

ANTIMICROBIAL RESISTANCE AMONG INTENSIVE CARE UNIT PATIENTS IN A TERTIARY CARE HOSPITAL OF BANGLADESH

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Abstract:

Background: Antimicrobial resistance is a growing concern specially among the critically ill patients who are often treated by multiple antibiotics. But, the data regarding the pattern of antimicrobial resistance in this population are often insufficient.

Objective: To observe the pattern of antimicrobial resistance among the patients admitted into the intensive care unit (ICU).

Methodology: This prospective observational study was carried out in the ICU of a tertiary care hospital of Bangladesh over 6 months. Samples of blood, urine, tracheal aspirate, wound swab and pus were obtained from the patients, cultured and analyzed.

Results: Among 100 subjects, the most common primary diagnoses were aspiration pneumonia (29%) and urinary tract infection (UTI) (24%). Out of 315 samples, microorganisms were isolated from 125 samples (39.68%). The most common sample yielding positive culture was tracheal aspirate (67.2%), and the most frequently isolated microorganisms were *Pseudomonas* spp. (35%), *Escherichia coli* (28%), *Acinetobacter* spp. (24%) and *Klebsiella* spp. (18%). *Acinetobacter* spp., *Pseudomonas* spp. and *Klebsiella* spp. were the commonest resistant organisms. Overall prevalence of resistance to antibiotics were: ceftriaxone 72%, ceftazidime 78.4%, ciprofloxacin 81.6%, gentamicin 84%, meropenem 49.6% and netilmicin 39.2%. Meropenem was the most sensitive antibiotic against *Klebsiella* spp. (66.67%) but *Acinetobacter* spp. was still resistant to meropenem and amikacin but sensitive to cotrimoxazole (66.67%). Multidrug resistant *Pseudomonas*, *Acinetobacter* and *Klebsiella* species were found; piperacillin-tazobactam combination showed <40% resistance against them. No single antibiotic showed good efficacy against *Acinetobacter* spp.

Conclusion: The prevalence of antibiotic resistance is high among the ICU patients, and the majority of the isolated organisms are resistant to conventional antibiotics.

Keywords: Antimicrobial resistance, microorganism, antibiotic, intensive care unit.

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Introduction

The intensive care unit (ICU) is often called the epicenter of infection due to its extremely vulnerable population. The risk of infection increases because of multiple procedures and use of invasive devices e.g., intubation, mechanical ventilation, vascular access, central venous lines distorting the integrity of protective

barriers. In addition, several drugs are often administered, which predispose to infections. For example sedatives, muscle relaxants precipitate pneumonia by reducing cough and swallow reflexes or stress ulcer prophylaxis predispose to infection by distorting the normal nonpathogenic bacterial flora.¹ Consequently, the ICU population has one of

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the highest occurrence rates of nosocomial infections (20-30% of all ICU-admissions)^{2,3}, leading to an enormous impact on morbidity, hospital costs, and often, survival.⁴⁻⁶ According to the Extended Prevalence of Infection in Intensive Care (EPIC) II 1-day prospective point-prevalence study in 1,265 participating ICUs in 75 countries worldwide, 51% of the 12,796 patients were considered infected, although no subdivision was made for hospital-acquired infections.⁷ The patients in the ICU have a 5-to-7-fold higher risk of nosocomial infection compared with the other patients due to underlying illness, suppressed immune systems and frequent use of invasive devices, exposure to broad spectrum antibiotics and the colonization of resistant microorganisms. Suspected infection may be pneumonia, meningitis, intra-abdominal infection, urinary tract infection and catheter-related infections.⁸ Along with the problem of nosocomial infection, the ongoing emergence of resistance in the community and hospital is considered a major threat for public health. Due to the specific risk profile of its residents, the ICU is deemed the epicenter of resistance development, as well as, has even been described as a factory for creating, disseminating, and amplifying antimicrobial resistance.⁹ Both infection and multi-drug resistance (MDR) result in a considerable clinical and economic burden. As such, the presence of MDR boosts the deleterious impact of nosocomial infection.¹⁰ Due to the specific risk of infection, the additional cost of MDR in hospitalized patients with infections has been estimated at \$6,000 to \$30,000 per patient.¹¹ This burden of resistance, however, is probably more due to higher rate of inappropriate empiric antimicrobial treatment associated with infections caused by MDR pathogens than with the virulence of particular MDR strains.¹² In a study in an Indian ICU, the most common organisms were *Acinetobacter spp.*, *Escherichia coli*, *Klebsiella spp.*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Streptococcus pyogenes*.¹³ But in a European ICU, *Staphylococcus aureus* was found as the most frequently isolated organism (30.1%), followed by *Pseudomonas aeruginosa* (28.7%), Coagulase-negative *Staphylococcus* (19.1%) and Yeast (17.1%)¹⁴. In almost all cases, there is a need to initiate empirical antimicrobial treatment before obtaining the microbial culture results, but the situation is further complicated during the past decades, a shift in the MDR dilemma has been noted from gram-positive to gram-negative bacteria, especially due to the scarceness of new antimicrobial agents active against resistant gram-negative microorganisms¹⁵. Among gram-positive organisms, the *Staphylococcus aureus*, and

vancomycin-resistant enterococci are of great concern^{15,16}. In gram-negative bacteria, the resistance is mainly due to the rapid increase of extended-spectrum beta-lactamases (ESBLs) in *Klebsiella pneumoniae*, *Escherichia coli*, and *Proteus mirabilis*; high level third-generation cephalosporin beta-lactamase resistance among *Enterobacter spp.* and *Citrobacter spp.*, and MDR in *Pseudomonas aeruginosa*, *Acinetobacter spp.*, and *Stenotrophomonas maltophilia*¹⁶. Several other types of infections become more difficult to treat like anaerobic *Clostridium difficile*, and fungal species. Infections with resistant strains of microorganisms in the ICUs lead to increased mortality and cost.¹⁷ All these major reports indicate the need for obtaining data on resistant strains in the ICU along with the susceptibility pattern, to help in revising antibiotic policy and guiding clinicians for the better management of patients. Prevalent flora and antimicrobial resistance pattern may vary from region to region depending upon the predominant antibiotic use in that locality. Standard treatment guidelines of different microbes in ICUs are not sufficient for the purpose. Therefore, the present study was designed to determine the pattern of antimicrobial resistance among the ICU patients.

Materials and methods

Methodology

This observational study was carried out in the ICU of Dhaka Medical College Hospital, Dhaka, Bangladesh in 2015 over a period of 6 months. The objective was to determine the antibiotic resistance pattern among the adult ICU patients. The patients of either sex ageing 18 years or more suffering from various medical conditions and being treated with broad-spectrum antibiotics were included. Samples of blood, urine, sputum/tracheal aspirate and pus/wound swabs were collected from consecutive patients. The collected samples were cultured in standard culture media for isolation of potential pathogens following standard methods. For each isolate, antibiotic susceptibility was performed by disc diffusion method. Isolates showing sensitivity to all antibiotics, isolates from repeat culture of previously recruited patients and isolate identified as commensals, colonization or contaminants were excluded. Isolates with intermediate susceptibility were considered resistant.

The study protocol was approved by the Bangladesh College of Physicians and Surgeons (BCPS), and the Ethical Review Committee of Dhaka Medical College. Informed written consent was obtained from the patients or their attendants.

For the study, data were collected in a pre-designed structured data collection form, analyzed using SPSS for windows version 16.0.

Results

From the 100 ICU patients, 125 specimens were obtained. Among the collected specimens, 66% were from males and 34% from females. Twenty-one percent of the patients were within the 61-70 years of age group and 17% aged >70 years. The most common primary diagnoses were aspiration pneumonia (29%), and urinary tract infection (UTI) (24%), respectively (Table 1). The most common locations for infection were tracheal aspirate (67.2%), urine (16%), and blood (10.4%) (Table 2). The most frequent microorganisms isolated were *Pseudomonas spp.* (35%), *Escherichia coli* (28%), *Acinetobacter spp.* (24%), and *Klebsiella spp.* (18%) which were mostly found in sample from tracheal aspirate (Table 3).

Table 4, 5, and 6 show the sensitivity of different microorganisms to common antibiotics. In Table 7, out of 125 samples, 72% were resistant to ceftriaxone and 78.4% were resistant to ceftazidime. These organisms were mostly *Pseudomonas spp.*, *Escherichia coli*, *Acinetobacter spp.* and *Klebsiella spp.* *Klebsiella spp.* were resistant to ceftriaxone (83.33%), ceftazidime (44.45%), amikacin (72.22%), gentamicin (72.28%) and quinolones (82.22-83.33%) (Table- 4, 5, 6). *Acinetobacter spp.* were resistant to ceftriaxone (58.44%), ceftazidime (79.17%), meropenem (75%), amikacin (66.67%), gentamicin (75%) and quinolones (79.17-92.67%) (Table 4, 5, 6). *Pseudomonas spp.* were resistant to ceftriaxone (77.24%), ceftazidime (94.29%), amikacin (68.57%), gentamicin (74.29%), meropenem (74.29%) and quinolones (60-77.15%) (Table 4, 5, 6). Meropenem was the most sensitive antibiotic against *Klebsiella spp.* (66.67%) but *Acinetobacter spp.* were still resistant to meropenem and amikacin but sensitive to cotrimoxazole (66.67%) (Table 6). Table 4 and 5 show

Escherichia coli was mostly sensitive to netilmicin (71.43%) and meropenem (50%).

Table-I

Primary diagnosis of the ICU patients. (N=100)

Primary diagnosis	Frequency	Percentage
Aspiration pneumonia	29	29.0
UTI	24	24.0
Septicemia	12	12.0
Meningitis	12	12.0
Pneumonia	10	10.0
COPD with respiratory failure	8	8.0
Surgical wound infection	5	5.0
Total	100	100.0

Table-II

Sample profile and rate

Sample	Total number of samples	Growth of organism	
		Number	Percentage
Blood	100	13	10.4
Urine	100	20	16
Tracheal secretion	93	84	67.2
Wound swab Pus	1210	53	42.4
Total	315	125	39.68

Table 2 : Sample profile and rate of positive culture from different samples (N=315)

Table-III

Frequency of different microorganisms from various samples (N=125)

Microorganism	Blood	Tracheal aspirate	Urine	Wound swab	Pus	Total
<i>Pseudomonas</i>	8	21	6	0	0	35
<i>E.coli</i>	1	15	7	3	2	28
<i>Acinetobacter</i>	0	22	1	1	0	24
<i>Klebsiella</i>	0	16	2	0	0	18
<i>Staph aureus</i>	4	6	1	0	0	11
<i>Streptococcus pneumoniae</i>	0	2	0	0	0	2
<i>Proteus mirabilis</i>	0	2	0	0	0	2
<i>Morganella morganii</i>	0	0	2	0	0	2
<i>Citrobacter</i>	0	0	0	1	1	2
<i>Enterococcus</i>	0	0	1	0	0	1
Total	13	84	20	5	3	125

Table-IV*Distribution of microorganisms according to susceptibility to penicillins, cephalosporins and meropenem (N=125)*

Microorganisms	Piperacillin+tazobactam (N/%)		Ceftriaxone (N/%)		Ceftazidime (N/%)		Meropenem (N/%)	
	S	R	S	R	S	R	S	R
<i>Pseudomonas spp.</i>	26(74.28)	9(25.72)	8(22.86)	27(77.24)	2(5.71)	33(94.29)	9(25.71)	26(74.29)
<i>E.coli</i>	22(78.57)	6(21.43)	4(14.29)	24(85.71)	5(17.85)	23(82.15)	14(50)	14(50)
<i>Acinetobacter</i>	15(62.5)	9(32.5)	10(41.66)	14(58.44)	5(20.83)	19(79.17)	6(25)	18(75)
<i>Klebsiella spp.</i>	11(61.11)	7(38.89)	3(16.67)	15(83.33)	10(55.55)	8(44.45)	12(66.67)	6(33.33)
<i>Staph aureus</i>	0(00)	0(00)	6(54.55)	5(45.45)	6(54.55)	5(45.45)	10(90.9)	1(9.1)
<i>Strep. pneumoniae</i>	2(100)	0(00)	2(100)	0(00)	1(50)	1(50)	2(100)	0(00)
<i>Proteus mirabilis</i>	0(00)	2(100)	0(00)	2(100)	0(00)	2(100)	0(00)	2(100)
<i>Morganellamorganii</i>	1(50)	1(50)	1(50)	1(50)	0(00)	2(100)	0(00)	2(100)
<i>Citrobacter</i>	0(00)	0(00)	0(00)	2(100)	0(00)	2(100)	0(00)	2(100)
<i>Enterococcus</i>	0(00)	0(00)	1(100)	0(00)	0(00)	1(100)	0(00)	1(100)

S= Sensitivity, R= Resistance

Table 5*Distribution of microorganisms according to susceptibility to aminoglycosides. (N=125)*

Microorganisms	Amikacin(N/%)		Gentamicin(N/%)		Netilmicin(N/%)	
	S	R	S	R	S	R
<i>Pseudomonas spp.</i>	11(31.43)	24(68.57)	9(25.71)	26(74.29)	19(54.25)	16(45.75)
<i>E.coli</i>	8(28.57)	20(71.43)	4(14.29)	24(85.71)	20(71.43)	8(28.57)
<i>Acinetobacter</i>	8(33.33)	16(66.67)	6(25)	18(75)	12(50)	12(50)
<i>Klebsiella spp.</i>	5(27.78)	13(72.22)	5(27.78)	13(72.28)	11(61.11)	7(38.89)
<i>Staph aureus</i>	0(00)	0(00)	6(54.55)	5(45.45)	0(00)	0(00)
<i>Strep. pneumoniae</i>	1(50)	1(50)	0(00)	2(100)	1(50)	1(50)
<i>Proteus mirabilis</i>	0(00)	2(100)	0(00)	2(100)	0(00)	0(00)
<i>Morganellamorganii</i>	0(00)	2(100)	0(00)	2(100)	0(00)	2(100)
<i>Citrobacter</i>	0(00)	2(100)	0(00)	2(100)	0(00)	2(100)
<i>Enterococcus</i>	0(00)	1(100)	0(00)	1(100)	0(00)	1(100)

S= Sensitivity, R= Resistance

Table-VI*Distribution of microorganisms according to susceptibility to quinolones and other antibiotics (N=125)*

Microorganisms	Ciprofloxacin(N/%)		Levofloxacin(N/%)		Colistin(N/%)		Cotrimoxazole(N/%)	
	S	R	S	R	S	R	S	R
<i>Pseudomonas spp.</i>	8(22.85)	27(77.15)	14(40)	21(60)	20(57.14)	15(42.86)	9(25.71)	26(74.29)
<i>E.coli</i>	5(17.86)	23(82.14)	6(21.43)	22(78.57)	0(00)	0(00)	12(42.86)	16(57.14)
<i>Acinetobacter</i>	2(8.33)	22(91.67)	5(20.83)	19(79.17)	14(58.33)	8(41.67)	16(66.67)	8(33.33)
<i>Klebsiella spp.</i>	3(16.67)	15(83.33)	5(17.78)	13(82.22)	0(00)	0(00)	11(61.11)	7(38.89)
<i>Staph aureus</i>	4(36.36)	7(63.64)	6(54.54)	5(45.46)	0(00)	0(00)	8(72.72)	3(27.28)
<i>Strep. pneumoniae</i>	1(50)	1(50)	1(50)	1(50)	0(00)	0(00)	0(00)	0(00)
<i>Proteus mirabilis</i>	0(00)	2(100)	0(00)	2(100)	0(00)	2(100)	0(00)	0(00)
<i>Citrobacter</i>	0(00)	2(100)	0(00)	2(100)	0(00)	0(00)	0(00)	0(00)
<i>Morganellamorganii</i>	0(00)	2(100)	0(00)	2(100)	1(50)	1(50)	0(00)	0(00)
<i>Enterococcus</i>	0(00)	1(100)	0(00)	1(100)	0(00)	0(00)	0(00)	0(00)

S= Sensitivity, R= Resistance

Table-VII

Antibiotic resistance pattern of the major organisms isolated from different samples

Antibiotic	No./percentage of isolates showing resistance
Ciprofloxacin	102/81.6%
Levofloxacin	88/70.4%
Ceftriaxone	90/72%
Ceftazidime	98/78.4%
Amikacin	81/64.8%
Gentamicin	105/84%
Netilmicin	49/39.2%
Meropenem	62/49.6%

Discussion

This study provides an analysis of epidemiology and microbiology of infections in the ICU patients of Dhaka Medical College Hospital. In this study, aspiration pneumonia, and UTI are the predominant infections; these findings are consistent with those of Kumari et al.¹⁸ In recent years, a rising trend of infection by gram negative organisms and increase in their resistance pattern has been observed.⁹ The organisms that have emerged as most problematic for patients within the ICU include *Acinetobacter spp.*, *Klebsiella spp.*, *Pseudomonas spp.*, and *Escherichia coli*.¹⁹ In our study, the most frequent microorganisms derived from samples were the gram-negative organisms consisting of *Pseudomonas spp.* (28%), *Escherichia coli* (22.4%), *Acinetobacter spp.* (19.2%), and *Klebsiella spp.* (14.4%); these findings correlate with those of a study done in a private hospital in Dhaka.²⁰ In recent years, *Acinetobacter spp.* have emerged as important pathogens of ICUs, most of them being resistant to ampicillin, carbenicillin, cefotaxime, chloramphenicol, and gentamicin.^{18,21} In our study, *Acinetobacter spp.* was the number one cause of pneumonia based on samples gathered from the tracheal aspirate and shows resistance to ceftriaxone (58.4%), ceftazidime (79.17%), amikacin (66.67%), gentamicin (75%) and fluoroquinolones (79.17-91.67%). These findings are consistent with the results of similar studies conducted in India and Bangladesh.^{18,20,22} In our study, *Acinetobacter spp.* were resistant to meropenem (75%) but sensitive to cotrimoxazole (66.67%); similar results were found in other study done in Bangladesh (79.3% resistance to meropenem and 60% sensitivity to cotrimoxazole)²⁰

Gram-negative bacilli are frequently associated with nosocomial infections in ICUs. Data from a multicenter Intensive Care Unit Surveillance Study (ISS) in the

United States demonstrated that *Pseudomonas spp.* are frequently isolated from ICU samples and they are especially resistance to fluoroquinolones.²³ The isolates of *Pseudomonas spp.* in this study were 28%, mostly from tracheal aspirate (21%), blood (8%) and urine (6%). In this study, *Pseudomonas spp.* were resistant to ceftriaxone (77.24%), ceftazidime (94.29%), amikacin (68.57%), gentamicin (74.29%), quinolones (60-77.15%) and meropenem (74.29%), which is closely consistent with other studies.^{19,20}

Another commonly seen resistant pathogen among ICU patients is *Klebsiella spp.* producing extended-spectrum beta lactamases (ESBLs).²² Dramatic rise in ESBLs has led to multidrug resistant *Escherichia coli* and *Klebsiella pneumoniae* making optimal therapy selection difficult. Our isolates of *Klebsiella spp.* showed high resistance to broad-spectrum cephalosporins (44.45%-83.33%) and gentamicin (72.28%), but sensitive to meropenem (66.67%). Again, these findings are very similar to those of a recent study carried out in Dhaka (resistance against cephalosporins and gentamicin 82.6%-84.6% and 66.6%, respectively)²⁰

In our observation, *Escherichia coli* was the most frequent pathogen obtained from patients with UTI. This is similar to the findings of previous studies.^{20,24} In the study by Islam et al, *Escherichia coli* was fully susceptible to meropenem, but resistant to ceftriaxone.²⁰ In our study, *Escherichia coli* was mostly sensitive to meropenem (50%) and netilmicin (71.43%), but resistant to ceftazidime (82.15%), ceftriaxone (85.71%), levofloxacin (78.57%) and ciprofloxacin (82.14%).

Multidrug resistant *Pseudomonas*, *Acinetobacter* and *Klebsiella* species have given new dimensions to the problem of hospital-associated infections. Hope is there that piperacillin-tazobactam combination showed <40% resistance against these 3 organisms. The alarming issue is the infection with *Acinetobacter spp.*, where no single antibiotic showed effective sensitivity.

Our study has got some important limitations. The sample size is relatively small, and is a single-centre study. So, the findings may not be generalizable. Anaerobic cultures and cultures suitable for isolating the fastidious organisms were not done. Some antibiotics which are less commonly used but having increasing importance in concurrent patient management might have been omitted from the sensitivity study. Also, the disc diffusion method, not the broth dilution method was used to determine the antibiotic sensitivity, accordingly, information regarding the minimum inhibitory concentration of antibiotics is lacking.

Conclusion

Antibiotic resistance is common among the ICU patients. Gram negative organisms constitute a major portion of the antibiotic resistant organisms. Commonly isolated organisms are often resistant to the commonly available antibiotics. When possible, antibiotics selection should be used based on the results of culture and sensitivity testing. For empirical use, third generation cephalosporins or carbapenems (e.g., meropenem) may be the optimal initial choice. Colomycin (colistin) and piperacillin-tazobactam combination should be kept preserved for further use. Antibiotic usage guidelines may be formulated according to the resistance pattern in individual institutions. These should be based on further, well-designed studies. Rational use of antibiotic is the key to combat Antimicrobial Resistance.

Conflict of interest: We have no conflict of interest.

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