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# PRESCRIBING PATTERN OF CEPHALOSPORINS AND CARBAPENEM ANTIBIOTICS IN THE CRITICAL CARE UNIT OF A TERTIARY CARE HOSPITAL

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## ABSTRACT

The aim of present study was to develop clinical pharmacist intervention to improve the prescribing pattern of Cephalosporins and Carbapenem antibiotics in Critical Care Unit (CCU). We focus on 224 patients who received Cephalosporin or Carbapenem antibiotics in CCU. Prescribing pattern was evaluated through descriptive analysis, t-test, modified t-test and chi square techniques. APACHE 2 Score was used for the prediction of mortality rate of patients admitted to CCU. The result shows 128 male and 96 female patients admitted to CCU during the study period. The average age of the patients was 61.32 years ± 15.85 SD and the median APACHE II score was 12, and the most common diagnosis at admission was respiratory diseases (60 patients). The average length of stay (LOS) in the CCU was 7.37 days. A total of 1780 drugs were prescribed at admission in 224 patients, that is, an average of 7.95± 2.90 SD drugs/prescription. One hundred and thirty two patients (58.92%) were prescribed an antibiotic at the time of admission into the CCU. In all, 293 antibiotics, at an average of 1.32 ± 0.56 SD antibiotics/prescription were ordered, and antibiotics constituted 16.46% of the total drugs prescribed. The study concluded as clinical pharmacist interventions had a great importance in improving the prescribing pattern and reducing the emergence of resistance.

**KEY WORDS**: Prescribing pattern, Cephalosporins, Carbapenem, Critical Care Unit (CCU), APPACHE 2 Score.

## INTRODUCTION

Patients on Intensive Care Unit (ICU) were suffering from serious diseases and were critically ill. These patients were most frequently prescribed with antibiotic during their hospital days.[1] These antimicrobial agents were most often prescribed inappropriately and also inadequately in medical practices; hence they have become highly abused drugs.[2]

The wide spread and inappropriate use of antibiotics were resulted in antibiotic resistance pathogens. These also leads to prolongation of illness, exacerbation of present disease, ineffective treatment, high risk of morbidity, increased patient cost and patient harm.[3] Antibiotic resistant pathogens are one of the major concerns in ICU and will leads to antibiotic resistance.

Cephalosporins and Carbapenem were most commonly prescribed antibiotics in Critical Care Unit because of its wide spectrum of activity for both Gram positive $G^+$ and Gram negative $G^-$ microbes. They are most commonly prescribed as empirical therapy for most of infections in Critical Care Unit.

Cephalosporins are β-lactam antibiotics, and are bactericidal and have similar mechanism of action as penicillin ie, inhibition of cell wall synthesis. However, they bind to different proteins than those which bind penicillins. This may explain difference in spectrum, potency and lack of cross resistance. Cephalosporins are mainly classified into five generations according to spectrum of activity. The spectrum of activity widens from $G^+$ve and $G^-$ve bacteria as the generations rise from the first to fifth.[4]

Carbapenems are beta lactam antibiotics with broad spectrum of activity and coverage of $G^{-ve}$ and $G^{+ve}$ aerobic and anaerobic bacteria. Like other broad spectrum antibiotic, Carbapenem are prescribed as a part of empiric therapy in most serious nosocomial infections. Imipenem is a synthetic Carbapenem co-administered with Cilastatin, to prevent renal metabolism of Imipenem by dehydropeptidase I (DHPI). In contrast, this co-administration with the dehydropeptidase inhibitors, Cilastatin is not necessary with Meropenem, because this agent is not hydrolyzed by DHPI.[5]

The studies on prescribing pattern were conducted to evaluate and suggest valuable information for making rational and cost effective prescribing policies.[6] In many studies it was found that antibiotic prescribing is suboptimal, it refers to inappropriate spectrum antibiotic,

use of antibiotic for little or no sign of bacterial infection, over use of parenteral preparation, prolonged treatment for minor infections. The inappropriate prescribing leads to increased health care cost, antibiotic resistance and many ADR.

Prolongation of illness, disease exacerbation, ineffective and unsafe treatment is the result of indiscriminate prescribing of AMAs. Indiscriminate and inappropriate use of antibiotics is the major health concern in health care system in all over the world. Hence prescribing pattern studies have major role in improving therapeutic benefits, reducing adverse effects and optimizing health care services.

## MATERIALS AND METHODS

### Study design

❖This prospective cross sectional study on prescribing pattern of Cephalosporin and Carbapenem antibiotics was carried out in a critical care unit of a 360 bedded multispecialty hospital in south India. Our CCU is an open mixed medical surgical 23 bedded unit with approximately 1000 admissions per year. This was a six months study conducted between October 2014 and April 2015.

❖The study protocol was approved by Institutional Ethical Committee(IEC) of the respective hospital.

❖Inclusion and exclusion criteria were defined and a specially designed data collection form was prepared for entering the data on prescribing pattern of Cephalosporin and Carbapenem antibiotics.

### Sample size

Sample size was calculated for the accurate collection of cases according to average patient admissions in CCU during the study period. The sample size was calculated using the formula $N = Z_{\alpha}^{2}pq/ d^{2}$ with the assumption that an average of 142 patients were admitted per month. Hence total of 224 patients were included in the study for a period of 6 months.

### Inclusion Criteria

- Patients who are admitted in the Critical Care Unit prescribed with cephalosporin or carbapenem antibiotics with a minimal length of stay of 24hrs.

### Exclusion Criteria

- Patients below 15 years of age.
- Pregnant women.

### Data collection

✓The prescription data of total 224 patients admitted in CCU on scheduled time was audited.

✓Baseline demographic variables of all patients such as IP number, age, gender, department ,clinical diagnosis, culture sensitivity and antibiotic sensitivity test reports, duration of CCU days, and total number of drugs prescribed was collected.

✓It also involves the collection of data regarding antibiotic such as brand name, generic name, dose, route, frequency and duration.

✓APACHE II score (Acute Physiology And Chronic Health Evaluation Score)-standard tool to assess the severity of illness was used for the prediction of mortality rate of patients admitted to Critical Care Units. An integer score from 0 to 71 was assigned based on several measurements; higher scores correspond to more severe disease and a higher risk of mortality.

✓Antibiotics can be prescribed both in their generic name as well as in brand name. It is evaluated by auditing the prescriptions and classified them accordingly.

✓Antibiotics in CCU are prescribed according to the clinical symptoms and condition of the patient (empirical therapy) and also using the culture and sensitivity test reports (definitive therapy). By auditing case files, selection of antibiotic therapy was recorded according as empiric therapy and definitive therapy.

✓Pharmacist interventions were made to optimize therapy by performing prescribing pattern analysis.

### Statistical analysis

This is a cross sectional study and therefore it have to describe fully the characteristics of the patients in the descriptive part in this research. For this purpose we have used methods of tabulation, graphical procedures and calculation of summary indices (mean, median, and standard deviation) where ever appropriate. For describing the categorical variables(sex, diagnosis, antibiotics etc) we have used percentage and for describing quantitative variables (age, number of antibiotics, total number of drugs) mean, median and standard deviation respectively where ever appropriate.

For data entry we had used the software Microsoft excel and for the analysis SPSS (Statistical Package for Social Science). In inferential part we had used t- test, chi square test appropriately. All p values were set at 5% and we have used 2 tailed tests for this purpose.

## RESULTS

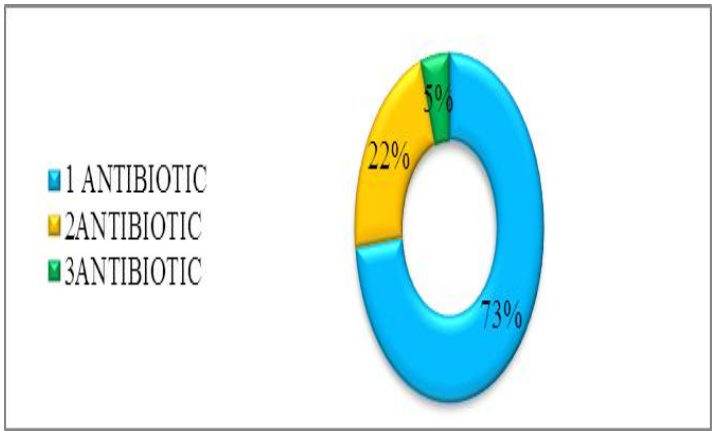
The prescriptions of 224 consecutive patients admitted into the CCU were analyzed. This included 128 male and 96 female patients. The average age of the patients was 61.32 years ± 15.85 SD and the median APACHE II score was 12. Most of our patients were admitted to the CCU from the medical specialty (90.17%) and the most common diagnosis at admission was respiratory diseases (60 patients). The average length of stay (LOS) in the CCU was 7.37 days. The demographic data and patient characteristics are given in table 2.

**Table 2: Demographic data and patient characteristics**

| VARIABLE | NUMBER (N=224) | PERCENTAGE (%) |
|---|---|---|
| **GENDER** | | |
| Male | 128 | 57.1 |
| Female | 96 | 42.9 |
| **AGE DISTRIBUTION(in years)** | | |
| ≤ 30 | 10 | 4.46 |
| 31-45 | 22 | 9.82 |
| 46-60 | 70 | 31.25 |
| 61-75 | 79 | 35.26 |
| >75 | 43 | 19.19 |
| **APPACHE 2 SCORE** | | |
| 0-9 | 60 | 26.78 |
| 10-19 | 124 | 55.35 |
| 20-29 | 32 | 14.28 |
| ≥30 | 8 | 3.57 |
| **DEPARTMENT OF ORIGIN** | | |
| Medical | 202 | 90.17 |
| Surgical | 22 | 9.83 |
| **DRUGS PRESCRIBED** | | |
| 1-5 | 49 | 21.87 |
| 6-10 | 139 | 62.05 |
| 11-15 | 30 | 13.39 |
| >15 | 6 | 2.68 |
| **ANTIBIOTICS PRESCRIBED** | | |
| 1 | 164 | 73.2 |
| 2 | 49 | 21.9 |
| 3 | 11 | 4.9 |
| **LENGTH OF ICU STAY(In Days)** | | |
| 1-5 | 33 | 14.73 |
| 6-10 | 178 | 79.46 |
| 11-15 | 11 | 4.91 |
| >15 | 2 | 0.72 |
| **OUTCOME FROM ICU** | | |
| Discharged | 186 | 83 |
| Expired | 38 | 17 |

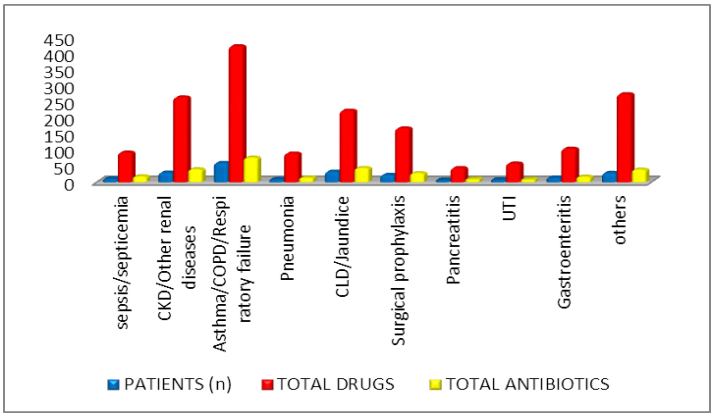
**PRESCRIBING PATTERN ANALYSIS**

A total of 1780 drugs were prescribed at admission in 224 patients, that is, an average of 7.95± 2.90 SD drugs/prescription. One hundred and thirty two patients (58.92%) were prescribed an antibiotic at the time of admission into the CCU. In all, 293 antibiotics, at an average of 1.32 ± 0.56 SD antibiotics/prescription were ordered, and antibiotics constituted 16.46% of the total drugs prescribed. 73% of the cases were prescribed with one antibiotic and the distributions of patients according to the number of antibiotics were shown in graph 1.




**Graph 1 : The distribution of patients according to the number of antibiotics prescribed.**

The influence of various clinical factors, such as diagnosis at admission and APACHE II score in determining the number of drugs and antibiotics prescribed was studied. Patients admitted with respiratory diseases were prescribed the most number of antibiotics graph 2.




**Graph 2: Distribution of patients, total number of drugs and total antibiotics according to different diagnosis**

**FACTORS AFFECTING PRESCRIBING PATTERN**

The average number of drugs were prescribed irrespective of APPACHE II Score (t= 1.235, p = 0.218). However, the average number of antibiotics prescribed in these patients were having a significant relation between the APPACHE II Score (modified t = 3.615; p= 0.0001). For patients with APPACHE II Score >15, the average number of antibiotics prescribed were high, than that with lower APPACHE II Scores. Both male and female have no significant difference in their APPACHE II Scores (Chi-square value = 0.028, p = 0.867). The factors affecting prescribing pattern were shown below Table 3.

**Table 3: Factors affecting prescribing pattern**

| **Relation between APPACHE II Score and Total number of drugs prescribed** | | | |
|---|---|---|---|
| **APPACHE II SCORE** | **N** | **Mean** | **SD** |
| ≤15 | 155 | 7.79 | ± 2.74 |
| >15 | 69 | 8.30 | ± 3.23 |
| t= 1.235 ; p = 0.218 | | | |
| **Relation between APPACHE II Score and Total number of antibiotics prescribed** | | | |
| **APPACHE II SCORE** | **N** | **Mean** | **SD** |
| ≤15 | 155 | 1.21 | ± 0.44 |
| >15 | 69 | 1.55 | ± 0.72 |
| t= 3.615 ; p = 0.0001 | | | |
| **Relationship of gender difference and mortality** | | | |
| **GENDER** | **APPACHE II SCORE** | | |
| | ≤15 | >15 | |
| Male | 88 | 40 | |
| Female | 67 | 29 | |
| Total | 155 | 69 | |
| **Chi-square value = 0.028 ; p = 0.867** | | | |

**MOST FREQUENTLY USED ANTIBIOTICS (ACCORDING TO NUMBER OF PRESCRIPTIONS)**

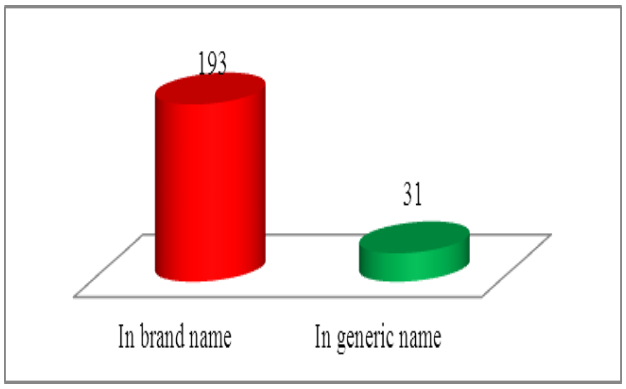
The most commonly prescribed antimicrobial at ICU admission was Cefoperazone/ Sulbactam (47.8% of all prescriptions) and 321 units of the same were consumed among the patients studied. Table 4 enlists the 10 most commonly prescribed antibiotics along with their DDD per 100 bed-days.

**Table 4: Most frequently used antibiotics (according to number of prescriptions)**

| **NAME** | **ATC CODE** | **DDD(gm)** | **NO.OF PRESCRIPTIONS** | **UNITS** | **DDD/100 BED-DAYS** |
|---|---|---|---|---|---|
| Cefoperazone/sulbactam | J01DD62 | 4 | 107 | 321 | 11.34 |
| Ceftriaxone | JO1DD04 | 2 | 21 | 42 | 4.45 |
| Cefotaxime | J01DD01 | 4 | 34 | 68 | 3.60 |
| Meropenem | J01DH02 | 2 | 41 | 123 | 13.04 |

| | | | | | |
|---|---|---|---|---|---|
| Ertapenem | J01DH03 | 1 | 4 | 4 | 0.848 |
| Imepenem/cilastatin | J01DH51 | 2 | 11 | 16.5 | 13.41 |
| Doripenem | J01DH04 | 1.5 | 3 | 4.5 | 0.65 |

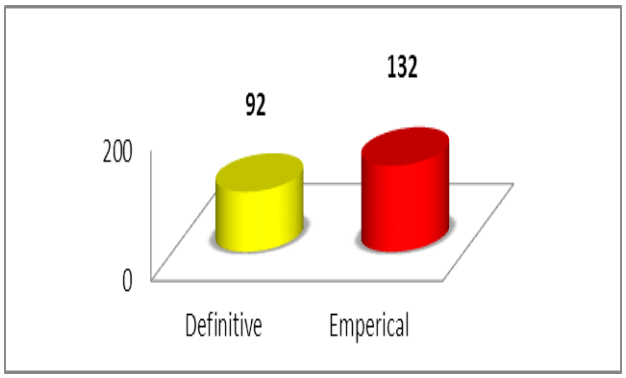
**TYPE OF ANTIBIOTIC PRECRIPTION (GENERIC AND BRAND NAME):** Drugs were prescribed as generic names in 31(13.8%) of cases and it was prescribed in other brand names in 193(86.2%).




**Graph 8: Type of antibiotic prescription**

**EMPIRIC VERSUS DEFINITIVE THERAPY**

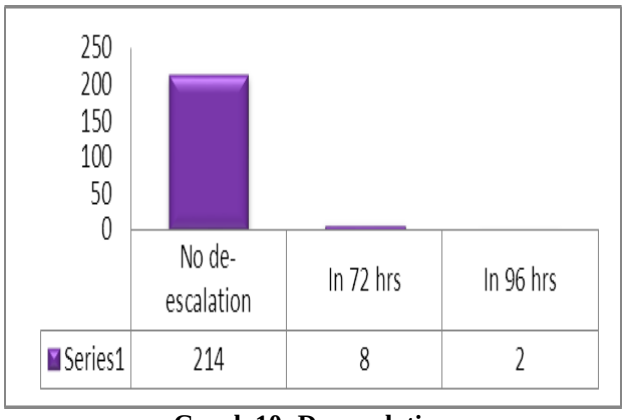
Antibiotics were prescribed empirically in 132(58.9%) cases and definitive therapy (after culture and antibiotic sensitivity reports) was chooses in 92 (41.1%) cases.




**Graph 9: Empiric versus Definitive therapy**

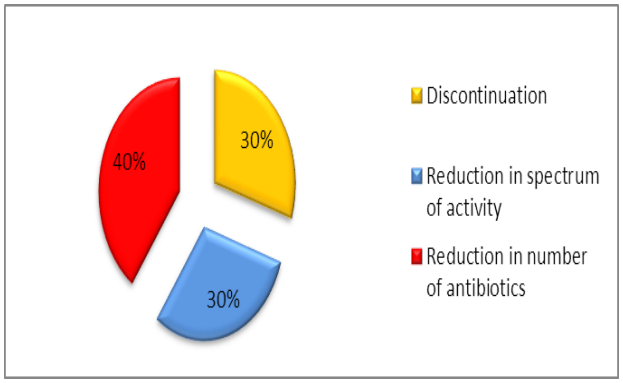
**DE-ESCALATION**

De-escalation after sensitivity reports was done in 10(4.5%) cases and was not done in 214 cases (95.5%).




**Graph 10: De-escalation**

The most commonly used mode of de escalation was reduction in number of antibiotics in 4(40%) patients.




**Graph 11: Mode of de-escalation**

**DISCUSSION**

Antimicrobial resistance is one of the major global preventable problems. Unnecessary use, inappropriate doses, inadequate duration of therapy and irrational fixed dose drug combinations are the causes of antimicrobial resistance. Hence this study was undertaken to improve the quality of medication and to promote the prescription of drugs.[7] The emergence of drug resistance is having a greatest concern as it increase health care cost, increased length of stay and increases the likelihood of ADR and Drug interactions.[8]

In order to prevent or minimize antimicrobial resistance, the prescribing pattern of antibiotics should be properly analyzed. A total of 224 prescriptions of consecutive ICU admissions were analyzed over 6 month period. The demographic results of patients admitted during this period revealed male preponderance [128 male: 96 female] with a mean age of around 61years. This was similar to the study conducted by *Pandiamunian et al*[9]on prescribing pattern of antibiotics on medical ICU with male preponderance and the mean age was around 53 years, similarly *Ansari et al*[10]conducted a study revealed average age of patient was 51.9 years and with a male preponderance. In our study more patients are from the medical department which indicates that most patients are prescribed with antibiotics for infection than surgical prophylaxis. The average length of ICU stay (LOS) of the patients in our study was found to be 7.37 days. Similarly in a study by *Bergmans et al*[11] the average length of ICU stay was 7days and having similar APPACHE II score. Similar result was obtained from the study conducted by *Ansari et al*,[10]ie. the average length of ICU stay was 7.5 days. It was found that out of 224 patients 186 patients were discharged and 38 patients were dead, it does not indicates that prescribed antibiotic is not sufficient, it may due to some other factors.

The average number of drugs per prescription in our study was found to be 7.95 ± 2.90 SD. *Vandana et al*[12] conducted a study on prescribing pattern of antimicrobials in medicine ICU in central India revealed the average number of drugs per prescription was 7.5. The average number of drugs per prescription is having an important role in health care outcome, as the number of drugs per prescription increases the risk for drug interactions, development of bacterial resistance and hospital cost also increases. Hence the number of drugs per prescription should be kept as low as possible.

The average number of antibiotics per prescription was found to be 1.32 ± 0.56, and 1-2 antibiotics constitute 95% of total cases. *Ansari et al*[10] conducted a study on prescribing pattern revealed average number of antibiotics was 1.59. The antibiotics constituted 16.46% of total drugs prescribed. The study conducted by *Admane et al*[7] revealed 30.25% drugs were antimicrobials among the total drugs in the prescription. This result has wide variation from the result obtained in our study. The study conducted by *Aparna et al*[13] on prescribing pattern on antibiotics revealed average of 2.09 antibiotics/prescription were ordered, and antibiotics constituted 33.54% of the total drugs prescribed. The average number of antibiotics should also kept low as possible, as it increase the emergence of resistant organisms. But according to the severity of infection in patients admitted to ICU, physicians may prescribe more antibiotics in order to reduce the severity of infection.

While auditing the prescriptions most patients were prescribed with only one antibiotic and the most commonly prescribed antibiotic at ICU admission was Cefoperazone/sulbactam, which is a 3rd generation cephalosporin. Similarly the most commonly prescribed antibiotics in ICU from study conducted by *Vandana et al*[12] was also found to be 3rd generation cephalosporin, Cefotaxime(32%). *Shankar et al*[6] also found cephalosporins as the most commonly prescribed antibiotics especially ceftriaxone(57%). 3rd generation Cephalosporins have wide spectrum of activity, hence it was most commonly selected and prescribed as empirical therapy in Intensive Care Units. Cefoperazone differs from other 3rd generation Cephalosporins in having stronger activity on Pseudomonas. Sulbactam is a semisynthetic β-lactamase inhibitor. The use of combination antimicrobial therapy has been proposed as a strategy to reduce the emergence of bacterial resistance. The important advantages of combination antibiotic therapy include achieving synergistic action, to reduce the severity or incidence of adverse effects, to prevent the emergence of resistance, and to broaden the spectrum of activity.[4]

The most common diagnosis in our study was respiratory disorders (60 patients). The results were similar to the study on sensitivity pattern of antibiotics in ICU conducted by *Radji et al*[14]and also study on prescribing pattern of antibiotics in ICU conducted by *Ansari et al*[10] revealed Respiratory infections was the most common infection as the most common diagnosis.

APPACHE II (Acute Physiology and Chronic Health Evaluation II) score is a predictor of mortality in patients admitted to ICU. Patients with higher APPACHE II score have more chance for the severity of disease; hence the number of antibiotics per prescription may vary according to the score. Patient who had higher APPACHE II scores (>15) at admission were prescribed significantly 2 or more antibiotics than with lower scores. That is there was a significant relation between APPACHE II Score and total number of antibiotics prescribed. This similar result was found in study conducted by *Tavallaee et al*[15] on drug use pattern in ICU of a hospital in Iran. But in contrast to our study, the study conducted by *Ansari et al*[10] found no association between number of antibiotics prescribed and the mortality risk (APPACHE II Score).

Our study reveals there is no significant relation between APPACHE II Score and total number of drugs prescribed, but the study conducted by *Aparna et al*[13] reveals a significant relation between total number of drugs and APPACHE II Score.

In our study majority of antibiotics were prescribed in brand name (86.2%), only 13.8% antibiotics were prescribed in generic name. Similar results were obtained from the studies by *Saurabh et al*[16] and *Patel et al*[17]that over 90% prescriptions were only in brand names. But an opposing result was obtained in a study by *admane et al*[7] in which 79.18% prescriptions was in generic name. In order to improve the quality of prescribing and to reduce the cost of therapy drug prescription in generic name should be promoted. Generic medicines are 40-60% cheaper than the innovator brand name with equal efficacy.[16]

Empiric therapy is therapy based on experience and more specifically, therapy begun on the basis of a clinical educated guess in the absence of complete or perfect information. Empirical therapy is most often used when antibiotics are given to a person before the specific bacterium causing infection is known. A broad spectrum antibiotic that cover both Gram positive and Gram negative bacteria were chosen as an empiric antibiotic. Antibiotics were prescribed empirically in 58.9% of cases and prescribing after culture and antibiotic sensitivity reports were chosen only in 41.1% of cases. Since the patients were critically ill, the physicians may start an empiric antibiotic therapy inorder to reduce the severity of infection. But inappropriate initial empiric antibiotic selection can adversely affect the patient health status and economic consequences. Hence the drug choice according to culture and sensitivity is having an important role. Antimicrobials prescribed empirically and prophylactically without performing culture sensitivity pattern may increases the chances of

antimicrobial resistance. Inappropriate antibiotic therapy was defined as the use of an antimicrobial to which the documented pathogen was resistant, or as the failure to provide coverage against an identified pathogen. Hence the importance of performing culture sensitivity for patients especially admitted to ICU should be emphasized.

De-escalation was not performed in most cases, ie. in 95.5%, only 4.5% cases were de-escalated. But in a study conducted by *Morel et al*[18] on de-escalation strategy in ICU 45% cases were de-escalated. The most common mode of de-escalation in our study was reduction in number of antibiotics. Reduction in number of antibiotics as the major mode of de-escalation in studies conducted by *Leone et al*,[19] *Kollef et al*[20] and *Gjantsou et al.*[21] De-escalation was possible irrespective of the severity of the infection, and more frequently translated into a reduction of the number of antibiotics rather than a reduction of the spectrum. Although the study was not powered for clinical outcomes, de-escalation seems to be safe with no excess of mortality and might even allow a reduction in recurrent infections. De-escalation therapy was defined as either a switch to a narrower spectrum agent, or the reduction in the number of antibiotics, or the early arrest of antibiotic treatment.

As a part of improving the quality of prescribing of antibiotics, we have made suggestions including documentation of antibiotic sensitivity and culture sensitivity reports in a specific format. We have designed various forms that can help in improving the quality of antibiotic prescribing. Antibiotic order form, Antibiotic allergy chart, Antibiotic conversion form, antibiotic history form were developed. Antibiotic order form provides information on all antibiotics that have been ordered to the specific patient. The rationality of prescribing can be easily measured through this document. Antibiotic allergy chart provide a rapid identification of antibiotics that have found allergic reaction to a specific patient. The prior identification of allergic antibiotic can minimize the adverse outcome and health care costs. Antibiotic conversion forms were designed to improve the proper intravenous to oral and oral to intravenous conversions. As a part of improving current knowledge on antibiotics among health care professionals we developed antibiotic newsletter, which provide current information on antibiotics. For better use of antibiotics among patients antibiotic general information leaflets were prepared. As a part of improving the safe use of antibiotics we suggest these ideas to our institution.

## CONCLUSION

This study reveals that antibiotics were widely prescribed in critically ill patients and form a significant proportion of the total drugs consumed in CCU. Elderly and critically ill patients were prescribed more drugs and antibiotics. The high utilization rates and cost of antibiotics prescribed at admission in the CCU are a matter of great concern and need to be urgently addressed by the use of guidelines, protocols, educational initiatives, surveillance and antibiotic restriction policies at all levels of health care. Clinical pharmacist interventions had a great importance in improving the prescribing pattern and reducing the emergence of antibiotic resistance.

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## REFERENCES

1. Krivoy N, El-Ahal WA, Bar-Lavie Y, Haddad S. Antibiotic prescription and cost patterns in a general intensive care unit. Pharmacy Practice 2007; 5(2): 67-73.
2. Joshi MC, Tariq K, Ejaj A. Restricted antibiotic policy: Rational approach towards antibiotic resistance - Policy - Express Healthcare Management. Indian Express, Business Publications Division, Issue dtd. 1st to 15th June 2005.
3. De Vries TPGM, Henning RH, Hogerzeil HV, Fresle DA.WHO. Action Programme on Essential Drugs. Guide to good prescribing: programme WHO/DAP 94.11. Geneva: WHO; 1994.6-64.
4. Tripathi KD. Antimicrobial drugs, Essentials of Medical Pharmacology.7 th Edition, 12. New Delhi JAYPEE Brothers medical publishers, 2013; 688-704.
5. Mahini SH, Hayatshahi A, Torkamandi H, Gholami K, Javadi MR. Carbapenem Utilization in Critically Ill Patients. J Pharm Care 2013; 1(4): 141-144.
6. Shankar R.V, et al. Prescribing patterns of antibiotics and sensitivity patterns of common microorganisms in the Internal Medicine ward of a teaching hospital in Western Nepal: a prospective study. Ann ClinMicrobiolAntimicrob, 2003; 2:7.
7. Admane PD et al.: Prescription pattern of antimicrobials in tertiary care hospital in central India. International Journal of Pharmacological Research, 2015; 5(2).
8. Sheth VK et al.: Antibiotic Sensitivity Pattern of Bacterial Isolates from the Intensive Care Unit of a Tertiary Care Hospital in India. Tropical Journal of Pharmaceutical Research December 2012; 11(6): 991-999.
9. Pandiamunian et al.:a study on prescribing pattern of anti microbial agents in the medical intensive care unit of a tertiary care teaching hospital in puducherry union territory, south india International Journal of Pharmacy and Pharmaceutical Sciences, 6(3): 235-238.
10. Ansari et al.:Antibiotic prescription pattern in an Intensive Care Unit in the kingdom of Bahrain: an observational prospective study. International

journal of scientific research 2013; 12(2): 2273-8179.
11. Bergmans DCJJ, Bontena MJM, Gaillard CA, Van Tiel FH, Van der Geesta S, De Leeuwa PW et al. Indications for antibiotic use in ICU patients: A one year prospective surveillance. J AntimicrobChemother 1997; 39: 527.
12. Vandana et al.:Study of Prescribing Pattern of Antimicrobial Agents in Medicine Intensive Care Unit of a Teaching Hospital in Central India. JAPI. april 2012; 60.
13. Williams A, Mathai AS, Phillips AS. Antibiotic prescription patterns at admission into a tertiary level intensive care unit in Northen India. J Pharm BioallSci 2011; 3: 531.
14. Radji M et al.:Antibiotic sensitivity pattern of bacterial pathogens in the intensive care unit of Fatmawati Hospital, Indonesia. Asian Pac J Trop Biomed. 2011 Jan; 1(1): 39–42.
15. Tavallaee M, Fahimi F, Kiani S. Drug-use patterns in an intensive care unit of a hospital in Iran: an observational prospective study.Int J Pharm Pract. 2010.
16. Saurabh et al,:study of prescribing habits and assessment of rational use of drugs among doctors of primary health care facilities.Asian Journal of Pharmaceutical and Clinical Research Vol. 4, Issue 4, 2011.
17. Patel et al.: Irrational drug use in India: a prospective survey from Goa. J postgrad med. March 2005; 51(1).
18. Morel et al.: De-escalation as part of a global strategy of empiric antibiotherapy management. A retrospective study in a medico-surgical intensive care unit. Critical Care 2010; 14: R225.
19. Leone M, Garcin F, Bouvenot J, Boyadjev I, Visintini P, Albanese J, Martin C: Ventilator-associated pneumonia: breaking the vicious circle of antibiotic overuse. Crit Care Med 2007; 35: 379-385, quizz 386.
20. Kollef MH, Morrow LE, Niederman MS, Leeper KV, Anzueto A, Benz-Scott L, Rodino FJ: Clinical characteristics and treatment patterns among patients with ventilator-associated pneumonia. Chest 2006; 129: 1210-1218.
21. Giantsou E, Liratzopoulos N, Efraimidou E, Panopoulou M, Alepopoulou E, Kartali-Ktenidou S, Manolas K: De-escalation therapy rates are significantly higher by bronchoalveolar lavage than by tracheal aspirate. Intensive Care Med 2007; 33: 1533-1540.