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Antimicrobial Resistant Pattern of Isolates from Intensive Care Unit of Tertiary Care Hospital

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Abstract

Background: Patients in intensive care units are more vulnerable and have a higher risk of Hospital acquire infection in comparison to non-critical patient's wards. We determine the Microbial spectrum and their antimicrobial resistant pattern of isolates from intensive care units of tertiary care hospital in Peshawar, Pakistan.

Methods: A cross-sectional study was carried out for a period of 6 months and a total of 65 patients from the surgical intensive care unit and medical intensive care unit of tertiary care hospital were sampled for the possible pathogen. Non-probability convenient sampling techniques were used to enrolled patients and samples were transported to the pathology department for culture and anti-microbial resistant pattern. Data were analyzed on SPPS version 19 using descriptive and inferential statistical tools. Chi-square test were used for possible association and p value of < 0.05 were considered statistically significant.

Results: Both gram-positive and gram-negative isolates additional to fungi were prevalent in the intensive care unit with the most frequent isolates being *Acinetobacter* species followed by *Enterobacteriaceae* and *P. Aeruginosa* respectively. Amikacin, Doxycycline, Linezolid, Tigecycline, and Vancomycin have a low resistant pattern for both *Staph aureus* and coagulase-negative staphylococci (CoNS) while Cephalosporin including cefepime (58%), and minocycline (35%) along with polymyxin B shows the lower resistance pattern for *Acinetobacter* and other gram-negative isolates.

Conclusion: Tigecycline, vancomycin, cefepime, and polymyxin B were used as empiric therapy agents in severe conditions however a larger scale study is required for calculating optimized therapeutic regime for each agent. The physician and hospital guidelines should adhere to the monitoring of antimicrobials to limit the upsurge of resistance patterns among different pathogenic organisms.

Introduction

Hospital-acquired infections (HAI) are most frequently encountered by both gram-positive and gram-negative bacteria. Hospitalized patients are vulnerable to be affected by certain infections due to immunocompromised status accompanying serious underlined illness, especially in case of admission in intensive Care Unit (ICU) [1-2]. Studies from various epidemiologic sources are required for local surveillance and resistant pattern of antimicrobial for improvement in empiric therapy. Such information is also necessary for infection control purposes and creating local guidelines to limit the spread of infection by adhering to such guidelines.

Patients admitted to both the surgical intensive care unit (SICU) and Medical intensive care unit (MICU) are always susceptible to hospital-acquired infection associated with increased morbidity and mortality. The rate of infection is five to ten times greater than non-ICU patients admitted for various reasons [3-4]. Multiple risk factors such as Intensive interventional procedures, age, and primary disease are associated with an increased rate of HAI.

The incidence of HAI in intensive care units is the median rate of 9 patients per 100 discharged ICU patients [5]. Several studies reported a rate of nosocomial infection related to ICU patients with an approximate prevalence of 5 to 30 % [6]. The infection ranges from a urinary infection, respiratory illness to septicemia which accounts for 19% prevalence of ICU patients [6-7].

Use of Antimicrobial agents re in parallel to the development of their resistance as reported by the United States National Nosocomial Infection Surveillance System in their report [8-9].

Gram-positive and gram-negative bacteria were the most frequently encountered microbiologic agents for causing ICU to acquire infection with the prevalence of 34% in comparison to all hospital-acquired Gram-negative bacteremia's [10]. Moreover, a study reported a higher mortality rate of 7-fold increase in comparison to admitted patients without gram-negative septicemia [11].

MDR phenotype creates a challenging scenario and limits therapeutic options for treating hospital acquire infection and has an economic and social burden [12]. Information regarding the current antimicrobial resistant pattern against various isolates from intensive care unit are scarce and required updated study to optimize the therapeutic strategy for empiric treatment. This study was designed to determine the frequently encountered organism in ICU and their resistance pattern along with multi-drug resistant (MDR) phenotype against commonly prescribed antimicrobial agents.

Methods

A cross-sectional study was done in SICU and MICU of Rehman Medical Institute Peshawar Pakistan from 05-august-2017 to 05-December-2017. Patients were selected after reviewing their hospital stay in both Surgical and medical intensive care units for greater than 48 to 72 hours of admission. 65 patients were enrolled in the study irrespective of gender and age. Different samples including blood, urine, pus, sputum, body fluids, bronco alveolar lavage were screened for bacterial and fungal isolates. All Samples were transported to the Pathology department for determination of culture and antimicrobial susceptibility testing. All cultures were processed in accordance with the standard microbiological protocol defined by CLSI (Clinical Laboratory standard Institute) guidelines. Urine samples were inoculated and cultured on CLED (Cysteine-lactose-electrolyte Deficient agar) and MacConkey agar while CLED, MacConkey, and Blood agar were used for sputum samples. Blood cultures were processed on BD BACTEC™ Automated Blood Culture System. Inoculated media were kept overnight for incubation at 35C for 24 hours. After overnight incubation of the plate's bacterial growth was isolated and identified based on gram staining, Colony morphology, and biochemical characteristics as per CLSI guidelines.

Coagulase tests were used for catalase-positive gram-positive cocci. For fungal isolation cultured was carried on Sabouraud dextrose agar. After microbial isolation, all isolated were subcultured on MHA (Muller Hinton agar) media for antimicrobial susceptibility testing. For standardization of an approximate number of bacteria in a liquid suspension of 0.5 McFarland turbidity standard which provides an optical density comparable to the density of a bacterial suspension with a 1.5 x 10^8 colony forming units (CFU/ml) were used.

The antibiotics used for antibiogram determination were: fosfomycin 50ug, nitrofurantoin 300ug, ampicillin 10ug, ceftazidime 30ug, tazobactam/piperacillin 10/100ug, imipenem 10ug, gentamicin 10ug, ciprofloxacin 5ug, amikacin 30ug andcontrimaxazole1.25/23.75ug. The plates were incubated at 37c for 24 hours. For quality control purpose different ATCC strains were used for positive control such as staphylococcus aureus ATCC 25923; *Escherichia coli* ATCC 25922. Data were analyzed on SPSS v19 software and variables for analyzed based on descriptive and inferential statistical tools. Chi-square tests of association were used in order to reveal a significant association between the categorical variables. A P-value of <0.05 was considered statistically significant.

Results

A total of 65 patients were sampled for different clinical samples. The isolates were obtained from different sites i.e., blood (16%), followed by urine (15%), BAL and tracheal secretions (13%), pus (12%), and others (7%) respectively. Coagulase-negative staphylococci, pseudomonas, and staphylococcus aureus were the 3 common isolates from blood. *Enterobacteriaceae* family was the predominant isolates in urine and Acinetobacter in BAL. *Acinetobacter* species, *Pseudomonas Aeruginosa* and *Enterobacteriaceae* family were the most common isolates among gram-negative organisms, while *Staph aureus* and Coagulase-negative staphylococci (CoNS) were the two leading gram-positive isolates. For *enterococcus* spp, there were no VRE isolates found. The most frequent species isolated from ICU was *Acinetobacter*. The frequency of gram-positive was 22% and gram-negative was 70% while fungal isolates were 8% respectively. Table 1 shows the percentage of antibiotic resistance to gram-positive isolates resistance to the antibiotics tested. Both Staphylococcus aureus and coagulase-negative staphylococcus show 0% resistance to vancomycin, linezolid, and tigecycline.

Antimicrobial drug	Antimicrobial resistant pattern	
	Staph Aureus	CoNS
Amikacin	0%	0%
Erythromycin	80%	60%
Gentamicin	20%	40%
Ciprofloxacin	100%	40%
Clindamycin	0%	20%
Amoxicillin-clavulanate	100%	80%
Ceftriaxone	80%	20%
Doxycycline	20%	0%
Fusidic acid	60%	20%
Linezolid	0%	0%
Tigecycline	0%	0%
Vancomycin	0%	0%

Table 1: Antimicrobial resistant pattern of Isolates from different clinical samples.

Discussion

Reduction in antimicrobial resistance predominantly in ICUs has been a goal for all intensive care units as it improves outcome and cost to all patients in terms of the expenses for costly antibiotics as the duration of ICU stay. Various epidemiological studies reported the antimicrobial resistance to ICU isolates due to increasing utilization as prophylactic and therapeutic strategies. In our study, the most frequent pathogen isolated from ICU were *Acinetobacter, E. coli*, and *Pseudomonas Aeruginosa*. *Staph aureus* and coagulase-negative *staphylococci* were predominant isolates. This observation was agreed with the finding of a previous study that reported the bacterial spectrum and antimicrobial susceptibility pattern in Saudi Arabia [13]. The frequency of gram-positive and gram-negative bacilli in our study was 22% and 70% respectively.

Antimicrobial drug	Antimicrobial resistant pattern		
	Enterobacteriaceae	*Pseudomonas*	*Acinetobacter*
Amikacin	95%	60%	94%
Ciprofloxacin	82%	58%	100%
Gentamicin	68%	70%	63%
Doxycycline	62%	-	65%
Cefepime	10%	12%	58%
Ceftriaxone	82%	-	82%
Piperacillin	58%	22%	58%
Polymyxin B	28%	-	60%
Sulzon	38%	20%	-
Minocycline	-	-	35%
Meropenem	48%	25%	55%
Tigecycline	20%	-	-
Imipenem	35%	25%	-

Table 2: Antimicrobial resistant pattern of Isolates from different clinical samples.

A multicenter surveillance study from china ICUs also reported the rate of infection by gram-negative was greater than gram-positive i.e. 63.2% and 36.8% respectively which is almost similar to our finding [14]. In our study all gram-positive isolates were found sensitive to vancomycin, tigecycline, linezolid and amikacin while resistant to ciprofloxacin, erythromycin Amoxicillin-clavulanate, and Ceftriaxone. Our findings are in agreement with the findings of a study from Secondary Care Hospital in Saudi Arabia [15]. They reported the resistance pattern for erythromycin 40% and ciprofloxacin 56% respectively. Higher resistance to ciprofloxacin was observed for *staph aureus* than CoNS. This observation is agreed with the finding of a study on the antimicrobial resistance pattern of surgical ICU in Turkey [16].

Overall vancomycin, tigecycline, and linezolid can effectively use as a therapeutic choice for Gram-positive infections while high resistance to amoxicillin-clavulanate, ciprofloxacin implies their averting their choice of drug for treating ICU related infections in our settings. Similar findings were reported by Japoni A et al to use vancomycin as a control for gram-positive infections [17]. In our study, *Acinetobacter* isolates were resistant to ampicillin, amoxicillin-clavulanate, and ciprofloxacin, whereas minocycline, polymyxin B, tigecycline shows a least resistant pattern. *Enterobacteriaceae* shows higher resistance to ceftriaxone, amikacin, and ciprofloxacin. similar findings were reported by mehr et al [18] reported higher resistance to ciprofloxacin, ceftriaxone while amikacin shows least resistance. The gram-negative bacteria were the major cause of infections in the ICU. The commonest isolates were *S.aureus, Acinetobacter, Enterobacteriaceae, and Pseudomonas Aeruginosa*. The best empirical therapy should include vancomycin, Tigecycline, cefepime, and polymyxin B can be used as first-line drugs with carbapenems as second-line agents. The high frequency of multidrug resistance bacteria in ICU suggests that we need to prescribe broad-spectrum antibiotics more wisely to reduce pressure on sensitive strains. This could be beneficial for saving ICU patients and preventing the spread of resistant isolates in critical wards.

Competing interest

The author declares that there is no conflict of interest regarding the publication of this paper.

Authors' Contribution

Conceived and designed the experiments: Shehryar Ahmad, Ujala Rasheed, Sajid Ali
Performed the experiments: Iram Naz and Nasir Ali
Analyzed the data: Shehryar Ahmad, and Iram Naz
Contributed materials/analysis/tools: Ujala Rasheed and Atif Aziz
Wrote the paper: Shehryar Ahmad, Critical Review: Nasir Ali

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