Research Article

A Study on Evaluation of Appropriateness of Antibiotics Used in the Intensive Care Unit Settings of a Tertiary Care Teaching Hospital

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ABSTRACT

To evaluate the appropriateness of antibiotics used in the intensive care unit (ICU) settings of a tertiary care teaching hospital and identify the different parameters of inappropriateness in prescribing pattern of antibiotics. To observe pathogen specific anti-biograms in ICUs. A prospective hospital based was done for 6 months in patients admitted in intensive care units and prescribed with antibiotics, excluding the paediatric and neonatal ICUs. Data was collected, the appropriateness of antibiotic treatment was analysed based on the hospital antibiotic prescribing guidelines and the Database 'Up-to-date guidelines'. The primary outcome measure was the appropriateness of indication, dose, frequency, duration, culture not done, de-escalation and antibiotic therapy started. Of the 380 patients studied, 67.6% were males and 32.3% were females. They received 34 different class of antibiotics (n=733) during their ICU stay. Empirical antibiotic therapy was given for 68% and only after infection was proven microbiologically in 32% of patients. E. coli (32.28%) was the most common micro-organism causing infection in the ICU settings. The most frequently prescribed antibiotics were ceftriaxone (20.3%), Piperacillin + tazobactam (10.2%), Imipenem (6.4%) and levofloxacin (6.0%). Overall, appropriateness of antibiotic prescribing was (84.4%) and inappropriateness was (15.6%). Inappropriateness in dose (7.0%), frequency (3.5%), duration (21.9%), indication (15.7%), culture not done (39.4%), de-escalation (3.5%) and antibiotic therapy started late (8.7%) were the parameters for inappropriateness in antibiotic prescribing. The current study identified 84% of the antibiotic prescribing patterns to be appropriate and also gave an insight to prevent microbial resistance.

Keywords: Antibiotics, Antibiograms, Appropriateness, Intensive care units.

INTRODUCTION

Antibiotics are chemical substances derived from living micro-organisms, which inhibits or completely stops growth or kills bacteria when present in very minute concentrations; these are mostly metabolites produced by micro-organism which antagonises the microbial growth itself if present in very low concentrations.

Most of the antibiotics are modified structurally to alter its pharmacokinetic or stability and antimicrobial properties so as to produce a most effective antibiotic; almost most of them can be synthesized in laboratories.

The rates of nosocomial infections range from 5 to 30% among the ICU patients. Although ICUs generally comprise 5% of all the hospital beds, they account for 20 to 25% of all nosocomial infections.[1] Antibiotics are among the most commonly prescribed drugs in hospitals and around 30% of the hospitalized patients are treated with these antibiotics.[2] Irrational use of antibiotics is one of the most central factors for the development and spread of resistance in the hospitals and communities. The World Health Organization has established antibiotic use as a priority in its campaign for the rational use of medications.[3] Antibiotic prescribing in the ICU is usually empirical.[1]

The inappropriate use of antimicrobials is of special importance in the intensive care unit because of prescribing antibiotics in large number, the chance for errors in selecting the antibiotics and the likelihood for the development of drug resistance.[4] The medically inappropriate, ineffective and economically inefficient use of antimicrobials is commonly observed in the health care system throughout the world, especially in developing countries.[5]

A study on the prescribing practices in the ICU is vitally important in guiding antibiotic selection and usage and therefore, in the achievement of the above stated goals. The relative prevalence of predominant pathogens and their susceptibility towards antimicrobial has a wide institutional diversity within each specific ICUs, where there are patient populations with varying risks and susceptibilities to infections and specific pathogens. Hence appropriate prescription practices should be formulated based on studies and research in the ICUs.[1]

Methodology

Study Design

Prospective hospital based study.

Study Place

Six Intensive Care Units of a Tertiary care University hospital

Inclusion Criteria

- Patients above 18 years of age, admitted in intensive care units and prescribed with antibiotics

Exclusion Criteria

- Patients admitted in paediatric and neonatal ICUs
- Patients in wards
- Out patients

Methods

A hospital based prospective study was conducted in 380 patients with the approval of the Institutional Ethics Committee and the consent of the study participants.

Data collection

Patients admitted in the ICUs who were prescribed with antibiotics were included and the data was collected regarding patient demographics, hospital and ICU admission date, past and present medical history, the primary admitting diagnosis and the reason for ICU admission and all other reports regarding their clinical condition. The patients were followed up till discharge to monitor the type and duration of the antibiotics used in ICU, the reasons for stopping or changing antibiotics based on their clinical condition, microbiological results and the sensitivity pattern of the organisms which were isolated from these patients.

The appropriateness of antibiotics prescribed to the patients were evaluated following the hospital antibiotic prescribing guidelines of the University hospital and the Database 'Up-to-date guidelines' from Drugs and Poison Information Centre of the University. The data collected were tabulated and expressed as descriptive statistics.

RESULTS

A prospective study was conducted for a 6 month period in 380 patients (257 males and 123 females), who were admitted in 6 different ICUs as mentioned in Table 1 and followed up till discharge. Out of 380 patients, 114 (30%) patients were in Multi specialty 1 ICU, 136 (35.7%) patients were in Neurology and Neurosurgery ICU, 38 (10%) patients were in Cardiology ICU, 24 (6.3%) patients were in Cardiothoracic ICU, 67 (17.6%) patients were in Multi specialty 2 ICU and 1 (0.2%) patient in Oncology ICU.

A total of 733 antibiotics were prescribed for 380 patients during their ICU stay. Out of 34 different class of antibiotics, the most frequently prescribed were ceftriaxone (20.3%), piperacillin + tazobactam (11.8%), cefaperazone + sulbactam (10.2%), imipenam (6.4%) and levofloxacin (6.0%) (Table 2). Of the 380 patients, 163 patients received one antibiotic, 143 patients received two antibiotics, 43 patients received three antibiotics, 12 patients received four antibiotics, 9 patients received five antibiotics, 8 patients received six antibiotics and 2 patients received seven antibiotics, during their hospital stay.

In Multi specialty 1 ICU maximum numbers of patients were prescribed with two antibiotics. In Neurology and Neurosurgery ICU maximum numbers of patients were prescribed with one antibiotic. In Cardiology ICU maximum numbers of patients were prescribed with one antibiotic. In cardiothoracic ICU maximum numbers of patients were prescribed with two antibiotics and In Multi specialty 2 ICU maximum numbers of patients were prescribed with two antibiotics.

Table 1: Specialty Wise Distribution of Patients in Intensive Care Units

ICUS	Department	No. Of patients (N=380)
Multi specialty 1	General Medicine	52
	Nephrology	31
	Neurology	7
	General Surgery	7
	Gastroenterology	8
	Radiology	3
	Vascular Surgery	1
	Chest & TB	3
	OBG	2
Neurology and Neurosurgery	Neuro Surgery	116
	Neurology	20
Cardiology	Cardiology	37
	General Surgery	1
Cardiothoracic	Cardiothoracic	24
Oncology	Oncology	1
Multi specialty 2	Nephrology	4
	Neurology	6
	General Medicine	28
	General Surgery	9
	Cardiology	4
	OBG	3
	Vascular Surgery	2
	Surgical Gastroenterology	5
	Medical Gastroenterology	2
	Others	4

Out of 733 antibiotics, 619 were found to be appropriate (84.4%) and 114 were found to be inappropriate (15.6%). Out of 114 inappropriate antibiotics, 21 (18.4%) were observed in Multi specialty 1 ICU, 43 (37.7%) in Neurology and Neurosurgery ICU, 10 (8.7%) in Cardiology ICU, 14 (12.2%) in Cardiothoracic ICU and 26 (22.8%) in Multi specialty 2 ICU. In the multi specialty 1 ICU, appropriateness was 91% and inappropriateness was 9%, In Neurology and Neurosurgery ICU, appropriateness was 84% and inappropriateness was 16%, In Cardiology ICU, appropriateness was 82% and inappropriateness was 18%, In Cardiothoracic ICU, appropriateness was 63% and inappropriateness was 37%, In multi specialty 2 ICU, appropriateness was 79% and inappropriateness was 21% (Table 3).

The parameters, which have been considered as reasons for inappropriateness were dose (7.0%), frequency (3.5%), duration (21.9%), indication (15.7%), culture not done (39.4%), de-escalation (3.5%) and antibiotic started late (8.7%) (Table 4).

Table 2: Antibiotics Prescribed In Intensive Care Units

Antibiotics	No. Of cases
Ceftriaxone	149
Piperacillin + Tazobactam	87
Cefaperazone + Sulbactam	75
Imipenam	47
Levofloxacin	44
Clindamycin	39
Metronidazole	35
Cefixime	32
Linezolid	26
Amoxicillin + Clavulanic acid	23
Cefuroxime	21
Amikacin	20
Cefotaxime	20
Polymyxin B	16
Doxycyclin	16
Cefazolin	12
Clarithromycin	9
Nitrofurantoin	8
Ciprofloxacin	8
Cefepime	8
Azithromycin	5
Ampicillin	5
Tigecycline	5
Vancomycin	5
Cefaperazone	3
Meropenam	3
Ofloxicin	3
Moxifloxacin	2
Cloxicillin	2
Cefepime + Tazobactam	1
Cefalexin	1
Gentamicin	1
Colistin	1
Ertapenam	1

Table 3: Percentage of Appropriateness and Inappropriateness in Different Intensive Care Units

ICUS	Total no. Of antibiotics	No of Appropriate	No of Inappropriate
MS 1	239	218 (91%)	21 (9%)
Neuro	274	231 (84%)	43 (16%)
Cardio	56	46 (82%)	10 (18%)
CT	38	24 (63%)	14 (37%)
MS 2	124	98 (79%)	26 (21%)
Onco	2	2 (100%)	0 (0%)

The micro-organisms isolated from the cultures of various biological fluids of the study population were discussed in Table 5. The biological samples included 75 (33.6%) urine cultures, 58 (26%) blood cultures, 45 (20.1%) wound and pus cultures, 36 (16.1%) CSF cultures and 9(4.03%) Tracheal aspirate cultures.

The organisms isolated were as follows: Acinectobacter sp in 27(12.10%) (in 15 blood cultures; 3 Tracheal aspirates; 3 wound and pus cultures; 6 CSF cultures); Pseudomonas sp in 18 (8.07%) (in 3 tracheal aspirate samples; 6 wound and pus samples; 9 urine samples); E.coli in 72 (32.28%) (in 15 Blood samples; 3 tracheal aspirate samples; 12 wound and pus samples; 33 urine samples; 9 CSF samples); Klebsiella sp in 24 (10.76%) (in 3 blood samples; 12 urine samples; 9 CSF samples); Enterococcus sp in 24 (10.76%) (in 6 blood samples; 12 wound and pus samples; 6 urine samples); Staphylococcus sp in 30 (13.45%) (in 9 blood samples; 9 wound and pus samples; 12 CSF samples); Candida Sp in 12 (5.38%) 12 urine samples; Proteus sp. in 10(4.48%) blood samples; Other organisms like Corynbacterium and Providencia Sp. in 6 (2.69%) (in 3 wound and pus samples; 3 urine samples) of biological samples. Overall, E.coli (32.28%) was found to be the most common micro-organism causing infection in our ICU settings.

The antibiotic sensitivity patterns of the micro-organisms isolated from the biological samples of the study were discussed in Table 6.

Acinetobacter sp was found to be highly sensitive to piperacillin + tazobactam, amikacin, cefaperazone + sulbactam and polymixin B (33% each), followed by cefotaxime (22%), ampicillin and ceftazidime (11% each).

Pseudomonas sp was found to be highly sensitive to Amikacin (50%) followed by piperacillin + tazobactam, ciprofloxacin and cefoperazone + sulbactam (33.3% each), polymixin B (27%), ampicillin and ceftazidime (16% each).

E. coli was found to be highly sensitive to piperacillin + tazobactam and amikacin (37% each) followed by cefaperazone + sulbactam (33%), cefotaxime (16%), ampicillin, ceftazidime, cefapime, ciprofloxacin and polymixin B (8% each).

Table 4: Reasons for Inappropriateness in Different Intensive Care Units

Reasons	Multi specialty 1	Neurology and neurosurgery	Cardiology	Cardiothoracic	Multi specialty 2
Dose	2	-	1	1	4
Frequency	-	2	1	-	1
Duration	6	12	4	-	3
Indication	5	10	1	-	2
Culture not done	8	9	3	13	12
De-escalation	-	-	-	-	4
Antibiotic started late	-	10	-	-	-

Table 5: Microbial Pattern in Cultures of Biological Fluids

Organism	Blood	Tracheal aspirate	Wound & pus	Urine	CSF	Total	
						N	%
Acinetobacter sp	15	3	3	-	6	27	12.10
Pseudomonas sp	-	3	6	9	-	18	8.07
E.coli	15	3	12	33	9	72	32.28
Klebsiella sp	3	-	-	12	9	24	10.76
Enterococcus sp	6	-	12	6	-	24	10.76
Staphylococcus sp	9	-	9	-	12	30	13.45
Candida sp	-	-	-	12	-	12	5.38
Proteus sp	10	-	-	-	-	10	4.48
Others	-	-	3	3	-	6	2.69
Total	58	9	45	75	36	223	100

Table 6: Sensitivity Patterns of Micro-Organisms Isolated From Various Biological Samples

Antibiotics	Acinetobacter sp (N=27)		Pseudomonas sp (N=18)		E. coli (N=72)		Klebsiella sp (N=24)		Proteus sp (N=10)		Enterococcus sp (N=24)		Staphylococcus sp (N=30)	
	n	%	N	%	n	%	n	%	n	%	n	%	n	%
Ampicillin	3	11	3	16	6	8	-	-	3	30	3	16	1	3.3
Cefotaxime	6	22	-	-	12	16	3	12.5	1	10	-	-	-	-
Ceftazidime	3	11	3	16	6	8	-	-	2	20	3	16	2	6.6
Cefepime	-	-	-	-	6	8	-	-	-	-	-	-	-	-
Piperacillin + tazobactam	9	33.3	6	33	27	37	6	25	2	20	-	-	3	10
Imipenem	-	-	-	-	-	-	-	-	1	10	-	-	-	-
Amikacin	9	33.3	9	50	27	37	6	25	5	50	3	16	6	20
Ciprofloxacin	-	-	6	33.3	6	8	3	12.5	-	-	-	-	1	3.3
Cefaperazone + sulbactam	9	33.3	6	33.3	24	33	3	12.5	-	-	-	-	2	6.6
Linezolid	-	-	-	-	-	-	6	25	-	-	3	16	1	3.3
Vancomycin	-	-	-	-	-	-	6	25	1	10	3	16	1	3.3
Polymixin B	9	33.3	5	27	6	8	3	12.5	-	-	3	16	2	6.6

Klebsiella Sp was found to be highly sensitive to piperacillin + tazobactam, amikacin, linezolid and vancomycin (25% each), followed by cefotaxime, ciprofloxacin, cefoperazone + sulbactam and polymixin B(12.5% each).

Proteus sp was found to be highly sensitive to amikacin (50%) followed by ampicillin (30%), piperacillin + tazobactam and ceftazidime (20% each), cefotaxime, imipenam and vancomycin (10% each).

Enterococcus sp was found to be equally sensitive to ampicillin, ceftazidime, amikacin, linezolid, vancomycin and polymixin B (12.5%).

Staphylococcus sp was found to be more sensitive to amikacin (20%) followed by piperacillin + tazobactam (10%), ceftazidime, cefaperazone + sulbactam and polymixin B (6.6% each), ampicillin, ciprofloxacin, linezolid and vancomycin (3.3% each).

The antibiotic resistant patterns of the micro-organisms isolated from the biological samples of the study were depicted in Table 7.

Acinetobacter sp was found to be highly resistant to cefepime (66.6%) followed by ceftazidime (55.5%), ciprofloxacin (33.3%) ampicillin, imipenem and gentamicin (22.2%each) and piperacillin + tazobactam (11.1%).

Pseudomonas sp was found to be highly resistant to ceftazidime, piperacillin + tazobactam, cefepime and imipenem (66.6% each) followed by ampicillin, cefotaxime, gentamicin and ciprofloxacin (33.3% each) and amikacin (16.6%).

E.coli was found to be highly resistant to ampicillin (83.3%) followed by cefepime and ciprofloxacin (66.6% each), ceftazidime (62.5%), piperacillin + tazobactam and gentamicin (29.1% each) and cefotaxime (25%).

Klebsiella sp was found to be highly resistant to amipicillin (100%) followed by cefepime (62.5%), ceftazidime (50%), piperacillin + tazobactam (37.5%), cefotaxime, gentamicin and ciprofloxacin (25% each) and imipenem (12.5%).

Proteus sp was highly resistant to ampicillin (50%) followed by ciprofloxacin (40%), ceftazidime (30%), cefotaxime, cefepime and amikacin (20% each), piperacillin + tazobactam and gentamicin (10% each).

Enterococcus sp was found to be highly resistant to ampicillin (75%) followed by gentamicin (58.3%), ciprofloxacin (45.8%), cefotaxim (37.5%), piperacillin + tazobactam (33.3%), ceftazidime and amikacin (20.8% each) and cefepime (16.6%).

Staphylococcus sp was found to be highly resistant to ampicillin (36.6%) followed by piperacillin + tazobactam (23.3%), cefotaxim (20%), ciprofloxacin (16.6%), ceftazidime and cefepime (13.3% each) and amikacin (6.6%).

Table 7: Resistance Patterns of Micro-Organisms Isolated From Various Biological Samples

Antibiotics	Acinetobacter sp (N=27)		Pseudomonas sp (N=18)		E. coli (N=72)		Klebsiella sp (N=24)		Proteus sp (N=10)		Enterococcus sp (N=24)		Staphylococcus sp (N=30)	
	n	%	N	%	n	%	n	%	n	%	n	%	n	%
Ampicillin	6	22.2	6	33.3	60	83.3	24	100	5	50	18	75	11	36.6
Cefotaxime	-	-	6	33.3	18	25	6	25	2	20	9	37.5	6	20
Ceftazidime	15	55.5	12	66.6	45	62.5	12	50	3	30	5	20.8	4	13.3
Cefepime	18	66.6	12	66.6	48	66.6	15	62.5	2	20	4	16.6	4	13.3
Piperacillin tazobactam	3	11.1	12	66.6	21	29.1	9	37.5	1	10	8	33.3	7	23.3
Imipenem	6	22.2	12	66.6	-	-	3	12.5	-	-	-	-	-	-
Gentamicin	6	22.2	6	33.3	21	29.1	6	25	1	10	14	58.3	-	-
Amikacin	-	-	3	16.6	-	-	-	-	2	20	5	20.8	2	6.6
Ciprofloxacin	9	33.3	6	33.3	48	66.6	6	25	4	40	11	45.8	5	16.6

DISCUSSION

A prospective study was conducted for a period of 6 months, to study the appropriateness of antibiotics in intensive care units of a tertiary care University hospital. The study population comprised of 380 patients prescribed with antibiotics in different ICUs, who were followed up until discharge or death. A similar study was conducted by Balinga Shrikala et al.,[6] on evaluation of antibiotics prescription practices in 262 patients of an intensive care unit of a tertiary care hospital with the chief objective of rational prescribing practice of antibiotics and to prevent microbial resistance.

In this study, out of 380 patients, 67.6% were males and 32.3% were females. This is in concordance with the observations of the study conducted by H. Dupont et al.,[7] who reported that, out of 111 patients, 74 (66.6%) were male patients and 37 (33.4%) were female patients.

In the current study, antibiotics were started empirically in 68% of the cases, whereas in the rest of the 32%, only after infection was proved microbiologically. The most common antibiotics which were prescribed in our settings were ceftriaxone, cefaperazone-sulbactam or piperacillin-tazobactum. Infections caused by gram negative organisms (75.78%) were more common than those caused by gram positive organisms (24.21%). This is similar to the observations of Balinga Shrikala et al.,[6] who reported that antibiotics were started empirically in 64%. The infections were microbiologically confirmed in 45.91% of the cases. The most common antibiotics prescribed at admission were cefaperazone-sulbactam or piperacillin-tazobactum and infections caused by gram negative organisms (57.14%) were more common than those caused by gram positive organisms (42.85%).

Of the gram negative organisms identified in this study, E.coli (32.28%), was predominant, followed by

Acinetobacter sp (12.10%), Klebsiella sp (10.76%), Pseudomonas sp (8.07%), and Proteus sp (4.48%), whereas in the study done by Balinga Shrikala et al.,[6] Acinetobacter sp (21%) was predominant, followed by Pseudomonas sp (13%), E.coli (12.4%), Klebsiella sp (9.9%) and Proteus sp (6.2%).

Organisms isolated from various biological samples showed high sensitivity to amikacin, piperacillin + tazobactam and cefaperazone + sulbactam and were highly resistant to antibiotics like ampicillin, ceftazidime and cefepime. A. Erbay et al.,[8] also reported that the organisms isolated from the biological samples of their study population were mostly resistant to ampicillin, cefotaxime and ceftazidime and the study did not focus on the sensitivity patterns of the micro-organisms.

In our study with a chief objective to evaluate the appropriateness of antibiotic prescribing, it was observed that antibiotics prescribed empirically were based on infection parameters like elevated WBC count, temperature (> 98.6^{0}F or >37^{0}C) and culture report. This is in accordance with the observation of a study conducted by A. Erbay et al., [8] who also considered parameters of infection like elevated temperature, higher leukocyte count and culture results for empirical antibiotic prescribing.

In the present study, among 380 patients, majority of the population were admitted in multispecialty ICUs (181 patients (47.6%). Of the733 antibiotics prescribed , third generation cephalosporins (ceftriaxone) were predominantly used in 39.2% patients, followed by an external spectrum penicillin and beta-lactamase inhibitor (Piperacillin + Tazobactam) in 22.9% patients. This is in accordance with the findings of the study conducted by V Chini et al.,[9] which stated that the most commonly prescribed antibiotics were third generation cephalosporins (ceftriaxone (31.7%), followed by piperacillin + tazobactam (31.2%). A study done by A Erbay et al.,[8] had observed that the most common prescribed antibiotics were first generation cephalosporin (cephazolin (16.1%) which is contradictory to the present study.

The criteria used to determine the inappropriate antibiotic use in the present study were, antibiotics prescribed to patients whose vital parameter found to be normal and the culture result which seemed to have no sign of infection, laboratory parameters which seemed to be normal, the total count was within normal limit and de-escalation of the antibiotics. This is concordant with the study of A.Erbay et al.,[8] where the antibiotic prescribing was judged to be inappropriate when the patient had no evidence of infection, if a more effective antibiotic was available based on either the culture and susceptibility results of the isolated pathogen or by the identity of the expected pathogen.

Out of 733 antibiotics prescribed, 619 were found to be appropriate (84.4%) and 114 were found to be inappropriate (15.6%) in our study, which is not in concordance to the findings of the study conducted by A. Erbay et al.,[8] in which they have reported that the antibiotic use was inappropriate for 47.3% of prescriptions. The percentage of inappropriateness in our study was found to be less as compared to their study.

Of the 144 inappropriate antibiotics prescribed, it was identified that 31.2% were due to culture not done, 17.3% were due to duration, 12.5% were due to indication, 6.9% were due to antibiotic started late, 5.5% were due to dose, 2.7% were due to frequency and 2.7% were due to de-escalation.

In the present study, of the 74 patients with renal impairment, 4 patients had dose related inappropriateness of antibiotics on considering creatinine clearance as a measure to calculate dose for those patients.

The present study which was conducted in a tertiary care teaching hospital set up with National Accreditation Board for Hospitals and Healthcare Providers (NABH) and Joint Commission International (JCI) accreditation has proved the efficient handling of antibiotics by the physicians, by taking appropriate measures like periodic auditing and providing awareness regarding microbial resistance by the clinical pharmacists and the medication safety team. This tangible approach has resulted in strict adherence to standard guidelines for the usage of antibiotics thereby ensuring rational use of antibiotics and reducing the emergence of microbial resistance.

CONCLUSION

Monitoring of antibiotics in health care setup is mandatory due to increased rates of microbial resistance, a herculean task to overcome. Appropriate antibiotic usage can be achieved by following standard guidelines and periodic assessment of their prescribing practices. Hence studies to evaluate and bring discipline in the prescribing patterns of antibiotics are highly warranted.

In the current study with a chief objective of monitoring the antibiotic appropriateness in intensive care units of a tertiary care teaching hospital, 84% of the antibiotic prescribing pattern was found to be appropriate, indicative of strict adherence to the standard guidelines and optimal pharmaceutical care.

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