

## Drug Use Evaluation Study in a Tertiary Care Corporate Hospital with Special Reference to Use of Antibiotics in ICU Department

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### ABSTRACT

Patients admitted to the intensive care unit (ICU) are seriously ill and often suffer from chronic critical illnesses. Antibiotics are the most frequently prescribed drugs among hospitalized patients especially in intensive care and surgical department. Inadequate antibiotic use can also lead to increased morbidity, mortality, length of hospital stay (LOS) and healthcare expenditures. To study the (1) determine the most commonly prescribed antibiotics in ICU Department. (2) calculate average costs of antibiotics prescribed in ICU Department. (3) The correlation of antibiotic usage as well as costs incurred with respect to age and diagnosis. A private, tertiary care hospital, prospective study. 400 consecutive prescriptions on patients admitted to the ICU from 03/10/2011 to 03/04/2012, were audited. The total number of drugs and antibiotics, the class, dose route and cost of antibiotics were calculated. A total of 3332 drugs and 699 antibiotic were prescribed in the 400 patients studied, that is an average of 8.33 drugs/prescription and 1.74 antibiotics/prescription. Antibiotics were prescribed on three hundred seventy six patients (94%) at a admission. The average cost of the antibiotics was Rupees 4364.90 per patient and antibiotics expenditure accounted for 67.79% of the total drug costs. The number of drugs per prescription were much more than required which increased the risk of drug interactions, development of bacterial resistance and the hospital costs.

**Keywords:** Antibiotic Usage, Antibiotic Audit, Intensive Care Unit, Prescriptions, Antibiotics Cost.

### INTRODUCTION

Patients admitted to the intensive care unit (ICU) are seriously ill and often suffer from chronic critical illnesses. Antibiotics are the most frequently prescribed drugs among hospitalized patients especially in intensive care and surgical department<sup>1</sup>. Resistance of common hospital-acquired bacteria to antibiotics is a worldwide problem. It can lead to increased morbidity, mortality, length of hospital stay (LOS) and healthcare expenditures<sup>2</sup>. An ICU of a developing country where health costs are borne by the patients and to some extent the hospitals, it is causing a huge economic burden<sup>3</sup>. The world has enhanced patient care through therapeutic optimization of the use of antimicrobial agents through the use of antibiotic restriction policies implemented widely throughout the hospital<sup>4</sup>. Knowledge of a ICUs most common bacterial isolates and their antibiotic susceptibility patterns facilitates effective empirical antibiotic therapy and

supports decisions to restrict or reduce the clinical availability of certain antibiotics<sup>5</sup>.

Hence, we proposed to study (1) determine the most commonly prescribed antibiotics in ICU Department. (2) calculate average costs of antibiotics prescribed in ICU Department. (3) The correlation of antibiotic usage as well as costs incurred with respect to age and diagnosis.

### MATERIALS AND METHODS

**Study design:** A prospective study was undertaken 16 bedded Medical Intensive Care Unit (MICU), 16 bedded Neurosurgery Intensive Care Unit (NSICU), 4 bedded Surgical Intensive Care Unit (SICU) and 4 bedded Cardiac thoracic vascular surgery (CTVS) of Fortis Hospital, over a period of six months.

**Sample Size:** A total of 400 prescriptions were included in the study and were

followed for the drug use evaluation to study the antibiotics use pattern.

### Data Collection

A Performa were designed and pretested to be used for entry of patient's specific information.

The format provided the following information:-

- Patient's name, IPID/UHID number, bed number, ICU room name, age, sex, date of admission (DOA) and date of discharge (DOD) or death.
- Different specialties and consultant name.
- Previous drug allergy.
- Diagnosis.
- Past history.
- Type of surgery.
- Date and time of surgery.
- Antibiotics prescribed before and after surgery.
- Dose of the drug.
- Dosage form.
- Route of administration.
- Frequency of administration.
- Antibiotics prescribed at the time of discharge.

### Testing Tool

The prescribing indicators were utilized as a tool to assess the drug utilization pattern.

Data were entered in excel sheet and following indicators were analyzed:-

- Total number of ICU rooms.
- Total number of patients included in the study.
- Total number of patients who underwent surgery.
- Overall population sex categorization of the patients included in the study.
- Average age of the patients (mean; in years).
- Total number of patients in different specialties during the study period.
- Total number of drug prescribed during the study.
- Total number of antibiotics prescribed during the study.
- Average duration of patient's stay in the ICU (in days).

- Average number of drugs prescribed during his/her stay in the ICU.
- Average number of antibiotics prescribed during his/her stay in the ICU.
- Average number of antibiotics prescribed without surgery during his/her stay in the ICU.
- Average number of antibiotics prescribed with surgery during his/her stay in the ICU.
- Most commonly prescribed antibiotics.
- Number of patients who received 10 or more than 10 drugs.
- Minimum number of antibiotics prescribed to the patient.
- Maximum number of antibiotics prescribed to the patient.
- Total number of patients who received more than one antibiotic.
- Total number of patients who received single dose of antibiotic.
- Percentage of patients in which single dose of antibiotic was used in operation.

### Calculation of the average costs of antibiotic use in ICU Department.

The total treatment of antibiotic cost per patient was calculated by the multiplication of the cost per unit and the number of doses that were used in each patient. The unit prices of each antibiotic used was obtained from the hospital pharmacy.

### Statistical Analysis

The results for prescribing indicators was calculated as a percentage as applicable. The data were analyzed using Open Source Epidemiologic Statistics for Public Health, Version 2.2 and Epi Info 4 DOS software. Fisher's exact test (Two sample independent t test) was performed to compare the patient groups.

### RESULTS

The prescriptions of 400 consecutive patients admitted into the ICU were analyzed. This included 255 male and 145 female patients. The average age of the patients was 66.6 years. The average length of stay (LOS) in the ICU was 5.65 days. Total number of patients was discharged

61.75% and expired was 38.25%. A total of 3332 drugs and 699 antibiotic were prescribed in the 400 patients studied, that is an average of 8.33 drugs/prescription and 1.74 antibiotics/prescription. Antibiotics were prescribed on three hundred seventy six patients (94%) at a admission. Antibiotics

constituted 20.97% of total drugs prescribed. 88 patients received more than 10 drugs and 64 patients received 3 or more than 3 antibiotics during their stay in the hospital (ICU Department). The demographic data and patient characteristics studied are as given in Table 1.

**Table 1: Demographic data and patient characteristics**

Variable	Number (n=400)	Percentage
<b>Gender</b>		
Male	255	63.75%
Female	145	36.25%
<b>Age distribution</b>		
0-15	15	3.75%
16-30	37	9.25%
31-45	77	19.25%
46-60	90	22.50%
61-75	137	34.25%
76-90	44	11.00%
<b>Distribution of patients in different specialties</b>		
Neurosurgery	68	17.00%
CTVS	52	13.00%
Orthopedics	49	12.25%
Critical care unit	48	12.00%
Nephrology	23	5.75%
Cardiology	23	5.75%
Neurology	20	5.00%
Surgical oncology unit	20	5.00%
Medical oncology	20	5.00%
Internal medicine unit	19	4.75%
Gastroenterology	12	3.00%
Pulmonology	10	2.50%
General surgery	7	1.75%
Kidney transplant	6	1.50%
Paediatric	5	1.25%
GI surgery and liver	3	0.75%
ENT	3	0.75%
Thoracic surgery	3	0.75%
Gynecology	2	0.50%
Plastic surgery	2	0.50%
Urology	2	0.50%
Vascular surgery	1	0.25%
Hematology	1	0.25%
Radiation oncology	1	0.25%
<b>Length of ICU stay of patients</b>		
1-5	233	58.25%
6-10	146	36.25%

11-15	17	4.25%
> 15	4	1.25%
<b>Outcome from ICU</b>		
Discharged	247	61.75%
Expired	153	38.25%
<b>Drugs prescribed</b>		
1-5	94	23.50%
6-10	208	52.00%
> 10	98	24.50%
<b>Antibiotics prescribed</b>		
0	24	6.00%
1	126	31.50%
2	186	46.50%
3	55	13.75%
4	9	2.25%

Amikacin was the most commonly prescribed antibiotic. The details of most commonly prescribed antibiotics in ICU Patient are given in Fig No1.

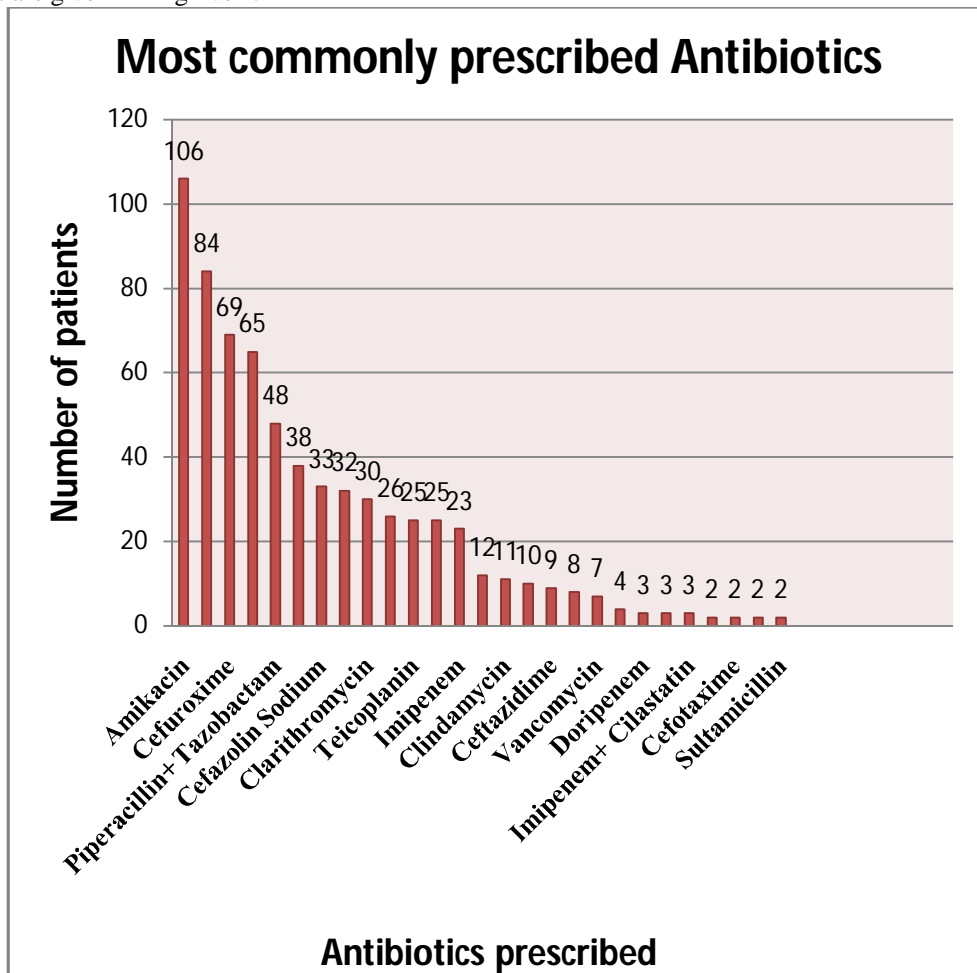


Fig. 1: Most commonly prescribed antibiotics in the ICU Department

141 Surgical Prophylaxis patients out of the 400 patients included in the study, 109 (77.30%) of them have received single dose of antibiotics before surgery which lasted for 4 hours or less. 32 (22.70%) patients received 2 or more than 2 doses of antibiotics before the surgery. Minimum number of

antibiotics prescribed to a patient was 01. Maximum number of antibiotics prescribed to a patients were 04. The details of most commonly prescribed antibiotics for surgical prophylaxis are given in Fig No 2.

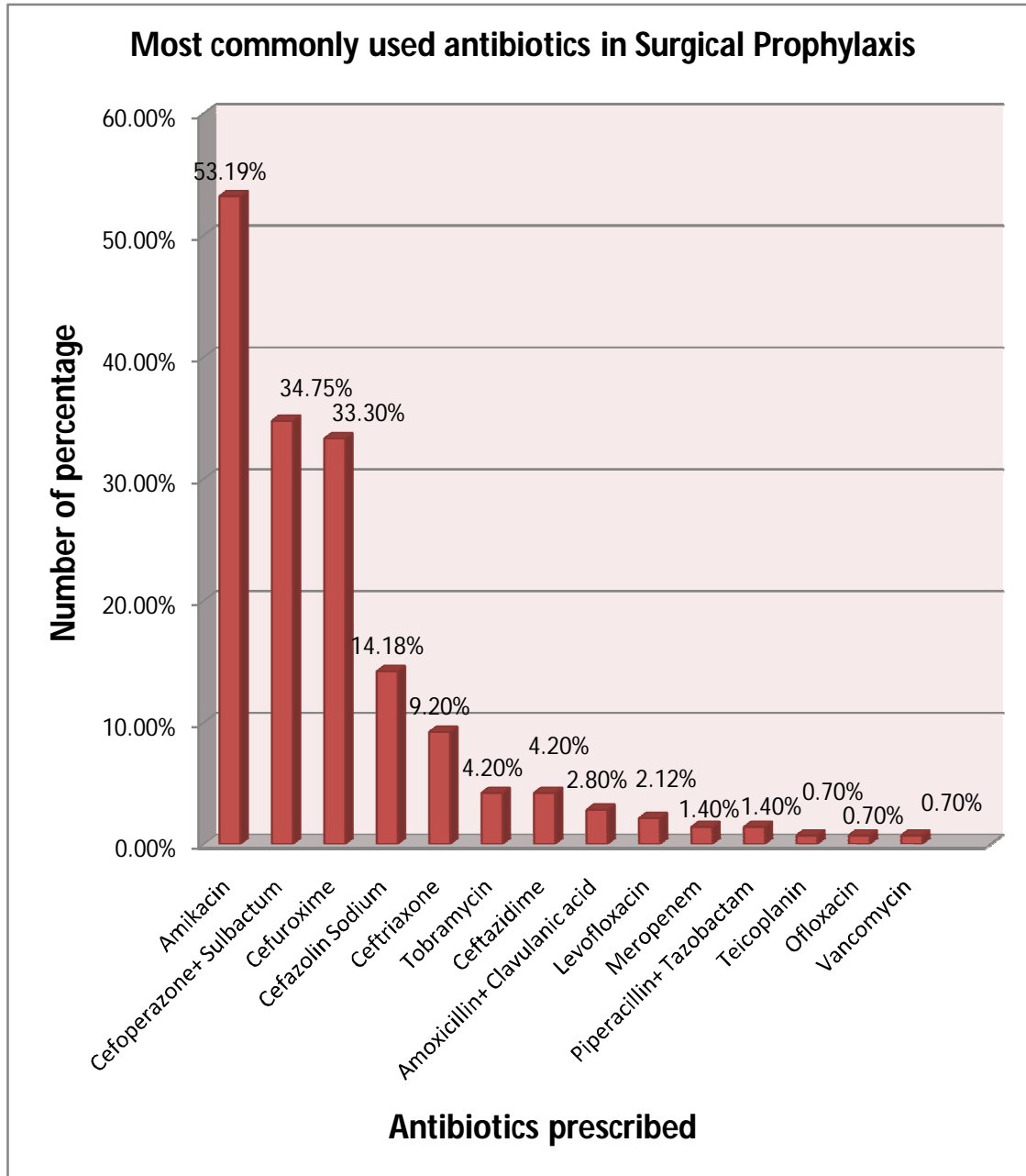


Fig. 2: Most commonly prescribed antibiotics for Surgical Prophylaxis

**The factors affecting the number of antibiotics prescribed in patients.**

The number of patients who were prescribed 1-2 antibiotics did not vary from those prescribed 3 or more antibiotics with respect to their age, gender and

total days of ICU stay. However, the number of antibiotics prescribed significantly correlated with medical and surgical ICU patients. The details of the factors affecting the number of antibiotics prescribed in patients are given in Table No. 2

**Table 2: The factors affecting the number of antibiotics prescribed in patients**

Variables	1-2 antibiotics (n=312)	>3 antibiotics (n=64)	P value
<b>Age (years)</b>			
≤ 45/>45	96/216	18/46	0.7659
<b>Gender</b>			
Male/Female	193/119	47/17	0.0875
<b>Total ICU days</b>			
≤ 5 days/≥ 5 days	175/137	33/31	0.5812
<b>Diagnosis</b>			
Medical/ Surgical	187/125	48/16	0.0238*

\*P value <0.05 is considered significant.

**Calculation of the average costs of antibiotic use in ICU Department.**

The total cost of antibiotics prescribed in all patients was Rs 17,45,961.21, an average of Rs 4364.90/patient. The total cost of all drugs was Rs 25,75,203.00, with an average of Rs 6438/patient. Thus the total cost incurred by antibiotics was nearly

67.79 % of the total drug costs in these patients. Piperacillin+ Tazobactam was the most expensive drug prescribed among these patients ( Rs. 3,70339.84), accounting for 20.97 % of the total cost of antibiotics. The details of Costs of Antibiotic use in ICU Department patients are given in Table No.3.

**Table 3: Costs of Antibiotics use in ICU Department patients**

Name of Antibiotic	Costs(in Rs.)	Percentage
Piperacillin+ Tazobactam	3,70339.84	21.21%
Meropenem	3,16992.00	18.15%
Cefoperazone+ Sulbactam	2,93617.50	16.81%
Teicoplanin	1,41128.00	8.08%
Clarithromycin	99,198.75	5.68%
Ertrapenem	72,000.00	4.12%
Doripenem	65,000.00	3.72%
Imipenem	43,680.00	2.50%
Imipenem+ Cilastatin	34,800.00	1.99%
Ceftazidime	34,374.00	1.96%
Amikacin	28,950.00	1.65%

Ceftriaxone	28,142.80	1.61%
Cefuroxime	27,497.60	1.57%
Vancomycin	22,100.00	1.26%
Linezolid	20,509.50	1.17%
Clindamycin	19,781.00	1.13%
Amoxicillin+ Clavulanic acid	18,256.00	1.04%
Levofloxacin	13,276.80	0.76%
Cefazolin Sodium	8,576.00	0.49%
Ofloxacin	5,149.00	0.29%
Tobramycin	5,005.00	0.28%
Cefaclor	1,598.40	0.091%
Sultamicillin	1,140.00	0.065%
Ciprofloxacin	344.52	0.019%
Cefixime	118.80	0.016%
Cefotaxime	117.96	0.015%
Sulfamethoxazole+ Trimethoprim	19.71	0.010%

**Comparison of the total drug and antibiotic costs with respect to age and diagnosis.**

The average cost of the total drugs prescribed and antibiotics prescribed were significantly lower in younger patient (< 45 years) (p=0.0176 and 0.0302). Although the total cost of antibiotics and drugs was

lower in surgical patients and this was not a statistically significant difference. The details of comparison of the total drug and antibiotic costs with respect to age and diagnosis are given in Table 4.

**Table 4: Comparison of the total drug and antibiotic costs with respect to age and diagnosis**

Variable	Cost of antibiotics	Cost of total drugs
<b>Total</b>	4364.90 (1745961.21)	6438 (2575203.00)
<b>Age</b>		
≤ 45 (n=129)	3764.90 ± 3892.42	5675.15 ± 5441.96
>45 (n=271)	4650.51 ± 4612.17	6801.14 ± 6553.69
<b>P value</b>	0.0302777*	0.0176838*
<b>Diagnosis</b>		
Medical (n=259)	4673.66 ± 4353.15	6675.71 ± 6600.45
Surgical (n=141)	3797.73 ± 4012.54	6001.36 ± 5929.39
<b>P value</b>	0.2836	0.158075

\*P value <0.05 is considered significant.

**DISCUSSION**

Prescriptions of 400 consecutive ICU admissions were audited over a 6-month period to study drug utilization pattern in a tertiary care corporate hospital with special reference to use of antibiotics in ICU Department.

In present study average age of patients was 66.6 years and the average of ICU LOS was 5.65 days. Total number of patients was discharged 61.75% and was expired 38.25%. A study in a Department of Anesthesiology and Critical Care, Christian Medical College, Ludhiana, Punjab, the average age of patient

studied was 49 years with an average LOS of 5.75 days, total number of patient discharged 60.50% and expired 39.50%<sup>6</sup>. A study in a Deenanath Mangeshkar Hospital, Mehendale Garage, Maharashtra, the average age of patient studied was 62.2 years with an average LOS of 8.8 days<sup>7</sup>. A study in a Indira Gandhi Government Medical College and Hospital, Nagpur, the average age of patient studied was 50 years<sup>8</sup>. Drug use patterns study from an ICU in Iran, the average age of patients studied was 50 years with an average LOS of 6 days<sup>9</sup>. A study in a University Hospital in Maastricht, the average duration of patient stay in the ICU was 7 days<sup>10</sup>.

The average number of drugs per prescription is an important index of a prescription audit. It is recommended that the number of drugs per prescription should be kept as low as possible to minimize the risk of drug interactions, development of bacterial resistance, and hospital costs<sup>11</sup>. In our study, 400 patients were enrolled who received 3332 drugs and 699 antibiotics during their stay in the ICU. The average number of drugs and antibiotics prescribed per patient were 8.33 and 1.74, antibiotics constituted 20.97% of the total drug prescribed. There were 98 patients in total who received more than 10 drugs and 64 patients who received 3 or more than 3 antibiotics during their stay in the ICU. There were 24 patients who received without antibiotics during their stay in the ICU. A study in a Department of Anesthesiology and Critical Care, Christian Medical College, Ludhiana, Punjab, 200 patients received 1246 drugs and 418 antibiotics during their stay in the hospital, the average number of drugs and antibiotics prescribed per patient were 6.23 and 2.09, antibiotics constituted 33.54% of the total drug prescribed. There were 14 patients in total who received more than 10 drugs and 51 patients who received 3 or more than 3 antibiotics during their stay in the ICU<sup>6</sup> and other data reported in literature, ranging from 5.1 to 12, according to the type of patient population and the geographical location studied<sup>12,13</sup>.

Most commonly prescribed antibiotics in the present study were amikacin, cefoperazone+sulbactam, cefuroxime, amoxicillin+clavulanic acid and piperacillin+tazobactam. A study in a Department of Biochemistry, Kasturba Medical College, Manipal, India, the most commonly prescribed antibiotics in ICU were Beta-lactams and fluoroquinolones<sup>14</sup>. A study in a Indira Gandhi Memorial Hospital, Shirpur, Maharashtra, the most commonly prescribed antibiotics in ICU were tobramycin, cefuroxime, amikacin, cefoperazone+ sulbactam, amoxicillin+clavulanic and ceftriaxone<sup>15</sup>. A study in a Department of Pulmonology, Khyber Teaching Hospital, Peshawar, the most commonly prescribed antibiotics

in ICU were Penicillin, 1st generation Cephalosporins and quinolones<sup>16</sup>. A study in a Brazilian University Hospital, the most commonly prescribed antibiotics in ICU were cephalosporins, aminoglycosides and fluoroquinolones<sup>17</sup>. A study in a Department of Anesthesiology and Critical Care, Christian Medical College, Ludhiana, Punjab, the most commonly prescribed antibiotics in ICU were 3<sup>rd</sup> generation cephalosporins, levofloxacin, meropenem and ceftriaxone<sup>6</sup>. A study in a Postgraduate Institute of Medical Education & Research, Chandigarh, the most commonly prescribed antibiotics in ICU were cefotaxime, amoxicillin+clavulanic acid, cefipime and ciprofloxacin<sup>18</sup>. A study in a RD Gardi Medical College, Ujjain, the most commonly prescribed antibiotics in ICU were third-generation cephalosporins, aminoglycosides and quinolones<sup>19</sup>.

Our study revealed that a large number of patients were prescribed an antibiotic at admission (94%). A study in a Department of Anesthesiology and Critical Care, Christian Medical College, Ludhiana, Punjab, a number of patients were prescribed an antibiotic at admission 95%<sup>6</sup>. Data from other countries report 60%-75% rates of antibiotic prescription in the ICU<sup>20,21</sup> and studies from Europe report an average antibiotic use of 58%-61%<sup>22,10</sup>. A study in a Department of Clinical Microbiology, Bispebjerg Hospital, University of Copenhagen, Denmark, 615 patients admitted, 434 (71%) received antibiotics, 220 (36%) for infections and 222 (36%) for prophylaxis<sup>23</sup>.

In our audit, most patients (78%) received 2 or less antibiotics. A study in a Department of Anesthesiology and Critical Care, Christian Medical College, Ludhiana, Punjab, most patients (70%) received 2 or less antibiotics<sup>6</sup>. A study in a Caribbean ICU, 60% of the patients received two antimicrobials, 26% received three and 14% of patients were prescribed four or more antimicrobials<sup>24</sup>. A study in a German surgical ICU, 36.7% of cases were treated with only one antibiotic agent, 14.1% were given a combination of 2 and 7.2% were given a combination of  $\geq 3$  antibiotic agents<sup>22</sup>.

The cost analysis of the antibiotics and the total drugs prescribed at admission revealed that patients were prescribed drugs and antibiotics worth nearly Rs 6438 per patient and Rs 4364.90 per patient respectively and antibiotic costs accounted for 67.7% of the total drug expenditure. A study in a Department of Anesthesiology and Critical Care, Christian Medical College, Ludhiana, Punjab, the cost analysis of the antibiotics and the total drugs prescribed at admission revealed that patients were prescribed drugs and antibiotics worth nearly Rs



2725 per patient and Rs 1995 per patient respectively, antibiotic costs accounted for 73.2% of the total drug expenditure and meropenem was the most expensive drug ordered (accounting for 34.7% of the total antibiotic costs)<sup>6</sup>. A study in a Postgraduate Institute of Medical Education & Research, Chandigarh, the patients spent about Rs 19,725 on total drug costs and antibiotics contributed to 51.3% of the total drug expenditure<sup>18</sup>. A study in a Deenanath Mangeshkar Hospital, Mehendale Garage, Maharashtra, the total cost of antibiotics prescribed in all patients was Rs 1455160, an average of Rs 39328 per patient<sup>7</sup>. A study in 2005 in a Manipal Teaching Hospital, Pokhara, Nepal, an average expenditure of Rs 1958.53 ± 1267.8 on the drugs prescribed in ICU<sup>12</sup>. A study in 2010 in a Manipal Teaching Hospital, Pokhara, Nepal, the mean cost per prescription of drugs was 1702.57 ± 1286.4 Nepalese rupees (USD 26.6 ± 20.1) [64 Nepalese rupees = 1 USD]. The mean cost of antibiotics was 681.52 ± 584.3 Nepalese rupees (USD 10.6 ± 9.13). Antibiotics accounted for approximately 40% of the total amount of money spent on drugs<sup>25</sup>. A study in 2007 in a Manipal Teaching Hospital, Pokhara, Nepal, that the mean cost of antibiotics was 13.1 US\$ and flouroquinolone contributed to 36.7% of the total drug cost<sup>26</sup>. A study in a Department of Pharmacy and Therapeutics, University of Pittsburgh, USA, ICU drug costs per patient-day ranging from \$208 to \$312<sup>27</sup>. The costs incurred due to antibiotic usage in blood stream infections in 310 patients in an ICU in Belgium, the mean overall daily antimicrobial cost was €14.25, with higher costs in patients with nosocomial infection<sup>28</sup>. In a Turkish university hospital, the mean daily antibiotic cost was \$89.64, with higher costs for patients with nosocomial infections and meropenem was the most expensive drug for treatment in this group<sup>29</sup>. A study in a Turkish University Hospital, Turkey, the cost of antibiotic therapy of \$1190 per infected patient, accounted for about 75% of the total extra cost<sup>30</sup>. A study in a Turkish University Hospital, Turkey, the daily antibiotic cost of nosocomial infections was \$70 per patient<sup>31</sup>. A study in a French prevalence survey, an average daily antibiotic between FF 520 to 1085 (about \$86 to \$160) per nosocomial infection<sup>32</sup>. A study in a University of Ilorin Teaching Hospital, Ilorin, Nigeria, the mean cost of antibiotics was US\$ 6.72. Average antibiotics make up 72.7% of total cost of drug in a prescription sheet<sup>33</sup>. A study in a Public Hospital in the Capital City of Brazil, the total cost of antimicrobial treatment for all patients was US\$ 1113221.55 along three years. Patients with multi-drug resistant organisms (MDRO) had a greater total cost than patients without it (p= 0.010)<sup>34</sup>. A study in a Department of Internal Medicine, University of

Texas Southwestern Medical Center, Dallas, USA, an average cost of treatment antibiotics \$190 and between \$72 to \$128 per nosocomial infection<sup>35</sup>.

## CONCLUSION

In the present study the drug utilization pattern in tertiary care corporate hospital with special reference to use of antibiotics in ICU Department was observed. The data of 400 patients was evaluated.

Our study reveals that the number of drugs per prescription were much more than required which increased the risk of drug interactions, development of bacterial resistance and the hospital costs.

The results also highlight several areas that need improvements. Most importantly, there is a need to formulate strict antibiotic restriction policy and implement protocols for antibiotic usage in order to streamline the judicious use of these drugs.

Use of antibiotic rotation policies in the ICU, regular audits and feedback reviews are useful tools to check the use of irrational antibiotic therapy in the ICUs. Education of the prescriber is the cornerstone of any successful antibiotic stewardship program and teaching of guidelines and clinical pathways will aid in improving antimicrobial prescribing behavior to a large extent.

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