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PRESCRIPTION PATTERNS OF ANTIBIOTICS AMONG ADULT PATIENTS IN HIGH RISK UNITS IN A TERTIARY CARE HOSPITAL

Microbiology

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ABSTRACT

Introduction: Antimicrobial resistance is a neglected global crisis that requires urgent attention and action. The scope of this study suggests that the prescribing patterns of antibiotics should be assessed regularly and it is a crucial step against the battle of antibiotic resistance among microbes. **Aim :** 1.To evaluate the patterns of antibiotic prescriptions given to adult patients admitted in medical and surgical ICU and post operative wards in a tertiary care hospital; 2.To evaluate the isolated microorganism and their sensitivity pattern, among patients admitted to the tertiary care departments. **Materials and methods:** This observational study was done in the ICU and post operative wards in a tertiary hospital in Chennai, Tamilnadu, from June 2019 to August 2019. 227 patients who were admitted in the respective wards were taken in as sample population based on the inclusion and exclusion criteria. **Results and interpretation:** Common classes of antibiotics used were observed to be Cephalosporins, Aminoglycosides and other combination of drugs. Prophylactic use of antibiotics was found to be the most common indicator of antibiotic prescription. The commonly isolated organism was found to be Klebsiella pneumoniae and Acinetobacter spp. The 3rd generation Cephalosporins was found to be highly used in high risk units. **Conclusion:** Lower antibiotics were commonly used which is an encouraging factor. However, prophylactic use of antibiotics was found to be the most common indicator in antibiotic prescriptions emphasizing the fact that antibiotic stewardship measures should be adopted.

KEYWORDS

Antimicrobial, Drug Resistant, Prescription, Pattern, Sensitivity.

INTRODUCTION:

The prevalence of antibiotic use is very high in India and ranges from 24% to 67% [1]. Hospital admissions increase the risk of health-care-associated infections and the transmission of multidrug-resistant organisms, which in turn lead to increased antimicrobial use [2].This calls for a regulatory measure in the use of antibiotics. Drug resistant strains and cross infections can result from an overuse of antimicrobials.

Objectives: To study the patterns of antibiotic prescriptions given to adult patients in ICU and Post operative wards in a tertiary care hospital. To identify the isolated microorganisms and their sensitivity pattern among the common infections in patients in ICU and post-operative wards.

MATERIALS AND METHODS:

This observational study was done in the ICU and post operative wards (of General surgery, Gynaecology, Orthopedics) in a tertiary care hospital in Chennai, from June - August 2019. 227 patients who were admitted in the respective wards represent sample population.

Inclusion Criteria – Patients taking prescribed antibiotics during their stay and are above 18 years. Patients who were only on topical antibiotics prescribed by dermatologists and ophthalmologists and who were referred from other hospitals and were already prescribed antibiotics were excluded.

Ethics committee approval was obtained from the Institutional Ethics committee and consecutive patients in the 12 bedded medical, six bedded surgical ICU units and post operative wards were included in the study. The sample size of 227 patients was included in the study after explaining to them about the aims and methods of the study and a written consent was obtained priorly. The sample size was calculated from the formula

$$\text{Sample size} = \frac{4xPxQ}{D^2}$$

Where, P= prevalence of patients prescribed antibiotics which is 30.6% [3].

The demographic details, age, gender, clinical diagnosis, no. of drugs prescribed on the day of admission, total no. of antimicrobial drugs prescribed, day on which the antibiotic was prescribed, any change in antibiotics, the generic name, dose, duration and route of administration of antibiotics and the year were entered into a patient indicator form (proforma) [4, 5] .The antibiotics prescribed to the patient from the time of admission till the time of exit from the hospital were collected. Their diagnosis, response to empirical treatment, indication, co morbidities and immunocompromised status, if present, were also recorded. The results of the microbiological culture samples isolated and sensitivity pattern test reports [4, 6, 7] were also collected and taken into consideration and analyzed. Any change in the antibiotic was also noted. The response to empirical treatment was taken into account to assess the indications. The antibiotics prescribed at the time of discharge were also taken into account.

STATISTICAL METHODS:

Entire data had been entered in an MS excel sheet. The collected data was entered, coded, tabulated and analyzed for descriptive analysis such as mean, median, mode and standard deviation, frequency and percentages using MS excel and spss statistics application. Tables and graphs representing the results were made using MS excel 10 and SPSS (21.0) application. No statistical test has been used in the study.

RESULTS:

The study population consisted of 227 patients who were admitted in their respective wards out of which 142 were female, 85 were male. . Patients in the age groups 30-40, 40-50, 50-60 were found to be 19.40%, 26.9%, and 22.90% respectively. 53.30% of the study population were earning members and 46.70% were dependents. The percentage of patients whose monthly income was in the range of 9000- 12000, 12000- 15000, 15000- 21000 were found to be 31.30%, 21.60%, 30.00% respectively.

Table 1: Descriptive statistics of age, monthly income and hospital stay

Statistics	Age	Monthly income	Hospital stay(days)
Sample size N	227	180*	227
Mean	48	12222	17
Median	48	11500	13
Mode	37	10000	5
Minimum	20	1500	1
Maximum	84	30000	100
Std. Error of Mean	1	329	1
Std. Deviation	14	4409	15

*47- monthly income not applicable for student, housewife

Proportion of study population across various high risk units: 45% of the patients were from the surgical post operative ward, followed by 20% from the orthopaedics post operative ward and 19% from the ICU, 14% gynaecology, 2% SICU. The distribution of various conditions in the study population were as follows: elective surgery-106(46.7%), emergency surgery- 29(12.8%), respiratory diseases- 13(5.7%), kidney diseases- 4 (1.8%), cardiovascular and metabolic diseases-22(9.7%) , orthopedic surgeries- 40 (17.6%), others -13(5.7%).The distribution of number of antimicrobial agents prescribed were found to be 1- 21.5%; 2-34.2%;3-21.5%; 4- 14.0% ; 5 – 5.3% ; 6-2.2%; 7-0.4% ; 9-0.4%

Table 2: Descriptive statistics of number of antimicrobials

Statistics	Antimicrobials
Mean	2.58
Median	2.00
Mode	2
Minimum	1
Maximum	9

The indications for prescribing antibiotic were found to be bacteriological proven (with culture) - 16.7% ; non bacteriological proven-clinical judgement (with culture)- 14.1%; non bacteriological proven – prophylactic – 69.2%.

Commonly prescribed antibiotics in 227 sample population were found to be Cefotaxime (53.7%) followed by metronidazole (38.3%) and amoxicillin /clavulanic acid (33%).Other antibiotics which were prescribed are Cefixime(27.8%), Ceftriaxone (11.5%), cephalexin (0.4%),Ciprofloxacin (4.8%) , levofloxacin (3.1%) , 0.4% ofloxacin, carbapenem antibiotics (imipenem 4.8%,meropenem 2.2%), aminoglycosides (amikacin 35%,gentamycin 5%), macrolides (azithromycin 11%,clarithromycin 1%), colistin (4.8%), linezolid (4.4%), doxycyline (4.0%), nitrofurantoin (1.8%),clindamycin(0.4%), vancomycin(0.4%), cefoperazone sulbactum and piperacillin tazobactum (11.9%), co trimoxazole(0.4%).

Piperacillin tazobactum (27.9%) and amoxicillin clavulanic acid (27.9%) was commonly used followed by azithromycin (20.9%), cefoperazone sulbactum(20.9%) ,metronidazole(18.6%), ceftriaxone(16.3%),levofloxacin(11.6%),cefotaxime(7.0%),ciproflox acin(7.0%), meropenem(7.0%), nitrofurantoin(7/0%), imipenem(4.7%), doxycyline(4.7%), amikacin(4.7%), colistin (4.7%), linezolid(2.3%), clarithromycin(2.3%), clindamycin(2.3) in the ICU. Cefotaxime (96.9%) and metronidazole (87.5%) were commonly followed by cefoperazone sulbactum (31.3%), cefixime (12.5%), linezolid (6.3%), piperacillin/ tazobactum (3.1%), amoxicillin clavulanic acid (3.1%), gentamycin (3.1%), amikacin (3.1%), co trimoxazole (3.1%) in gynaecology and obstetrics post operative wards.

Cefotaxime (82%) was the most commonly prescribed antibiotic followed by Cefixime (56%), Metronidazole (39%), Amoxicillin Clavulanic acid (25%), amikacin(15%), ceftriaxone (14%), piperacillin tazobactum (10%), cefoperazone sulbactum (9%), ciprofloxacin (8%), colistin (7%), doxycyline (6%), imipenem (4%),linezolid(4%), gentamycin(4%), azithromycin(2%), levofloxacin(2%), meropenem (2%),cephalexin(1%), nitrofurantoin (1%), ofloxacin(1%) in surgery post operative wards. Among the antibiotics prescribed, Amoxicillin clavulanic acid (75.6%) was the most commonly prescribed drug followed by amikacin (37.8%), metronidazole (17.8), cefotaxime (13.3%), cefoperazone sulbactum (13.3%), ceftriaxone (11.1%), and imipenem (11.1%) in orthopaedics wards.

DISCUSSION:

The study was undertaken to assess the prescription patterns of antibiotics among adult patients who were admitted in the high risk units such as ICU and post operative wards. The study population consisted of 227 patients who were admitted in their respective wards. Out of which 62.6% of the study population were female and 37.4% were male. The range of age group of patients was 20-84 where 26.9% of the patients were between the age group 40-50 years. The mean age was calculated to be 48. These results were approximately same seen in drug use pattern study in ICU of Northern India where average age was 49 years[3,5]. Most of the antibiotics were prescribed in their generic name except in cases of Piperacillin tazobactum and Amoxicillin-clavulanic acid. Prescription and resistance pattern of the study population were assessed during the study. Utilization of different classes of drugs as well as the individual drugs were processed, analysed and presented as percentages.

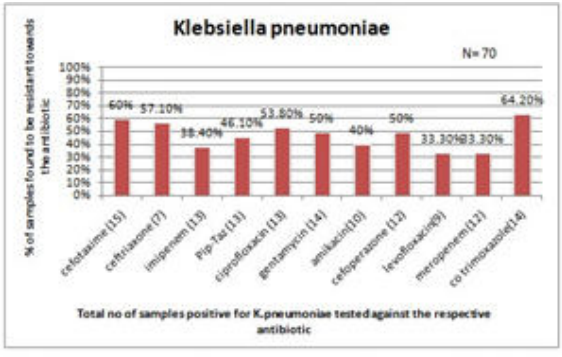
Table.3.1: Resistivity pattern of commonly isolated organisms.

Organism	Cefotaxime †	Ceftriaxone†	Imipenem †	Pip-taz †	Ciprofloxacin†	Linezolid †	Azithromycin †	Gentamycin †	Doxycyline†
Staphylococcus Aureus(MRSA)	nt	nt	nt	6\6 (100%)	6\6 (100%)	0/6 (0%)	4\5 (80%)	3\7 (42.8%)	0\6 (0%)
Staphylococcus Aureus(MSSA)	nt	nt	nt	1\3 (33.3%)	0\3 (0%)	0\3 (0%)	0\2 (0%)	0\3 (0%)	0\2 (0%)
Escherichia Coli	10\11 (90.9%)	8\11 (72.7%)	5\12 (41.6%)	6\12 (50%)	10\12 (83.3%)	nt	nt	6\12 (50%)	nt
Acinetobacter Spp	14\16 (87.5%)	7\9 (77.7%)	12\17 (70.5%)	12\17 (70.5%)	11\17 (64.7%)	nt	nt	15\18 (83.3%)	nt
Pseudomonas Aeruginosa	1\1 (100%)	nt	4\7 (57.14%)	2\10 (20%)	1\9 (11.1%)	nt	nt	1\4 (25%)	nt
Klebsiella Pneumoniae	9\15 (60%)	4\7 (57.1%)	5\13 (38.4%)	6\13 (46.1%)	7\13 (53.8%)	nt	nt	7\14 (50%)	nt
Enterococcus	nt	nt	nt	nt	5\6 (83.3%)	0\4 (0%)	nt	4\5 (80%)	nt
Pseudomonas Spp	nt	nt	4\8 (50%)	2\8 (25%)	4\8 (50%)	nt	nt	2\4 (50%)	nt
Proteus Mirabilis	2\4 (50%)	1\2 (50%)	0/4 (0%)	0/4 (0%)	2\3 (66.6%)	nt	nt	2\4 (50%)	nt
Proteus Vulgaris	1\2 (50%)	1\1 (100%)	0\2 (0%)	0\1 (0%)	1\2 (50%)	nt	nt	1\2 (50%)	nt
Streptococcus Spp	nt	nt	nt	Nt	1\1 (100%)	0\1 (0%)	nt	0\1 (0%)	nt

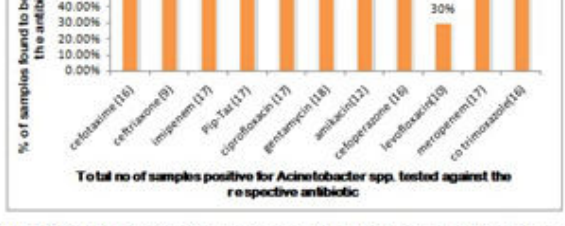
Table 3.2: Resistivity pattern of commonly isolated organisms.

Organism	Amikacin †	Cefoperazone Sulbactum†	Colistin †	Levofloxacin†	Meropenem†	Nitrofurantoin†	Co Trimoxazole†	Clindamycin†	Vancomycin †
Staphylococcus Aureus(MRSA)	nt	6\6 (100%)	nt	nt	nt	nt	6\6 (100%)	2\3 (66.6%)	0\6 (0%)
Staphylococcus Aureus(MSSA)	nt	0\3 (0%)	nt	nt	nt	nt	2\3 (66.6%)	0\1 (0%)	0\3 (0%)
Escherichia Coli	3\12 (25%)	5\6 (83.3%)	0\12 (0%)	7\9 (77.7%)	5\11 (45.4%)	0\6 (0%)	9\11 (81.8%)	nt	nt
Acinetobacter Spp	6\12 (50%)	10\16 (62.5%)	0\16 (0%)	3\10 (30%)	11\17 (64.7%)	nt	11\16 (68.75%)	nt	nt
Pseudomonas Aeruginosa	1\10 (10%)	0\2 (0%)	0\10 (0%)	3\10 (30%)	3\9 (33.3%)	nt	nt	nt	nt
Klebsiella Pneumoniae	4\10 (40%)	6\12 (50%)	0\13 (0%)	3\9 (33.3%)	4\12 (33.3%)	nt	9\14 (64.2%)	nt	nt
Enterococcus	nt	nt	nt	3\3 (100%)	nt	2\5 (40%)	nt	nt	0\4 (0%)
Pseudomonas Spp	3\8 (37.5%)	0\1 (0%)	0\9 (0%)	1\5 (20%)	3\7 (42.8%)	nt	nt	nt	nt
Proteus Mirabilis	1\4 (25%)	2\4 (50%)	4\4 (100%)	2\3 (66.6%)	0\2 (0%)	nt	2\3 (66.6%)	nt	nt
Proteus Vulgaris	1\2 (50%)	nt	2\2 (100%)	2\2 (100%)	0\2 (0%)	1\2 (50%)	1\2 (50%)	nt	nt
Streptococcus Spp	nt	nt	nt	nt	nt	0\1 (0%)	nt	nt	0\1 (0%)

*Resistant = no of cases/total no of cases in which it was isolated (percentage of resistant cases), nt – not tested



Graph 1: Drug Resistance in Klebsiella pneumonia- Out of 70 patients tested for culture and sensitivity, 64.20% with Co trimoxazole followed by 60% with Cefotaxime, 57.10% with Ceftriaxone.



Graph 2: Drug Resistance in Acinetobacter spp. - Out of 70 patients tested for culture and sensitivity, 87.50% with Cefotaxime, 83.30% with Gentamycin, 77.70% with Ceftriaxone.

The common indication for antibiotic use in this study was non bacteriologically proven- prophylactic use (69.2%) followed by bacteriological proven cases (16.7%) and non bacteriological proven – clinical judgement (14.1%).The results obtained were comparable to the result given by Gedam S *et al*[8]and Vandana AB *et al*[5]and Pandiamunian J[9]. Association between requesting culture report and indication for prescribing antibiotic was found to be statistically highly significant in this study.

In this study,21.5% of the study population was prescribed at least one antibiotic ,34.2% of the patients were prescribed 2 antibiotics , 21.5% of the patients were prescribed 3 antibiotics , 14% of the patients were prescribed 4 antibiotics during their stay in the hospital (antibiotics prescribed at the time of discharge was also taken into consideration). The study done by Bosu *et al*[10] showed the variation in average percentage of patients receiving at least one antibiotic as 41%,45%,79% and 98% respectively. 206 (60.1%) patients were receiving at least one antimicrobial in a study done in Fiji[11]

In this study, 100% of the antibiotics prescribed in the study population were found to be included in the WHO Essential Drug List[12].**ICU-**The most commonly prescribed antibiotic in the ICU was found to be Piperacillin tazobactum (27.9%) and Amoxicillin clavulanic acid (27.9%) A study from an ICU in Northern India, the most frequently prescribed antibiotics were found to be 3rd generation Cephalosporins followed by Metronidazole and Levofloxacin and in other Indian studies, the most frequently prescribed antibiotic was Metronidazole followed by Cefotaxime, Amoxicillin-clavulanic acid, Cefipime and Ciprofloxacin[5].Generic name of the drug was commonly used. Since patients who are diagnosed with serious conditions are present in the ICU, main route of administration was through IV (intravenous).

Surgery- Cefotaxime (79.6%) was the most commonly prescribed antibiotic in the surgical post operative patients followed by Cefixime (54.4%) and Metronidazole (37.9%).Usage of 2 antimicrobial agents was also common. More use of antimicrobials was found in surgical units in comparison with other units and higher number of 3rd generation cephalosporins for surgical prophylaxis. Vaccheri *et al.* [13], in their study, conducted in Italian hospitals, observed a similar finding. Surgical procedures often need antimicrobial coverage to avoid postoperative infections and complications. For surgical prophylaxis, international guidelines indicates that the use of 1st or at the most 2nd generation cephalosporins is suitable; other antimicrobials like vancomycin, metronidazole, aminoglycosides,ciprofloxacin and clindamycin can also be used for the purpose.[14,24]

Gynaecology-The most commonly prescribed antibiotics among gynaecology and obstetrics post operative patients was Cefotaxime (96.9%) followed by Metronidazole(87.5%) given orally and IV, In this study, the use of antibiotic was mostly prophylactic in gynaecology and obstetrics post operative patients. Most of the cases were indicated as non bacteriologically proven infection and prophylaxis**.**In Ecuadorian study, preoperative and postoperative indication of antibiotic were 69.90% and 100%[15].

Orthopaedics- Among the antibiotics prescribed, Amoxicillin clavulanic acid (75.6%) was the most commonly prescribed drug followed by Amikacin (37.8%), Metronidazole (17.8), Cefotaxime (13.3%), Cefoperazone sulbactum (13.3%),Ceftriaxone (11.1%) , Imipenem(11.1%) in orthopaedics wards. The most common indication was prophylactic use. Generic name was commonly seen in these prescriptions.

It was observed that cephalosporins were the most commonly prescribed drugs across the all the units.Similar results were found in studies from North, Central India and Serbia[2,5,16]. Of the 325 antimicrobial prescriptions, the most common agents were ampicillin (58/325, 17.8%), cloxacillin (55/325, 16.9%) and metronidazole (53/325, 16.3%)[11].Plachouraset al[17]reported that ceftriaxone was in third place of the list of antimicrobial agents accounting for 75% of antimicrobial use in acute-care hospitals in the European Union/European Economic Area countries during 2016–2017. Culture and sensitivity for 70(30.8%) patients was done in this study. Out of the 13 commonly isolated organisms, Klebsiella pneumoniae and Acinetobacter spp., were the most commonly isolated organisms seen in the study samples.Recent Indian studies from Chandigarh (34.8.7%), Puducherry (41.8%), and Jaipur (21%) found *Acinetobacter* as the most common organism followed by *Pseudomonas* (14%–24%), *Klebsiella* (19.7%), and *Escherichia coli* (15%–18%)[18,19,20]

The study conducted by Nooren sultana,S. Shafia *et al.*[21] showed similar results for the commonly prescribed antibiotics and the second generation Cefuroxime was found to be highly resistant when tested on E.coli and Klebsiella species. 3rd generation cephalosporin namely ceftazidime when tested against pseudomonas aeruginosa was found highly resistant and Enterococcus was highly resistant to levofloxacin and Staphylococcus aureus was highly resistant to penicillin. The most frequently identified bacteria in a Serbian study were *Acinetobacter* spp. (14.7%), *Klebsiella* spp. (11.1%)[16]. The most common single pathogens causing ICU-acquired infection in lower and middle income countries were *A. baumannii* (24%)*, P. aeruginosa* (16%)*, K. pneumoniae* (15%)*,* these caused the majority of infections[22]. and a similar result was found in a study by Fiji[11].

In this study, Acinetobacter spp (87.5%) was found to be highly resistant when tested with Cefotaxime and was found to be also resistant in E.coli and Klebsiella pneumoniae. However Pseudomonas aeruginosa was found to be highly resistant when tested with Ceftazidime as reported by Nooreen sultana et al[21]. In this study Enterococcus was found to be resistant when tested with ciprofloxacin whereas Linezolid, an oxazolidinone, was found to be sensitive to Enterococcus. Acinetobacter spp.and E.coli was also found to be highly resistant when tested with Ciprofloxacin and in Staphylococcus aureus(MRSA) & Klebsiella pneumoniae. Carbapenem resistance in acinetobacter spp. was noticed in this study and correlates with western studies. Pseudomonas spp. (P.aeruginosa) is highly sensitive when tested with Piperacillin tazobactum. Klebsiella pneumoniae was sensitive when tested with Imipenem and meropenem. Acinetobacter spp was found to be highly resistant when tested with Cefoperazone sulbactum and co trimoxazole whereas Colistin was highly sensitive to Acinetobacter spp. Klebsiella pneumonia was found to be resistant when tested with Co trimoxazole.

Drug resistance towards higher antibiotics were very minimal. The average number of drugs per prescription is an important index in a prescription audit. Preferably the number of drugs per prescription should be kept as low as possible to minimise the risk of drug interactions, development of bacterial resistance, hospital costs which causes great concern towards antibiotic resistance. This study concentrated only on antibiotics and not the co prescribed drugs.

Antibiotic resistance is one of the drastically alarming situations currently and there is an emerging trend of organisms becoming resistant to 3rd generation antibiotics in the high risk units. We are in the process of formulating an antibiotic prescription policy enlisting local antibiotic prescription guidelines and at present, national guidelines are being followed in the ICU. The study population consists of insured patients and the medicines were prescribed free of cost. Heng S.T *et.al(2021)*[23] has shown that As the pandemic continues, attention must be given to control the amount and appropriateness of antimicrobial use. Antimicrobial stewardship resources and efforts should be initiated and enhanced especially in areas where such practices are still in early stages of development[23].

CONCLUSION:

The 3rd generation Cephalosporins were found to be highly used in high risk units. The number of higher antibiotics prescribed was low. Lower antibiotics were commonly used which is an encouraging factor. Good antibiotic prescribing measures were observed in the ICU. Such measures could be modelled and practiced in other post surgical units also. Presently, With limited or no information on diagnosis of co-infections, antibiotic treatment may be indiscriminate and misinformed. There are chances that patients are given antibiotics that may not be effective for the particular infection causing bacteria. It is all the more worrisome in cases when the secondary infections are caused by drug-resistant bacteria.

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