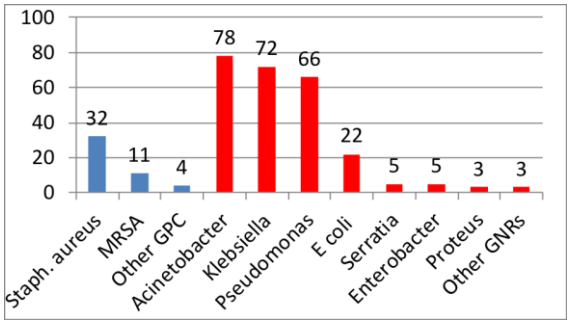

Fig 1. Distribution of Common Pathogens causing nosocomial pneumonia in ICU patients (n=301)

Table 1. Resistance pattern (%) of commonly used antibiotics against *Staph aureus* causing nosocomial pneumonia in the ICU patients

Microorganisms	*Antibiotics							
	P	FOX	ERY	DA	VAN	LZD	TE	DOX
Staph aureus	100	25	48	30	0	0	70	62

*P—Pinicillin, FOX—Cefoxitin, ERY—Erythromycin, DA—Clindamycin, VAN—Vancomycin, LZD—Linezolid, TE—Tetracycline, DOX—Doxycycline

Table 2. Resistance pattern (%) of commonly used antibiotics against Gram negative
Pathogens causing nosocomial pneumonia in the ICU patients

Microorganisms	*Antibiotics								
	AMC	TAZ	CTR	CEF	CFM	IMP	GEN	AK	CIP
Acinetobacter spp.	85	83	88	-	81	79	86	78	87
Pseudomonas	-	41	-	24	71	29	37	29	77
Klebsiella spp.	82	33	28	-	28	15	22	4	38
E coli	81	18	52	-	41	0	16	8	42
Serratia	80	0	40	-	0	0	40	80	40
Proteus	100	0	66	-	0	0	66	66	33
Enterobacter	80	40	60	-	40	0	80	60	60

*AMC—Amoxicillin + clavulonic acid, TAZ—Piperacillin-tazobactam, CTR—ceftriaxone, CEF—ceftazidime, CFM—cefepime, IMP—imipenem, GEN—gentamicin, AMC—amikacin, CIP—ciprofloxacin.

79% isolates of *Acinetobacter* species were resistant to carbapenem, while 3 were resistant to all the antibiotics tested including colistin and declared as pan-drug resistant *Acinetobacter.* Extended-spectrum beta-lactamase-producing *K. pneumoniae* accounted for 28% of all *Klebsiella* species isolated.
For Pseudomonas aeuroginosa, the resistance rates for imipenem, cefipime and ciprofloxacin were found 29%, 71%, and 77% respectively.

Discussion

The most common isolates observed in this study were *Acinetobacter spp, Klebsiella spp, P.aeruginosa,* and *Staph aureus* including MRSA. Some studies[6] presented results similar to ours, where the commonest isolated pathogens were *A. baumannii* (21.1%) and *P. aeruginosa* (17.4%), while the third place belonged to *S. aureus* (15.8%).
The frequencies of Gram-positive and Gram-negative bacteria in our study were 16% and 84% respectively. According to Chuon-Yi Lee *et al* the incidence of Gram positive and Gram negative bacteria was reported 30% to 47% and 40% to 48% respectively.[7]
Previous epidemiological studies have focused primarily on two common Gram positive antimicrobial resistant organisms; Methicillin-resistant *Staph aureus* (MRSA) and Vancomycin-resistant *Enterococcus* (VRE).[8]
Zorana *et al* [9] *and* Spellberg *et al.*[10]showed that multi drug resistance (MDR) among Gram-negative bacteria is becoming even a greater problem in health care facilities.
In this study, the percentage of *Staph aureus* is 14.2 % which is comparable to NHSN data 2006-2007 which is 14.5%.[11]
In the present study, 34% of the isolated *Staph aureus* were methicillin resistant. This MRSA rate was similar to that reported by Mumtaz et *al*. during a surveillance study from a Saudi ICU[12]. The contributions of methicillin-resistant *Staph aureus* (MRSA) to hospital acquired infection were demonstrated previously.[13]
In Europe, surveillance data shows a marked variability in MRSA rates among the various states, with ranging from 1% to 50%.The highest prevalence was seen in Portugal (49%),Greece (40%) and Italy (37%), whereas the lowest prevalence was observed in Norway, Sweden and Holland which was 1%.[14]
Patients with prolong use of antibiotics, hospitalization in a unit with high MRSA prevalence and patients on ventilator support are high risk for MRSA infections.[15] Our study showed 100%

susceptibility of MRSA to Vancomycin and linezolide, so efforts should be made to preserve efficacy of these antibiotics.

In our study, all Staph isolates were found sensitive to vancomycin contrary to 15.5 % resistant reported by Hossam M *et al*.[16]and comparable to Nermin K Saeed *etal*.[17]

The incidence of Gram negative bacteria in our study is 84% as compared to 40% to 48% reported by Chuon-YiLee *at al*.[7]However our findings were comparable to the study carried out in a secondary care hospital of Saudi Arabia[12]. In our study, *Acinetobacter spp* out stripped the other pathogens as the leading cause of nosocomial pneumonia (25.9%)**.** *Acinetobacter* spp. has recently advanced to one of the most common bug isolated from ICUs. *Acinetobacter* is an increasingly infectious threat, especially for patients receiving broad spectrum antimicrobial therapy and requiring life support.

A quite high percentage (79%) of *Acinetobacter* species were found resistant to carbapenem. Haeili *et al*.[18]also demonstrated low susceptibility rate of *Acinetobacter* to imipenem (25%), cephalosporins (3–25%), aminoglycosides (12–50%) and ciprofloxacin (below 35%), while susceptibility to polymyxin B was preserved (95.5%).

Infections by *Acinetobacter* have become difficult to treat as *Acinetobacter* can survive in the environment for long periods of time and develops multiple drug resistance.[19]

Carbepenams are usually the treatment of choice for *Acinetobacter.* However, if treatment fails due to the development of resistance, these can be substituted with polymyxins (colistin and polymyxin B), sulbactam and tigeycycline.[20]

The emerging Carbapenem-resistant *Acinetobacter spp* is an eye opener for doctors. These resistance patterns warn us that antibiotic resistance can become a global problem that requires bold and decisive global action. Implementation of effective infection control practices especially in critical care patient areas can control spread of *Acinetobacter* infections among patients.[21]

Extended-spectrum beta-lactamase-production was also tested. ESBL-Producing *Klebsiella pneumoniae* has been increased in recent years.[22] ESBL producing *K. pneumoniae* accounted for 28% of all *Klebsiella* species isolated. This observation is agreed with finding of Sarojamma V *et al*.[23] We did not find ESBL-Production in other gram negative rods, the reason may be the small sample size. ESBL producing isolates should be reported as resistant to all penicillins, cephalosporins, and aztreonam.[24]Carbapenems are the treatment of choice for infections due to ESBL-producing organisms if it is sensitive.[25]

In our study the resistance rates of *Pseudomonas aeruginosa* to imipenem, Ciprofloxacin, and Ceftazidine were found 29%, 77%, 24% respectively. These findings are consistent with other studies carried out in Saudi Arabia[12,17].

According to the National Healthcare Safety Network (NHSN) data, 71.6% *Pseudomonas aeruginosa* were susceptible to cefepime, 69.8% to carbapenems and 80.9% to piperacillin-tazobactam.[9]

Possible reasons for high resistance rate for carbapanem and other antimicrobial agents in *Pseudomonas aeruginosa* include more critical ill patients admitted to ICU and more patients being referred from other hospitals.

The increasing resistance rates of *Pseudomonas aeruginosa* strains to several antibiotics are expanding globally. Relevant figures for intensive care unit (ICU) isolates derived from Europe are even worse, because from 1990 to 1999, resistance to ceftazidime reached 57%, resistance to ciprofloxacin reached 56%, and resistance to imipenem reached 52%.[26]

Our study results are in agreement with reports from other countries that have shown high antimicrobial resistance rates in ICU patients. [27,9]

In fact, our ICU shows much higher resistance rates. Extended use of inappropriate antimicrobials and cross acquisition of resistance among admitted patients could be the possible reasons for emergence of MDR species. These reasons justify the need for establishing prompt infection control strategies in hospitals with special consideration in critical patient care areas. This single center study data may not reflect antibiotic susceptibility from whole of the country. As a consequence, a multi-site study is advised to compare and contrast from other hospitals.

Conclusion

In conclusion, the Gram negative bacteria remained more prevalent in ICU patients with nosocomial pneumonia. The reduced antibiotic susceptibility among Gram-negative bacteria alerts us that more effective strategies are needed to control the spread of antibiotic resistant organisms in critical patient areas.

Conflict of interest: The authors declare no conflict of interests**.**

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A. Conception/Study Designing/Planning
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C. Analysis/Interpretation/Discussion
D. Manuscript Writing
E. Critical Review
F. Facilitated for Reagents/Material/Analysis