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Original Article

Antibiogram of Intensive Care Unit of a Tertiary Care Hospital in Balochistan: an Overview of Rising Antimicrobial Resistance

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ABSTRACT

Objective: To formulate an antibiogram of the medical intensive care unit, indicating the prevalence and resistance patterns of bacterial pathogens that contribute to sepsis in critically ill patients. Study Design: Cross-sectional study.

Place and Duration of Study: Critical Care and Microbiology Departments of Combined Military Hospital Quetta, Pakistan, from May 2022 to May 2023.

Methodology: Cultures for susceptibility testing were collected from patients admitted to the intensive care unit with clinical suspicion of sepsis and on antibiotics. All specimens were processed as per standard laboratory protocols for identification and antimicrobial susceptibility testing.

Results: A total of 213 patients with positive cultures were included in the study, comprising 122 males (57%) and 91 females (43%). Of the 213 isolates, 49(23%) were Gram-positive, and 164(77%) were Gram-negative. Among the Gram-negative isolates, Burkholderia cepacia (43 cases, 26%) was the most frequently identified, followed by Acinetobacter baumannii (41 cases, 25%). Among the 49 Gram-positive isolates, Staphylococcus spp. was the most prevalent, with 33 cases (67%). All Staphylococci were found to be 100% resistant to methicillin, with no resistance observed to vancomycin. For Burkholderia cepacia, ceftazidime and cotrimoxazole exhibited low resistance rates, whereas colistin was the primary effective treatment for Acinetobacter baumannii in most cases.

Conclusion: An antibiogram serves as an evidence-based tool for guiding empirical antibiotic therapy. The increasing prevalence of multidrug-resistant microorganisms necessitates rational antibiotic use, achievable by identifying isolates in specific demographic areas and tailoring empiric therapy accordingly. Developing local antibiograms is crucial to combat antimicrobial resistance effectively.

Keywords: Antibiogram, Antibiotic Resistance, Intensive Care Unit.

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INTRODUCTION

Antibiotic resistance is emerging as a global crisis, primarily attributed to the indiscriminate use of antimicrobials.[1] Newly admitted patients to intensive care units (ICUs) are especially susceptible to nosocomial infections, as ICUs can harbor a multitude of drug-resistant pathogens.[2] These pathogens are often acquired from previously admitted critically ill patients, increasing the risk of sepsis and septic shock, leading to elevated morbidity and mortality. Additionally, prolonged hospital stays and increased nursing costs necessitate the rational use of antibiotics in ICUs.[3,4] In developing countries like Pakistan, there is limited availability of resources for comprehensive antimicrobial stewardship programs that further complicated by the country's high rates of healthcare-associated infections due to resistant organisms.[5]

While antibiotics have revolutionized medicine, resistance to these drugs threatens to reverse progress, potentially taking humankind back to an era where minor infections could be fatal. Antibiotics remain essential for improving patient outcomes in critical care settings.[6] Intensivists rely on tools and guidelines to support the rational use of antibiotics. Among these, antibiograms, which provide periodic summaries of microbial susceptibility profiles, are a highly valuable resource. They allow clinicians to track resistance trends and administer antibiotics judiciously.

The rationale of this study was to develop a standardized antibiogram for the ICU of our hospital, determining the prevalence of pathogens and their

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antimicrobial susceptibilities. This effort aims to improve practices, streamline antibiotic use, and refine clinical decision-making.

METHODOLOGY

This cross-sectional study was conducted in the Critical Care Department in collaboration with the Microbiology Department of Combined Military Hospital Quetta, Pakistan from May 2022 to May 2023. Approval was obtained from the hospital's ethical review board (IERB/06/2022).

Inclusion Criteria: was Adult patients of either gender admitted to the ICU with clinical suspicion of sepsis and positive cultures were included.

Exclusion Criteria: Pregnant females, specimens collected from urine bags, single blood cultures, and repeated specimens from the same patient were excluded.

Sample size was calculated using WHO calculator keeping the anticipated population proportion to be 16%, the sample size came out to be 206.[7] We collected a sample of 213 by non-probability consecutive sampling, after taking informed consent.

Various specimens, such as paired peripheral blood in the BacT/Alert automated system (BioMérieux SA, France), peripheral blood with CVP tips, secretions (endotracheal and endobronchial), non-directed bronchoalveolar lavage (NBL), cerebrospinal fluid (CSF), abdominal fluid, catheter venous pressure (CVP) tips, pus/ tissue aspirates specimens from clinically suspected critically ill patients, were collected aseptically and processed as per standard laboratory protocols.

Bacterial growth was identified using biochemical tests, and susceptibility testing was performed using the modified Kirby-Bauer disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) 2022 guidelines.[7-8] Highly resistant isolates identified via disk diffusion were further confirmed using the VITEK II system (BioMérieux, France), which provided minimum inhibitory concentration (MIC) results for commonly used antibiotics.

The key terminologies utilized in this study are defined as follows: Extended Spectrum Beta-Lactamase (ESBL) Producers: Bacteria that produce extended-spectrum beta-lactamases, identified in the laboratory using a phenotypic method. Resistance to third-generation cephalosporins was used as a screening test, and confirmation was performed using the double-disk synergy test according to CLSI guidelines 2022. Carbapenem-Resistant Organisms (CRO): These are bacteria resistant to imipenem, meropenem, or both. Methicillin-Resistant Staphylococci (MRSA/MRCoNS): Resistance in Staphylococcus species was determined using a cefoxitin disk (Fox). For Staphylococcus aureus, a zone diameter of ≥22 mm was considered susceptible, while for coagulase-negative Staphylococci (CoNS), a zone diameter of ≥25 mm was required. Vancomycin-Resistant Enterococci (VRE): Enterococci resistant to vancomycin or both vancomycin and teicoplanin. Extensively Drug-Resistant (XDR) Isolates: Bacteria resistant to at least one drug in all tested classes, with only one or two remaining options for treatment. Pan Drug-Resistant (PDR) Isolates: Bacteria resistant to all clinically available antibiotics. Not Tested (NT): Indicates that the isolate was not tested against a specific drug due to either the lack of CLSI-validated testing protocols or unavailability of the drug. Intrinsic Resistance (IR): Refers to inherent resistance of bacteria to specific drugs, rendering them clinically ineffective.

Data was analyzed using Statistical Package for Social Sciences (SPSS), version 26. Descriptive statistics were used to study the demographics of the study group, types and frequencies (percentages) of pathogens and susceptibility profiles of pathogens.

RESULTS

This study analyzed 213 patients, comprising 122 males (57.0%) and 91 females (43.0%), with ages ranging from 18-70 years. The majority of patients (69.0%) were between 51-70 years old followed by 62(29.1%) patients belonged to the age group of 31-52 years. Only 4 (1.9%) patients were between the ages of 18-30 year. Microbial cultures revealed 49(23.0%) gram-positive and 164(77.0%) gram-negative isolates from various specimens. Microbial growth was most commonly detected in 59 respiratory specimens, followed by 51blood and 34 pus/tissue aspirates. In contrast, 36 urine, 23 CVP tip and 10 abdominal fluids yielded positive results less frequently.

Among 164 gram-negative isolates, Burkholderia cepacia 43(26.0%) was the most prevalent, followed by Acinetobacter baumannii 41(25.0%), Klebsiella pneumoniae 32(19.5%), Escherichia coli 27(16.4%), and Pseudomonas aeruginosa 9(5.5%), shown in table-I. Coagulase-negative Staphylococci (47.0%) was the most common gram-positive isolate, followed by Staphylococcus a. Among 49 Gram-positive isolates,

Staphylococcus aureus (SA) and Coagulase-negative Staphylococci (CoNS) were predominantly methicillin-resistant (MR). Notably, 23 MR CoNS were exclusively detected in blood cultures and CVP tips, whereas MRSA was primarily isolated from pus/tissue aspirate specimens (10 cases). Urine specimens were the primary source of 10 Enterococcus species, which showed susceptibility to linezolid and tigecycline mentioned in Table-II. However, a concerning 50% of these isolates were found to be resistant to Vancomycin. Four (8.1%) Streptococcus pyogenes and (02) Streptococcus pneumonia were least common isolates, recovered from pus/tissue specimens and CSF, respectively (Table-II).

Antibiotic susceptibility testing revealed alarming rates of drug resistance among Gram-negative isolates, mentioned in Table-III. Notably, 43 Burkholderia cepacia, commonly found in blood (21), respiratory (15) and pus (7) specimens, showed maximum resistance, with ceftazidime and meropenem being the only effective treatments. Forty-one Acinetobacter baumannii, predominantly isolated from respiratory (24), pus (11), urine (6) specimens, exhibited extensive drug resistance, with colistin being the sole effective antibiotic. Twenty-seven Escherichia coli, mainly isolated from abdominal fluid (10),(13)

Table-I: List of Antibiotics

Abbreviation	Full Name	Abbreviation	Full Name
AK (30ug)	Amikacin	MEM (10ug)	Meropenem
CAP (30ug)	Chloramphenicol	MIN (30ug)	Minocycline
CAZ (30ug)	Ceftazidime	NIT (300ug)	Nitrofurantoin
CIP/LEV(5ug)	Ciprofloxacin/ Levofloxacin	PB/COL(2ug)	Polymyxin-B/Colistin agar
CFM (30ug)	Cefipime	PEN (10u)	Penicillin
CLI (2ug)	Clindamycin	SXT (25ug)	Co-trimoxazole
FOX (30ug)	Cefoxitin	TGC (15ug)	Tigecycline
CRO (30ug)	Ceftriaxone	TZP (110ug)	Piperacillin-Tazobactum
DOX (30ug)	Doxycycline	VAN (30ug)	Vancomycin
ERY (15ug)	Erythromycin	AMP (10ug)	Ampicillin
FD (10ug)	Fusidic acid	AMC (30ug)	Co-Amoxiclav
FOS (200ug)	Fosfomycin	TEC (30ug)	Teicoplanin
GEN (10ug) & (120ug)	Gentamicin	LZD (30ug)	Linezolid
IMP (10ug)	Imipenem	SAM (20ug)	Ampicillin-sulbactam

Table-II: Antibiotic Resistance and Sensitivities of Gram-positive Isolates (n=49)

Antibiotics	Gram positive isolates (n=49) (% Resistance to antimicrobials)				
	MRSA (10)	MR-CONS (23)	Streptococcus Pyogenes (04)	Streptococcus Pneumonia (02)	Enterococcus Spp (10)
Ampicillin	10(100)	100	0	0	5(50)
Cloxacillin*	10(100)	100	NT	NT	NT
Co-amoxiclav	10(100)	100	0	0	5(50)
Ceftriaxone	10(100)	100	0	0	IR
Levofloxacin	4(40%)	7(30%)	1(25%)	0	7(70)
Doxicycline	2(20%)	7(30)	2(50)	1(50)	4(40)
Gentamycin	4(40)	11(48)	NT	NT	3(30)*
Erythromycin	6(60)	13(56,5%)	3(75%)	1(50)	4(40)
Clindamycin	4(40)	11(48)	1(25)	1(50)	IR
Cotrimoxazole	3(30)	6(26)	3(75)	100	IR
Penicillin	100	100	0	0	6(60)
Linezolid	0(0)	8(35)	0	0	0
Vancomycin	0(0)	0	0	0	5(50)
Nitrofurantoin (urine only)	NT	NT	NT	NT	3(30)
Fosfomycin (urine only)	NT	NT	NT	NT	5(50)
Tigecycline	4(40)	3(13)	NT	NT	0
Teicoplanin	NT	NT	NT	NT	2(20)
Fusidic acid	2(20)	6(26)	NT	NT	IR

**MRSA = Methicillin resistant Staphylococcus aureus, *MRCoNS=Methicillin resistant Coagulase negative Staphylococci. **Resistance to Cloxacillin indicates MRSA.*

Table–III: Antibiotic Resistance And Sensitivities Of Gram positive isolates (n=164)

	Gram negative isolates (% Resistance to antimicrobials)									
Antibiotics	Klebsiella pneumoniae 32	Acinetobacter baumannii 41	Escherichia coli 27	Serratia marcesens 04	Pseudomonas aeruginosa 09	Enterobacter cloacae 02	Burkhulderia cepacia 43	Proteus mirabilis 02	Providentia rettgeri 02	Chyreseobaterium Indologenes 02
Ampicillin	IR	IR	100	IR	IR	IR	IR	100	IR	IR
Co-amoxiclav	30(94)	IR	24(89)	IR	IR	IR	IR	100	IR	IR
Ceftriaxone	30(94)	39(95)	24(89)	100	IR	100	IR	1(50)	100	IR
Chloramphenical	NT	IR	NT	NT	IR	NT	21(47)	NT	NT	NT
Cefipime	29(90)	34(83)	24(89)	100	6(67)	100	IR	1(50)	100	NT
Ceftazidime	NT	37(90)	NT	NT	4(44)	NT	9(21)	NT	NT	NT
Ciprofloxacin	22(69)	32(78)	21(78)	3(75)	5(55)	100	NT	1(50)	100	0
Cotrimoxazole	19(59%)	31(75.6)	19(70.4)	3(75)	IR	1(50)	9(21)	0	100	0
Doxicycline	21(65.6)	19(46)	16(59.2)	2(50)	IR	100	IR	IR	IR	IR
Amikacin	22(62.5)	21(65.6)	13(48)	1(25)	3(33)	0	IR	0	0	NT
Gentamycin	23(72)	33(80.5)	15(56)	2(50)	4(44)	1(50)	IR	0	0	NT
Imipenem	15(47)	23(56)	11(41)	2(50)	5(55)	0	IR	0	0	NT
Meropenem	13(42)	22(53.6)	9(33)	2(50)	3(33)	0	13(30.2)	0	0	NT
Piperacillin/ Tazobactum	30(94)	34(90)	24(89)	3(75)	3(33)	100	IR	1(50)	1(50)	0
Tigecycline	10(31)	25(61)	4(15)	0	IR	0	NT	IR	IR	NT
Polymyxin	1(3.1%)	2(4.8)	0	IR	1(11)	0	IR	IR	IR	IR
Nitrofurantoin (Urine only)	5(15.6)	NT	5(18.5)	IR	2(22)	0	NT	IR	IR	NT
Fosfomycin (Urine & XDR)	7(22%)	IR	4(15)	0	IR	0	IR	NT	NT	NT
Levofloxacin	22(69%)	31(75.6%)	19(70.4)	2(50)	2(22)	1(50)	11(26)	1(50)	1(50)	0
Ampicillin-sulbactam	NT	39(95)	NT	IR	IR	IR	IR	NT	NT	NT
Minocycline	10(31)	25(61)	5(18.5)	2(50)	IR	1(50)	11(26)	IR	IR	NT

**NT: the isolate has not been tested against the drug since the result is not validated by latest CLSI testing protocols or due to non- availability of that specific drug. *IR means the isolate is intrinsically resistant against the drug and it should not be used clinically.*

urine and (4) blood specimens. It showed minimal resistance to carbapenems, fosfomycin, amikacin, and nitrofurantoin, with no resistance to colistin or tigecycline. Whereas 32 Klebsiella pneumoniae, commonly found in respiratory (22), urine (7), and (3) blood specimens, also demonstrated high resistance rates in which colistin and tigecycline were the only effective antibiotics. Pseudomonas aeruginosa detected from 9 patients mainly from pus/tissue aspirates of burn patients.

The study also reported high rates of ESBL 149(91.0%), XDR 92(56.0%) and CRO 95(58.0%) strains among gram-negative organisms. PDR strains were found in only 7(4.0%) cases as shown in Figure.

DISCUSSION

The antibiogram developed in this study aimed to assist clinical practitioners in selecting the most effective empirical antimicrobial therapy against suspected pathogens. Additionally, the antibiogram supported the Antimicrobial Stewardship (AMS) program by simplifying resistance trends of common Gram-positive and Gram-negative organisms, thus promoting the judicious use of antibiotics.

One study showed Pseudomonas aeroginosa as a high-risk pathogen in the ICU settings of United states mainly associated with blood stream infections and respiratory infections.[9] In contrast, our medical ICU saw a predominance of Burkholderia cepacia, an environmentally resilient pathogen that readily inhabits water, soil, and vegetation. Though typically non-pathogenic to healthy individuals, it can cause pneumonia and septicemia in immunocompromised patients.[10,11] In our ICU, it was the most prevalent isolate (31.25%), predominantly recovered from blood and respiratory specimens. It exhibited intrinsic resistance to many antibiotics, including penicillins, aminoglycosides, cefepime, imipenem, and polymyxins.10 However, it was least resistant to

ceftazidime and cotrimoxazole, showing a resistance rate of 21%. This pattern differed from Pakistani data, where Acinetobacter spp. and E. coli were the most common isolates (15.3%). These variations underscore the importance of developing local antibiograms tailored to specific demographics.[12]

Acinetobacter baumannii, the second most prevalent pathogen in our study (25%), was isolated from a variety of specimens, including respiratory samples, pus, blood, and urinary samples. It exhibited over 60% resistance to all tested antibiotics except colistin and doxycycline. As a significant cause of multidrug resistance with a global mortality rate of up to 35%, we recommend combination therapy instead of monotherapy for treating infections caused by this organism.[12,13]

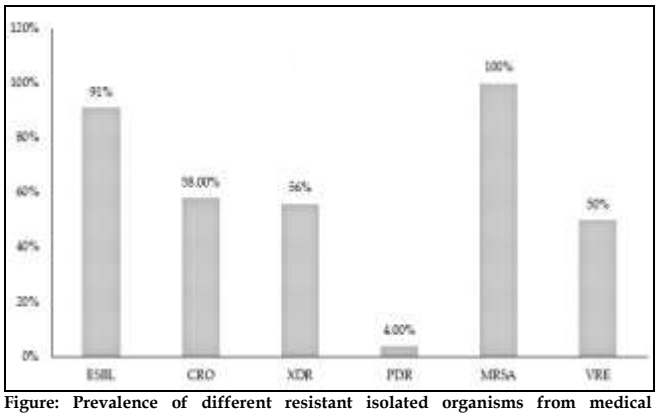

Figure: Prevalence of different resistant isolated organisms from medical intensive care unit

Klebsiella pneumoniae (19.5%) and E. coli (16.4%) were the third and fourth most common isolates, respectively. According to national surveillance data from Pakistan (2006–2018), resistance rates for these organisms exceeded 50% for third-generation cephalosporins, findings consistent with our data.[14] However, E. coli in our study showed minimal resistance to tigecycline, fosfomycin, and nitrofurantoin, and no resistance to colistin, making these effective treatment options. A comparative analysis with another ICU at a tertiary care hospital revealed distinct findings. Interestingly, E. coli was the most prevalent pathogen in their isolates (24%), differing from our results. However, both studies shared a commonality, with Acinetobacter being the second most common pathogen in their study (23%) and similarly prominent in our findings (25%).[14,15]

Enterococcus spp., primarily isolated from urine specimens, demonstrated 50% vancomycin resistance, which was lower than the 86.96% resistance rate reported by other studies in Pakistan. Susceptibility to linezolid was consistent across studies but inconsistent with vancomycin resistance.[16,17]

A study by Iqbal *et al.* included 150 patients with UTIs, in which the most common pathogen was E. coli followed by Klebisella pneumonia, showed better sensitivity to carbepenems and nitrofurantoin, which is similar to our findings.[18]

We observed a notable discrepancy in our results, with a higher CRO rate of 58% compared to only 18% reported in a previous Karachi-based study. Moreover, our Gram-positive isolates showed universal susceptibility to vancomycin and linezolid. In the same study, the most common pathogens were Klebsiella pneumoniae (34.6%), Pseudomonas aeruginosa (21.1%) and Escherichia coli (17.4%).[19]

In contrast to our results, which identified Burkholderia as the predominant pathogen, Zehra *et al.*'s study in an ICU setting found E. coli to be more common. Additionally, our isolates exhibited higher resistance rates, highlighting the need for localized antibiograms to guide antibiotic therapy.[20]

Mohamed *et al.* also investigated antibiograms in intensive care unit (ICU) patients at a tertiary care hospital, shedding light on the growing concern of antibiotic resistance, focusing on ESKAPE (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species) pathogens.[21] The study reports alarming rates of antibiotic resistance, with Klebsiella pneumoniae and Acinetobacter baumannii showing high levels of resistance to carbapenems, similar observations has been noted in our study.

In this Kenyan study, 45.5% of isolates were multidrug-resistant (MDR) with high mortality and prolonged hospital stay with 34.6% treatment failures whereas in this study it was way more than that indicating urgency of AMR surveillance and implementation of AMS.[22]

Saleem et al.'s study shared similarities with our research in terms of the high prevalence of Gram-negative organisms (73.1% vs. 77%). However, our study uncovered higher rates of ESBL (91%) and CRO (58%), indicating a more severe antibiotic resistance problem compared to their findings (ESBL: 57.1%, CRE: 21.4%).[23]

LIMITATION OF STUDY

This study focused on a single geographic region, limiting the generalizability of the antibiogram to

Balochistan. Additionally, the study centered solely on pathogens and their antibiotic susceptibilities, excluding patient comorbidities and disease states, which may have introduced bias.

CONCLUSION

The antibiogram serves as an essential, evidence-based tool for guiding empirical antibiotic therapy. The rising prevalence of multidrug-resistant organisms highlights the critical need for the rational use of antibiotics. Developing local antibiograms tailored to specific demographic areas is a high priority to combat AMR effectively.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

K & FS: Data acquisition, data analysis, critical review, approval of the final version to be published.

JA & KM: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MTAQ & FS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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