Evaluation of antibiotics and clinical outcomes along with various other Factors in critically ill intensive care unit patients

Muhammad Ali (qaziali17004@gmail.com)

1. Doctors Institute of Health Sciences, Sargodha, Pakistan. 2. 1. Faculty of Pharmaceutical Sciences, Riphah International University, Islamabad, Pakistan.

Quratulain Khan

2. Sindh Government Dispensary, District Central, Karachi, Pakistan

Muhammad Jamal

3. Jinnah College of Pharmacy, Sohail University, Karachi, Pakistan

Sabiha Gul

3. Jinnah College of Pharmacy, Sohail University, Karachi, Pakistan

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Research Article

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Abstract

Intensive care units (ICUs) are special hospital wards that provide desired treatment and close monitoring of patients who are critically ill. Drug Utilization Reviews (DUR) is an authorized, structured, ongoing review of patient medication to ensure appropriate and rational medication use to yield positive outcomes. The aim of this study is to evaluate the antibiotics and clinical outcomes in intensive care unit (ICU) patients. This study was cross sectional retrospective (cohort), descriptive and clinical study including patients admitted in ICU of tertiary care hospitals.A total 400 patients (Male 53%) and (Female 47%) were admitted in ICU were analyzed in this study. Majority of patients were from age group between 41 to 60 years i.e. 50.2%. Patients evaluated in this study were suffering from many diseases and comorbidities majorly including respiratory, infectious, nephrology and urology diseases. Antibiotics, majorly penicillins were administered to 185 (46.2%) patients, flouroquinolones 162 (40.5%), cephalosporins 287 (71.8%), carbapenems 102 (25.5%), vancomycin 61 (15.2%) and metronidazole 217 (54.2%) patients. Total 52 (12.5%) patients underwent Culture sensitivity test. Significant drug-drug interactions were seen in 64% patients. High mortality rate (72.8%) was seen in this study. It was observed that presence of NI and lack of CST enhanced mortality rate. CST is very important regarding choice of ICU patient's antibiotic therapy.Current study identified factors affecting the clinical outcomes in terms of morbidity and mortality in the ICU patients. Antibiotics are prescribed in ICU abundantly. Due to presence of drug-drug interactions, nosocomial infections, comorbidities, not having culture sensitivity test (CST) and adverse reactions mortality rate was enhanced. Pharmacist led medication review will help in avoiding all these issues.

Introduction

Intensive care units (ICUs) are special hospital wards that provide treatment and monitoring of patients who are critically ill. ICUs are also sometimes called critical care units (CCUs) or intensive therapy units (ITUs). ICUs are staffed with specially-trained healthcare professionals and equipped with sophisticated monitoring equipment. Staff of ICU comprises of consultants, nurses, physiotherapists, pharmacist, dietitians, microbiologist and medical physics technicians. They all work according to their expertise i.e. pharmacist expertise is to avoid drug interactions, side effects, adjustment of dose in renal and liver compromised patients and also consult with other healthcare professionals working in ICU. Antibiotics are medicines that fight against bacterial infections as they can save lives if used and prescribed properly. They can be either bacteriostatic or bactericidal but do not fight against infections caused by viruses, such as cold, flu, cough, sore throat etc. They may be used to treat bacterial infections that are unlikely to clear up without using antibiotics or affect others unless treated or taking too long to clear without treatment and carrying a risk of more serious complications. Antibiotics can be given orally, topically and as injectables [1]. Hospital-acquired infections (HAIs) are one of the most serious patient safety issues in health caretoday. They are the fifth leading cause of death in acute-care hospitals. Between 5% and 15% of hospital inpatients develop an infection during their admission, and critically ill, ICU patients are 5 to 10 times more likely to acquire an HAI than those in general ward [2]. Fever is a common problem faced in ICU. It causes changes in results of diagnostic tests and procedures. It also increases number of diagnostic tests and in appropriate use of antibiotics. Fever is pre requisite to almost every infection, there are both infectious and noninfectious causes of fever in the ICU patients [3]. Drug utilization review (DUR) is an authorized, structured review of prescribing,

dispensing and use of medication. It consists of three types i.e. prospective, concurrent and retrospective DUR. Three Rs (right dose, right drug, and right time) are mandatory parts of DUR which is an important part of clinical evaluation studies. In retrospective DUR, patient is evaluated after he/she has taken drug therapy [4]. DUR is involved in Comprehensive review of patients' prescription and medication data before, during, and after dispensing to ensure appropriate medication decision making. In this study the appropriateness of the antibiotic therapy was determined by using the American Society of Infectious Diseases (IDSA) guidelines [5]. Pharmacists play a key role in this process because of their expertise in the area of pharmaceutical care.

Importance of DUR / DUE: DUR programs play a key role in helping managed health care systems understand, interpret, and improve the prescribing, administration, and use of medications. Employers and health plans find DUR programs valuable because the results are used to foster more efficient use of scarce health care resources. DURs afford the managed care pharmacist the opportunity to identify trends in prescribing and administering antibiotics in ICU patients. Pharmacists can then, in collaboration with other members of the health care team of ICU, initiate action to improve drug therapy for patients. Previous studies suggested that Retrospective DUR is important because it deals with issues regarding therapeutic choices i.e. inappropriate drug/combination, inappropriate dose/frequency, unnecessary drugs, double medication etc. Pharmacist plays vital role in doing retrospective DUR and it helps the prescriber and policy makers to review drug therapies [6]. The aim of this study is to evaluate the antibiotics and clinical outcomes in intensive care unit (ICU) patients along with drug utilization review of antibiotics, which are being prescribed and administered to patients admitted in ICU.

Methods

Study design and sample: The present study was cross sectional retrospective done on patients admitted in ICU of tertiary care hospitals. The study sample included patient's data admitted either in medical or surgical ICU of tertiary care hospitals of twin cities, Islamabad/Rawalpindi, Pakistan.
The Sample size was determined using EPI info stat. calc. tool for the total population of twin cities i.e. 4 Million with a confidence interval of 95% (P value <0.05). The statistically significant sample size is calculated to be 387. Total data of 400 patients of ICU was collected.

Patient data consists of comprehensive information on hospital stay in ICU, drug therapy and lab diagnostics. Simple random sampling technique was employed to select patients and to remove chances of biasness. Evidence based checklist was developed. The clinical outcomes were analyzed using the clinical checklist upon follow-up data. Moreover, administration of antibiotics to ICU patients was evaluated according to Infectious Disease Society of America (IDSA) guidelines.

Ethical Review: NOC letters/Permission letters were obtained from ethical review boards of all public sector tertiary care hospitals from where patient data was collected. The study was conducted over a period of one year.

Inclusion Criteria

The patients fulfilling following criteria were studied

✓ Admitted in ICU (surgical or medical).

✓ Age range between 2 to 60 years

✓ Male and female.

✓ Total length of ICU stay between 2 to 30 days.

Exclusion Criteria

✓ Suffering from any tumor, cancer or autoimmune disease.

✓ Less than 2 years of age.

✓ Greater than 60 years of age.

✓ Length of ICU stay greater than 30 days.

✓ Length of ICU stay less than 2 days.

Statistical Analysis

Statistical analysis of data was performed using SPSS (version 16) to determine association between clinical outcomes, patient therapy and hospital related variables. Descriptive statistics were used to determine the frequencies, percentages, graphical representation, prevalence and incidence of variables. Correlation along with Pearson's chi-squared tests and cross tabulation were applied for results.

Results

A total 400 patients which were admitted in ICU due to acute nature of illness are analyzed in this study. The demographic characteristic of all the patients are provided below.

Table 1 Gender and Age groups of patients admitted in ICU

Variable		Number	%
Gender	**Male**	212	53
	Female	188	47
Age	**2 to 20 years**	50	12.5
	21 to 40 years	149	37.2
	41 to 60 years	201	50.2

Patients admitted to ICU were suffering from many diseases and comorbidities. Frequency and percentages are mentioned in table 02. According to data collected, following reasons were observed due to which patients were admitted in ICU. Frequency and % age are given in below table 03. Commonly faced nosocomial

infections by patients admitted in ICU were i.e. Hospital acquired pneumonia (HAP), Community acquired pneumonia (CAP), Ventilator associated pneumonia (VAP), MRSA, Surgical site infection (SSI), UTI and sepsis. Culture sensitivity test is important as for as antibiotics administration is concerned. In ICU, patients are admitted in compromised conditions so it is necessary to administer right antibiotics [7]. Number and % age of patients having NI and CST are given in table 04.

Table 2 Diseases of patients admitted in ICU

Diseases	Number	Percentage (%)
Respiratory	91	22.8
Infectious Disease	58	14.5
Nephrology and Urology	58	14.5
Gastroenterology	51	12.8
Central Nervous System	44	11
Surgical and Allied	34	8.5
Cardiovascular Disease	29	7.2
Endocrinology	13	3.2
Immunological	2	0.5
Hematology	1	0.2
Dermatological	1	0.2
Others	18	4.5

Table 3 Reason for hospital admission in ICU

Reason	Number of patients/ %age
Disease condition	344 (86.0%)
Surgery	37 (9.25%)
Burn	01 (0.2%)
Poisoning	10 (2.5%)
Gun shot	08 (2.0%)

Table 4 Frequency and percentage of Culture sensitivity test and Nosocomial infections

Variable		Number	%
Culture sensitivity Test	Yes	52	12.5
	No	348	87.5
Nosocomial infection	Yes	107	26.8
	No	293	73.2

Out of 400 patients, penicillins were administered to 185 (46.2%) patients, flouroquinolones 162 (40.5%), cephalosporins 287 (71.8%), aminoglycosides 96 (24.0%), macrolides 55 (13.8%), carbapenems 102 (25.5%), vancomycin 61 (15.2%), metronidazole 217 (54.2%), linezolid 14 (3.5%), lincomycin 2 (0.5%), colomycin 2 (0.5%), tetracyclines 7 (1.8%) and tigycyline 4 (1.0%) patients [8] [9]. DDI were analyzed or categorized using MED SCAPE classification. Frequency and percentage of DDI found in our collected patient data is mentioned below in table 05.

Table 5 DDI found in ICU patients

Drug-Drug interactions	Frequency	(%)
Serious (use alternative)	7	1.8
Major (Contraindicated)	46	11.5
Significant (Monitor Closely)	256	64
Minor	86	21.5

P value <0.05 was considered significant. P value of pearson chi-square test in above table shows that there is significant statistical difference between penecillins, aminoglycosides, cephalosporins, vancomycin, metronidazole and Clinical outcomes of patients.

Table 6 Clinical Outcomes (Death or Discharge) of patients admitted in ICU

Clinical outcome	Frequency	(%)
Death	291	72.8
Discharged	109	27.2

Table 7 Statistical inferences between antibiotics and clinical outcomes of patients (P-Value)

Drugs	Clinical outcomes (P- Value)
Penicillins	**0.000**
Flouroquinolones	0.13
Aminoglycosides	**0.000**
Macrolides	0.102
Cephalosporins	**0.001**
Carbapenems	**0.000**
Vancomycin	**0.000**
Metronidazole	**0.000**
Linezolid	0.085
Lincomycin	0.386
Colomycin	0.386
Tetracyclines	**0.008**
Tigecyline	0.219

Table 8 Statistical inferences between antibiotics and various clinical variables of patients

Antibiotics	Yes (n) (%)	No (n) (%)	P-value					
			Nosocomial	CST	Choice	ADRs	DDI	Death or Discharge
Penicillins	185 (46.2%)	215 (53.8%)	**0.031**	**0.000**	0.290	**0.002**	0.154	**0.000**
Flouroquinolones	162 (40.5%)	238 (59.5%)	0.540	0.233	**0.001**	0.218	0.338	0.13
Aminoglycosides	96 (24.0%)	304 (76.0%)	**0.003**	**0.000**	0.715	**0.001**	0.868	**0.000**
Macrolides	55 (13.8%)	345 (86.2%)	**0.000**	**0.001**	**0.012**	0.093	0.202	0.102
Cephalosporins	287 (71.8%)	112 (28.2%)	0.147	0.916	0.584	0.571	0.384	**0.001**
Carbapenems	102 (25.5%)	298 (74.5%)	**0.000**	**0.000**	0.571	0.002	0.896	**0.000**
Vancomycin	61 (15.2%)	339 (84.8%)	**0.002**	**0.012**	0.067	0.047	0.888	**0.000**
Metronidazole	217 (54.2%)	183 (45.8%)	**0.002**	0.258	0.580	0.299	0.429	**0.000**
Linezolid	14 (3.5%)	386 (96.5%)	0.647	0.340	0.510	0.318	0.662	0.085
Lincomycin	2 (0.5%)	398 (99.5%)	0.392	0.584	0.169	0.521	0.889	0.386
Colomycin	2 (0.5%)	398 (99.5%)	0.456	0.584	0.966	0.521	0.892	0.386
Tetracyclines	7 (1.8%)	393 (98.2%)	0.107	0.216	0.763	0.227	0.868	**0.008**
Tigecyline	4 (1.0%)	396 (99.0%)	0.937	**0.000**	0.952	0.363	0.686	0.219

Discussion

The purpose of this study is to identify factors effecting clinical outcomes and duration of hospital stay in ICU patients admitted in public sector hospitals of twin cities, Rawalpindi/Islamabad, Pakistan. Safety, efficacy of drugs and DUR is also studied in ICU patients. Antibiotic therapy is evaluated according to IDSA guidelines. To assess choice of appropriate drug therapy specifically antibiotics according to various diseased conditions IDSA guidelines are important and should be followed by practitioners. This will help in treating patients accordingly and will reduce mortality rate in the ICU settings of tertiary care hospitals. The ICU was the main

centre or source of infections especially NI. These infections were associated with morbidity, mortality, and healthcare costs [10]. It was observed from our collected data of 400 patients that 107 (26.8%) out of 400 patients were having NI. Nosocomial infections were main reason behind enhanced death rate in ICU patients and respiratory tract infections were most common in ICU [11]. In Fiji a study was carried out in which it was observed that NIs causes mortality in patients admitted to ICU and prevention of these infections was not an easy job [7]. CST along with NI is very important factor effecting mortality, morbidity and duration of hospital stay. CST was done to check weather which antibiotic was sensitive, susceptible and resistant to patient. By the help of this test it becomes easy for prescriber to choose appropriate drug therapy. As antibiotics are prescribed in ICU in large quantity so CST is very important test. Majority of patients in our data have not underwent CST which raised the mortality rate and lead to ADRs, DDI and irrational antibiotic therapy. In previous studies, all these factors were faced by patients of pneumonia admitted in ICU, mortality rate was enhanced due to inappropriate antibiotic therapy and not having CST. Whereas duration of hospital stay along with treatment cost was also increased [12] [13].

Antibiotics are prescribed excessively in ICU patients. Patients admitted to ICU are in compromised state and need high doses of drugs specially antibiotics. This overuse of antibiotics causes resistance and it is an alarming issue so it should be dealt seriously [14]. According to our data it was analyzed that multiple antibiotics were administered/prescribed to 400 patients who were admitted to ICU. Frequency and percentage of these antibiotics were calculated. Out of 400 patients, ceftriaxone was administered to majority of patients i.e. 287 (71.8%) patients, secondly metronidazole was administered to 217 (54.2%) patients, thirdly penicillins were administered to 185 (46.2%) patients but they are classified as empirical antibiotics by IDSA guidelines [15]. In Pakistan as age increases patient become more prone to comorbidities like hypertension, diabetes and stroke etc. Our Results also showed this trend, in third age group (41 to 60) years we observed increase in number of patients having hypertension, diabetes etc as a comorbidity i.e. hypertension was present in 29 (14.4%) patients, diabetes 14 (7.0%), others 1 (0.5%) and DM +HTN in 44 (21.9%) patients. Comorbidity was important factor effecting clinical outcomes and duration of hospital stay of patients [16]. DDI depends on poly pharmacy, unnecessary medications and poor therapeutic choice. Age has no relationship with DDI, it may vary from individual to individual, drug to drug and various other factors [17].

To avoid DDI it was necessary for prescriber to prescribe medicine according to guidelines. Other medical staff should monitor patient carefully, here the role of pharmacist is very important but unfortunately in Pakistan importance of pharmacist is neglected [18]. In ICU, patients were admitted in very serious or compromised state so in that scenario, therapeutic choice plays very vital role. Antibiotics are prescribed and administered abundantly in ICU. Out of 400 patients, 206 (51.5%) patients were administered antibiotics according to IDSA guidelines, whereas 194 (48.5%) patients were not administered antibiotics according to IDSA guidelines. So it was found that most of the patients were given antibiotics according to diagnosis/indications and they had not followed any specific guidelines. Multiple antibiotics were administered to ICU patients lead to DDI, increased treatment cost, increased hospital stay, mortality rate and various other complications, hence for decreasing mortality rate patients should be treated according to IDSA guidelines [19] [20]. Hence, it is cleared from our study that factors effecting clinical outcomes and length of hospital stay of patients in ICU are NI, CST, comorbidities, age related factors, ADRs and administration of antibiotics not according to IDSA guidelines.

Conclusion

In conclusion, Antibiotics are prescribed in ICU abundantly. This study identified the factors Affecting the clinical outcomes of patients in the ICU. This study will help health care teams to follow proper clinical guidelines and will also help health care policy makers to review and amend the guidelines. Moreover, it is also evident from this study that antibiotic stewardship is necessary and pharmacist should review medication.

Declarations

Disclosure:

✓ The authors declare that there are no conflicts of interest.

✓ No funding was received.

✓ Approval was obtained from the local ethics committee for the study.

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Figures

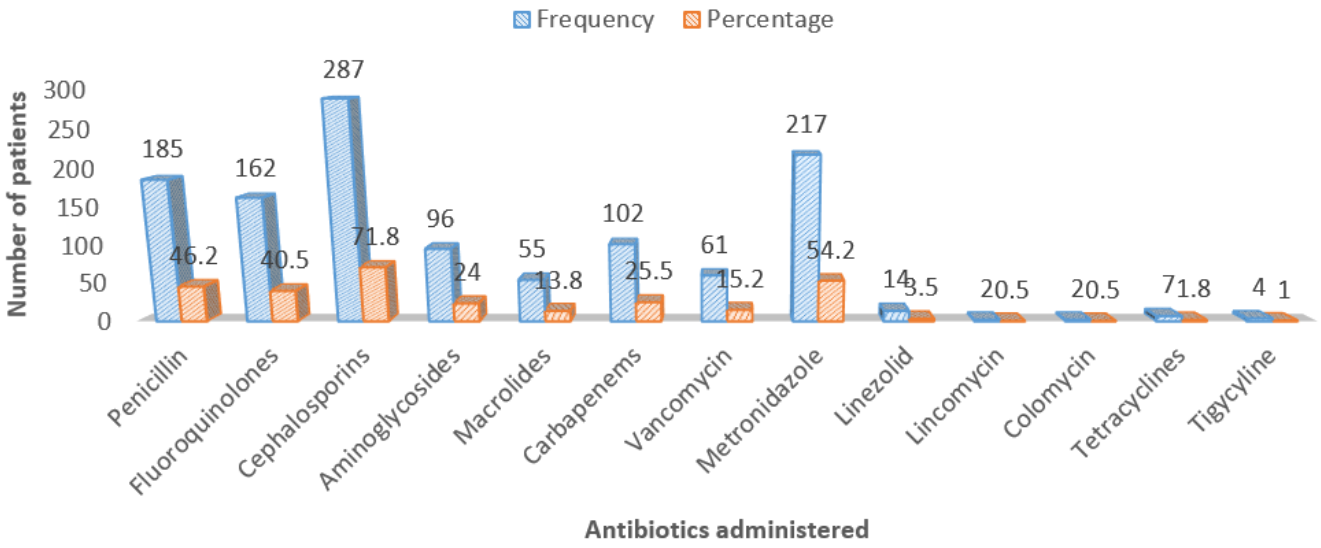

Figure 1

Legend not included with this version.