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Original Article

Increased burden of MDR bacterial infections; reflection from an antibiogram of ICUs of a tertiary care hospital

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Abstract

Introduction: Infectious disease management in intensive care units (ICUs) is becoming more difficult due to increasing antimicrobial resistance. Hence, the aim of this study was to explore the nature of pathogens mostly encountered in an ICU and determine their antibiotic susceptibility through the compilation of ICU-specific antibiogram.

Methodology: A descriptive cross-sectional study of the culture and sensitivity reports of ICU patients was conducted in a tertiary care hospital. An antibiogram was created according to the Clinical Laboratory Standards Institute (CLSI) M39-A4 guidelines.

Results: Of the total 597 reports, the most common specimen type were respiratory secretions (n = 174), followed by blood (n = 128), wounds (n = 108), and urine (n = 80). Out of 597 isolates, the most frequently isolated bacteria were *Klebsiella* species (n = 156), *Pseudomonas aeruginosa* (n = 117), *Escherichia coli* (n = 112), *Enterobacter* species (n = 56), *Acinetobacter* species (n = 52), *Proteus* species (n = 39), *Staphylococcus aureus* (n = 34) and coliform species (n = 31). An 84% multidrug resistance (MDR) rate was reported among the isolates studied, with *Acinetobacter* species being at the top with a 98% MDR rate.

Conclusions: A substantial and alarming MDR rate was observed in our study. Furthermore, our findings demonstrated a potential interest in developing an ICU-specific antibiogram that is informative to clinicians in their clinical decision-making related to antibiotic therapy.

Key words: antibiotics; antibiogram; antimicrobial resistance; multi-drug resistant organisms; intensive care units.

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Introduction

Infectious disease management in intensive care units (ICUs) is a rising challenge due to growing microbial resistance, for which an evidence based guiding principle on the selection of antibiotics is imperative for clinical decision-making [1-3]. In a period when antimicrobial drug development is stalled, a significant increase in Gram-positive and Gram-negative resistance with the additional burden of multidrug resistant (MDR) pathogens poses a worrisome clinical threat both to the individual patient and global health [4,5].

The growing prevalence of antibiotic-resistant bacteria is a pressing challenge for clinicians in intensive care settings. Knowledge of ICU-specific antibiotic resistance rates helps clinicians choose empiric antibiotics while waiting for culture and susceptibility results. In addition, hospital infection prevention and antibiotic stewardship programs employ such susceptibility data to track changes in resistance over time, perform surveillance for the emergence of antibiotic-resistant organisms, and identify areas for intervention. Local antibiotic susceptibility data obtained through a setting-specific antibiogram, aids in several ways in the management of patients with infectious illnesses, specifically in the scenario of intensive care as time is critical in clinical decision-making in such settings [6]. Antibiogram can also help enhance antibiotic formulary decisions in hospitals and local protocols like empiric therapy guidelines [7].

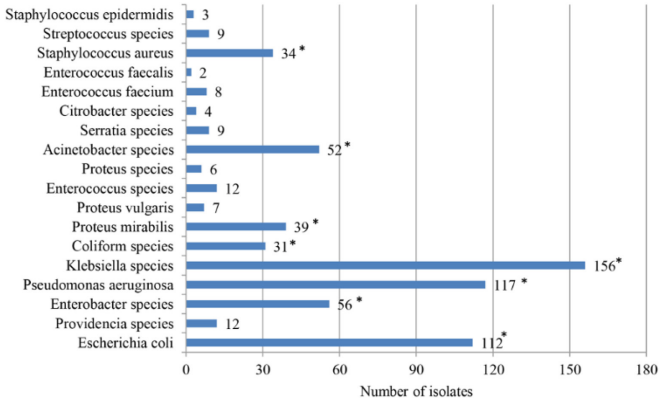
Furthermore, the availability of an ICU-specific antibiogram can assist clinicians in collaborating on issues linked to optimal selection of empiric antimicrobials and allow for the dissemination and sharing of prevailing resistance patterns. The scarcity of data in low and middle-income countries, particularly in a region like ours, has led us to explore this important aspect of public health concern. We, therefore, present here the nature and antibiotic susceptibility of pathogens mostly encountered in ICUs.

Methodology

We performed a descriptive cross-sectional analysis of culture and sensitivity reports of adult ICUs of the

Medical Teaching Institute-Hayatabad Medical Complex, which is a 1300 bed tertiary care public sector hospital located in the northwest region of the provincial capital of Khyber Pakhtunkhwa, Pakistan. The study was approved by the hospital's institutional review board (Ref#277/APP/2019). A total of 1008 reports were studied, which contained the culture and sensitivity data of all patients admitted under the care of ICUs over a period of one year (January 2020–December 2020) irrespective of infection type and source of infection. The antibiogram was set according to Clinical Laboratory Standard Institute (CLSI) M39-A4 guidelines [8]. There was a total of 760 positives culture reports, of which 669 reports met the inclusion criteria for the first isolate, defined in the CLSI M39-A4 guidelines as the initial microbial isolate of a particular species recovered from a patient during the time period analyzed regardless of the body source, specimen type, or antimicrobial susceptibility profile. However, a total of 597 out of 669 were included in the cumulative antibiogram after the exclusion of organisms with fewer than thirty isolates tested. Antibiotic sensitivity reports were assessed and recorded during routine clinical patient care for all diagnostic bacterial isolates obtained from patients admitted to the ICUs. Surveillance isolates, defined as organisms obtained from cultures of specimens that are collected for the purpose of determining if a patient is harboring a particular organism and are not from cultures that are obtained as part of the clinical evaluation of the patient's clinical illness, were excluded. Respiratory isolates were defined as isolates recovered from tracheal aspirates, bronchial aspirates, or broncho-alveolar lavage [9]. All specimens were tested in the central clinical microbiology laboratory of the hospital. Isolation and susceptibility testing of bacterial isolates were performed by the disc diffusion method; zone diameters were determined and interpreted according to the CLSI M100 guidelines. Intermediate susceptibility was categorized as non-susceptible [10]. MDR isolates were defined as those that were resistant to at least one antibiotic in three or more antimicrobial categories [11]. Percentage susceptibilities and the number of isolates tested were extracted from each report and analyzed in Statistical Package for Social Sciences (SPSS) version 21® through the application of descriptive statistics.

Figure 1. Total number of isolates versus isolates considered in antibiogram analysis.

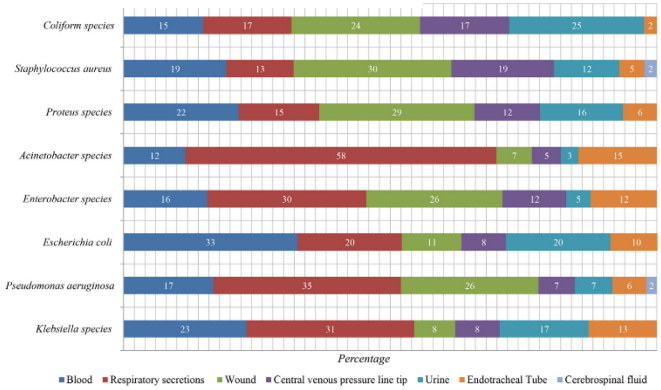


Results

Out of 597 isolates, the most common bacteria were *Klebsiella* species (n = 156), *Pseudomonas aeruginosa* (n =117), *Escherichia coli* (n =112), *Enterobacter* species (n = 56), *Acinetobacter* species (n = 52), *Proteus* species (n = 39), *Staphylococcus aureus* (n = 34) and coliform species (n = 31) (Figure 1).The clinical samples collected were mainly wound, urine, blood, respiratory secretions, central venous pressure (CVP) line tips, endotracheal tube (ETT),and cerebrospinal fluid (CSF) (Figure 2). The most common specimen type was respiratory secretions (n = 174) followed by blood (n = 128), wounds (n = 108) and urine (n = 80). Among the different specimens, blood specimens had high positivity for *E. coli* (33%), *Klebsiella* species (23%), *Proteus* species (22%) and *Staphylococcus* aureus (19%). Similarly, *Acinetobacter* species (58%) and *Pseudomonas* species (35%) were the predominant pathogens in respiratory secretions. Wound specimens yielded high positivity for *Staphylococcus aureus* (30%) and *Proteus* species (29%). Coliform species (25%) and *E. coli* (20%) predominated in the urine samples (Figure 2). Figure 3 depicts the percentage of MDR isolates observed; an overall 84% MDR rate can be seen among the studied isolates.

Table 1 presents the percent susceptibility profile of the studied isolates. Generally, isolates of *Klebsiella*

Figure 2. Percent of isolates in different clinical specimens.



species were susceptible to colistin (98%), polymyxin (97%), tigecycline (98%), and fosfomycin (80%), while a reduced susceptibility below which these agents cannot be considered empirically was noted for ceftazidime, ceftriaxone, cefepime, cefoperazone + sulbactam, gentamicin, amikacin, co-amoxiclav, oxacillin, piperacillin + tazobactam, meropenem, imipenem, ertapenem, nitrofurantoin and ciprofloxacin. Isolates of *Pseudomonas aeruginosa* demonstrated 99% susceptibility to colistin and polymixin only, and a grossly reduced susceptibility trend was observed for nitrofurantoin, cefotaxime, andceftriaxone. Overall, amikacin, colistin, fosfomycin, meropenem, imipenem, ertapenem, tigecycline, and nitrofurantoin retained 95%, 96%, 94%, 88%, 89%, 89%, 98%, and 94% susceptibility towards *E. coli*, respectively. *Enterobacter* species revealed resistance to cephalosporins (cefoperazone + sulbactam 64%, ceftriaxone 28%, cefepime 25%, ceftazidime 24%, and cefotaxime 19%), and ciprofloxacin (45%). However, a relatively good susceptibility trend was noted for carbapenems (meropenem and ertapenem 70%, imipenem 66%). Antibiotics with the highest susceptibilities against *Enterobacter* species were tigecycline (99%), colistin (97%) and fosfomycin (82%). Among the isolates of *Acinetobacter* species, 100% susceptibility was noted for colistin, fosfomycin, and nitrofurantoin, while a reduced susceptibility was observed against cephalosporins (cefoperazone + sulbactam 29%, ceftriaxone 8%), quinolones (ciprofloxacin 15%) carbapenems (meropenem 14%), and broad-spectrum penicillins (piperacillin + tazobactam 9%). *Proteus* species revealed 100% susceptibility to cefoperazone + sulbactam, fosfomycin, meropenem, imipenem, piperacillin + tazobactam and tigecycline. A reduced susceptibility pattern by *Proteus* species was observed against aminoglycosides (amikacin 81%, gentamicin 70%), and quinolones (ciprofloxacin 60%), cephalosporins (ceftriaxone 47%, ceftazidime 35%, cefepime 30%), and co-trimoxazole (25%). Antibiotic susceptibility patterns of Gram-

Figure 3. Multi-Drug Resistant (MDR)bacteria reflected in intensive care unit (ICU) antibiogram.

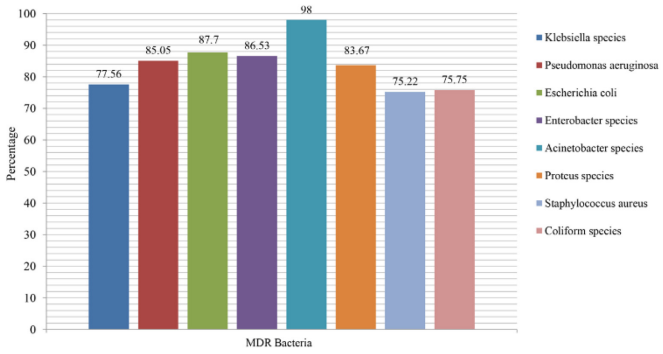


Table 1. Antibiogram of intensive care units.

Drugs	Percent susceptibility of isolates							
	Klebsiella species	*Pseudomonas aeruginosa*	*E. coli*	*Enterobacter* species	*Acinetobacter* species	*Proteus* species	*Staphylococcus aureus*	Coliforms species
Amikacin	75	57	95	76	50	81	78	59
Cefepime	22	62	24	25	NT	30	33	16
Cefoperazone + sulbactam	68	60	77	64	29	100	90	66
Cefotaxime	19	5	19	19	NT	48	25	18
Ceftriaxone	22	11	17	28	8	47	61	13
Ceftazidime	17	47	22	24	NT	35	NT	18
Co-triamoxazole	30	2	20	41	NT	25	65	38
Ciprofloxacin	44	42	28	45	15	61	NT	32
Fosfomycin	80	58	94	82	100	100	93	64
Ertapenem	62	55	89	70	NT	83	93	82
Meropenem	73	52	89	70	14	100	88	50
Imipenem + cilastatin	74	44	88	66	NT	100	88	49
Oxacillin	58	NT	73	72	NT	14	NT	64
Co-Amoxiclave	17	NT	24	17	NT	57	60	13
Piperacillin + tazobactam	63	67	79	69	9	100	100	51
Nitrofurantoin	67	5	88	76	NT	NT	94	47
Colistin	98	99	96	97	100	29	NT	100
Polymixin	97	99	96	92	100	25	NT	100
Teicoplanin	100	NT	NT	NT	NT	NT	95	NT
Tigecycline	98	NT	98	99	82	100	83	98
Vancomycin	NT	NT	NT	NT	NT	NT	99	NT
Linezolid	NT	NT	NT	NT	NT	NT	98	NT
Gentamicin	66	48	64	63	24	70	73	46
Clindamycin	NT	NT	NT	NT	NT	NT	52	NT
Rifampicin	NT	NT	NT	NT	NT	NT	89	NT
Doxycycline	NT	NT	NT	NT	NT	NT	87	NT
Chloramphenicol	NT	NT	NT	NT	NT	NT	95	NT

NT: not tested.

positive bacteria illustrated that *S. aureus* was almost completely susceptible to piperacillin + tazobactam (100%), vancomycin (99%), linezolid (98%) and teicoplanin (95%). Likewise, good susceptibility was demonstrated for nitrofurantoin (94%), ertapenem (93%), fosfomycin (93%), meropenem (88%), and imipenem (88%). However, a reduced susceptibility was demonstrated by *S. aureus* towards cephalosporins (ceftriaxone 61%, cefepime 33%, and cefotaxime 25%) except cefoperazone + sulbactam where susceptibility was 90%.

Discussion

Owing to the greater morbidity, mortality, and healthcare cost associated with difficult-to-treat infections, we aimed to explore the antibiotic resistance trends in critically ill patients. Such studies help in deciding optimal antibiotic use, lessening the drain on time and resources, and minimizing the use of broad-spectrum antibiotics, thereby, reducing selective pressure [12]. We opted to compile facility-specific (i.e., ICU-specific) antibiogram due to the fact that there has been significant variability in the susceptibilities of isolates among different healthcare units of the same hospital [13]. Hence, relying on the hospital-wide antibiogram may underestimate the resistance profile of specific pathogens.

An alarming MDR rate was noted across all the organisms included in the study (Figure 3). In a population like ours, where the healthcare system is not regulated at par, one could expect such an MDR rate. This could be due to the previous use of broad-spectrum antibiotics, and the utilization of invasive devices and procedures, which are risk factors for the acquisition of multidrug-resistant bacteria in the settings of ICUs [14]. High incidence of multidrug -resistant bacteria in ICUs has led to increased caution regarding the use of a few broad-spectrum antibiotics more wisely in order to reduce selective pressure on sensitive strains [15].

With *E. coli* and *Klebsiella* species, a diminished susceptibility to beta-lactams such as third- and fourth-generation generation cephalosporins was observed, illustrating evidence of extended spectrum beta-lactamases (ESBL). Out of all the antibiotics tested for these two organisms, only colistin, tigecycline, and Fosfomycin demonstrated a favorable susceptibility profile. Though explicit resistance testing for ESBL and carbapenem-resistant Enterobacteriaceae (CRE) was not reported in this study, reduced susceptibility to beta-lactams is suggestive of the ESBL and CRE resistance lurking in the region [16,17].

Acinetobacter species, a notorious pathogen to treat, alarmingly displayed reduced susceptibility to recommended agents such as carbapenems and other beta-lactams. We recommend using "last-line" antibiotics, i.e., colistin or tigecycline, in treating *Acinetobacter* infections. Although some studies reveal good in vitro activity of sulbactam, a β-lactamase inhibitor, against *Acinetobacter* species [18]and it has been successfully used in treating carbapenem-resistant strains [19], such a practice may not be adopted as an empiric practice and could be instituted based on an individual susceptibility report. Furthermore, we recommend adding all agents in the same class of antibiotics to the susceptibility testing panel, as evidence is suggestive of no cross resistance of *Acinetobacter* species among different agents of the same class of antibiotics [20]. As *Acinetobacter* species were the predominant isolates in respiratory samples, we suggest considering colistin as an empiric choice in patients with ventilator-associated pneumonia (VAP). It should be noted that only colistin displayed the greatest susceptibility against *Pseudomonas aeruginosa*isolates. With such a startling susceptibility pattern in *Pseudomonas* species, we are left with the last resort of colistin. In such infections, colistin could be adopted as an empiric choice, though at the expense of high cost and an undesirable safety profile [21]. Nevertheless, the risk of developing resistance to colistin still exists; hence it is necessary to ensure its prudent and judicious use in critical care areas.

Furthermore, our findings demonstrated potential interest in exploring ICU-specific antibiograms that are informative to participating facilities in devising empiric guidelines and strengthening antibiotics stewardship efforts. Not surprisingly, the ICUs-specific antibiogram came up with MDR isolates which are of global public health concern. Moreover, studies like ours can be utilized to compare antibiotic resistance among different ICUs in the region and to map the regional antibiotics susceptibility trend, which can help in devising evidence-based clinical guidelines. Future approaches for using this data include encouraging hospitals to periodically reveal their antibiotic susceptibility data in order to build a resistance trend relevant to intensive care settings.

The use of aggregate susceptibility data rather than raw isolate data from the microbiology laboratory is one of the limitations of this study. Furthermore, because this study is confined to a single setting and data from other hospitals is lacking, this influences the generalizability of the results.

A significant number of MDR isolates have been reported in our antibiogram, which can add to the risks of morbidity and mortality among critically ill patients. Overall, the findings of this study underscore the urgent need for proactive measures to address MDR infections in ICU settings. Therefore, periodic monitoring of resistance trends is crucial to prevent the emergence and spread of MDR in ICUs through a multidisciplinary approach involving clinicians, microbiologists, clinical pharmacists, infection prevention and control specialists, and hospital administrators.

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