A Comparison of Antimicrobial usage in ICUs and Wards of a Private Tertiary Care Hospital: A Prospective Study

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ABSTRACT

Introduction: Appropriate use of antimicrobials is the best possible way to safeguard the effectiveness of existing antimicrobials and to reduce the development of antimicrobial resistance. **Objective:** This study aims to evaluate and compare the utilization pattern of antimicrobial drugs in intensive care units (ICUs) and wards of a private tertiary care hospital. **Materials and Methods:** This is an observational prospective study carried out in ICUs and wards of private tertiary care hospital. In-patients receiving at least one antimicrobial agent were included in the study while patients with incomplete information were excluded out of the study. Utilization pattern of antimicrobial drugs was analyzed using RPM plus indicators recommended by World Health Organization. Student's *t*-test was used to determine statistical difference between continuous variables of ICUs and wards. **Results:** The number of patients studied in ICUs and wards was 405 and 561, respectively. In ICUs, the average number of medications prescribed was 13.49 ± 1.41, of which average number of AMDs was 2.49 ± 1.61. While in wards, the average number of medication was 10.51 ± 5.17, of which average number of AMDs was 1.91 ± 1.27. Overall 75% antimicrobials were administered by parenteral route. **Conclusion:** The findings of this study indicate that there is scope of improvement in extent of use of parenteral antimicrobial therapy.

Key words: Antimicrobials, Antimicrobial resistance, Antimicrobial sensitivity test, Intensive care unit, Antimicrobial drug utilization, Prescribing pattern.

INTRODUCTION

Antimicrobial resistance is one of the greatest threats to the global community.[1] On June 25, 2019, WHO had cautioned the world that antimicrobial resistance is an invisible pandemic.[2] It is a matter of concern that there are only limited numbers of new antibiotics which have been granted marketing approval during the last few years.[3] Hence, appropriate consumption of antimicrobials is the best possible way to safeguard the sustained use of existing antimicrobials. Appropriate use of the antimicrobials can help decrease the antimicrobial resistance and prolong their effectiveness through infection control, reducing cost, morbidity and mortality rate.

This study aims to evaluate and compare the utilization pattern of antimicrobial drugs in the intensive care units (ICUs) and wards of a private tertiary care hospital.

MATERIALS AND METHODS

This one year long observational prospective study was carried out at the wards and ICUs of a private tertiary care hospital. The study was approved by institutional ethics committee. In-patients receiving at least one antimicrobial agent were included in the study while patients with incomplete information were excluded out of the study.

Patient information regarding demographics (age, sex), disease (chief complaints, diagnosis and past history), duration of therapy and prescribed medication were collected from case record file by using a predesigned case record form. Patients were followed from date of admission till the time of discharge. Assessment of prescribing pattern was done by using RPM plus indicators recommended by the World Health Organization (WHO).

Results were presented as mean supported with standard error of mean (SEM) and numbers with percentages. Student's *t*-test was used to determine statistical difference between continuous variables of ICUs and wards. SPSS (Statistical Package for the Social Sciences) version 20 was used for performing statistical analysis.

RESULTS

Out of 1000 patients screened during the study period, 966 patients met the inclusion criteria. The data of 34 patients was excluded due to incomplete information. The results, therefore, are based upon a total of 966 patients' data. (Figure 1)

Profile of study population

Out of total 966, data of 561 patients' was obtained from wards while remaining 405 was from ICUs (58.6% vs. 41.9%).

The proportion of male patients in this study was higher than female patients (547 males and 419 females). Of 405 patients in the ICUs, 243 were male while 162 were female. Of 561 patients studied in wards, 304 were male and 257 female.

The average age of patients was found to be 56.43±0.60 years (*n*=966). The average age of female and male patients was 53.80±0.89and 58.40±0.81 years, respectively.

In case of patients from ICUs, the average age was 59.90±0.87 years. The average age of female and

male patients was 57.35±1.31 and 61.30±1.11 years, respectively. While in case of wards, the average age of patient was 53.81 ±0.81 years, (females had 51.32±1.14 and male 61.30±0.99 years).

Patients over 61years of age constituted the largest group (52%); while those under 18 years constituted smallest group of patients (6%).

The average length of stay of patients was 7.0±0.12 days in the overall study. Average length of stay was found to be more in ICUs (8.21±0.30 days) than wards (5.59±0.14 days). Majority of patients (45%) were hospitalized for a period of 1-5 days while only a few number of patients (2%) were hospitalized for >20days.

Close to two-thirds of the patients (66%) had at least 1 comorbidity while 34% patients did not have any comorbidity. Systemic hypertension was the most common comorbidity noted in more than half of patients (53%). It was also found that bronchial asthma and renal impairment were relatively rare comorbidities accounting for 5% and 6%, respectively.

Drug utilization pattern of antimicrobials

Antimicrobial utilization was assessed using RPM plus indicators (Table 1).

The average number of medications prescribed was 11.75±5.48, of which average number of AMDs was 2.10±1.40. It was found that antimicrobial drugs constituted 18% of the total number of medicines prescribed in the hospital. A very large number of antimicrobials were prescribed by their generic name. Half of the antimicrobials were from the National List of Essential Medicines 2015, India. As much as 75%
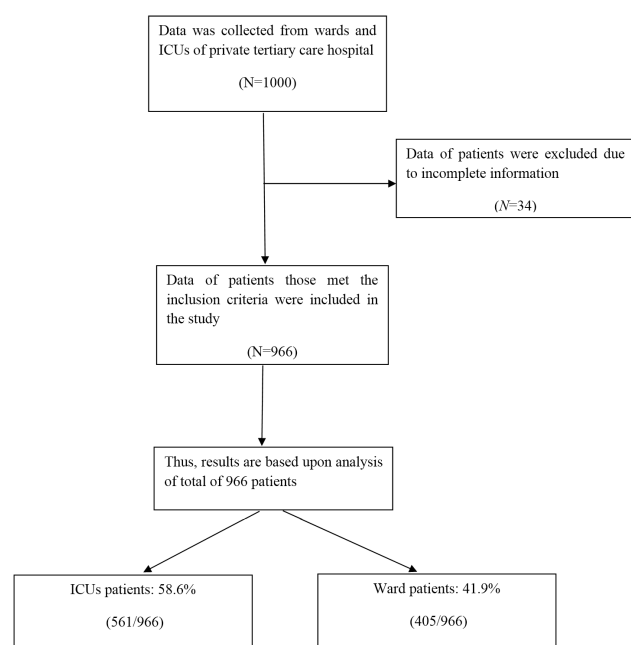

Figure 1: CONSORT Diagram showing enrollment of patients in the study.

Table 1: RPM Plus Indicators (N= 966).

RPM plus indicators	Values
Average number of medications per hospitalization	11.75±5.48
Average number of antimicrobials drugs prescribed	2.10±1.40
Percentage of antimicrobials consistent with National List of Essential Medicines (NLEM) 2015	50%
Percentage of antimicrobials administered by parenteral route	75%
Number of antimicrobials sensitivity tests reported per hospitalization including antimicrobial treatment	52
Percentage of antimicrobials prescribed by generic name	97%

of the antimicrobials were prescribed by the parenteral route. A small number of antimicrobial sensitivity tests (52) were reported per hospitalization.

Antimicrobial drug utilization was further compared between the two subgroups i.e. ICUs and wards (Table 2).

In ICUs, the average number of medications prescribed was 13.40±1.41, of which average number of AMDs was 2.40±1.61. While in wards, the average number of medications was 10.50±5.17, of which average number of AMDs was 1.90±1.27. Total 47.5% AMDs were consistent with NLEM 2015 in ICUs whereas it was 52.7% in wards and this difference was found to be statistically significant. Similarly, a significant difference was observed in number of antimicrobials sensitivity tests reported in ICUs (17) and wards (35).

Antimicrobial Sensitivity Test

Out of 966 patients, cultures of 107 patients from ICUs

and 216 from wards were sent for analysis to the hospital microbiological laboratory. Total 1081 cultures from 323 patients were analyzed. Out of these 1081 cultures, 298 (27%) were collected from ICUs while 783 (73%) from wards and 164 cultures were found to be positive.

Out of these 164 positive cultures, 48/164 (29%) and 116/164(71%) were of ICUs and wards patients, respectively and a total of 52 antimicrobials sensitivity tests were reported. Ward patients were found with more number of sensitivity tests reported i.e. 35 when compared to ICU ones. (Table 3)

Out of 52 sensitivity tests, majority of cultures were found to be resistant. *Klebsiella pneumoniae, Pseudomonas aeruginosa* and *Staphylococcus aureus* were resistant in 100% cultures. *Escherichia coli, Acinetobacter baumanii* and *Enterococcus faecalis* were found resistant in 93%, 86% and 86% cultures, respectively.

Further, *Escherichia coli, Klebsiella pneumonia* and *Pseudomonas aeruginosa* were found multi drug resistant in 16, 12 and 8 cultures, respectively. Extensive drug resistance was also seen in 9, 4 and 3 cultures of *Escherichia coli, Klebsiella pneumonia* and *Pseudomonas aeruginosa,* respectively.

In 114 patients, cultures were found positive, 78% patients (89/114) had monomicrobial infection while 22% (25/114) patients had polymicrobial infection. An infection with a maximum of 5 micro-organisms in a patient was also found in the study. Further, the occurrence of monomicrobial and polymicrobial

Table 2: RPM plus indicators in ICUs and Wards.

#	RPM plus indicators	ICUS N=405	Wards N=561
1	Average number of medications per hospitalization	13.49±1.41	10.51±5.17
2	Average number of antimicrobials drugs prescribed	2.49±1.61	1.91±1.27
3	Percentage of antimicrobials consistent with National List of Essential Medicines (NLEM) 2015	47.5%*	52.7%
4	Percentage of antimicrobials administered by parenteral route	76.5%	72.7%
5	Number of antimicrobials sensitivity tests reported per hospitalization including antimicrobial treatment	17*	35
6	Percentage of antimicrobials prescribed by generic name	96%	97%

*$P<0.05$ between ICUs and wards

Table 3: Distribution of cultures in intensive care units and wards.

Antimicrobial sensitivity test	ICUs	Wards	Total
Numbers of patient in which culture sent	107 (33%)	216(67%)	323 (100%)
Total cultures analyzed	298(27%)	783(73%)	1081 (100%)
Positive cultures	48(29%)	116(71%)	164 (100%)
Sensitivity test	17(33%)	35(67%)	52 (100%)

Table 4: Prescribing pattern of AMD in intensive care units and wards.

Class of AMD	ICU (%)	Wards (%)
Beta –lactams	50.09	59.47
Sulfonamides	0.29	0.65
Tetracyclins	1.28	0.28
Lincosamide	0.59	0.84
Glycopeptide and Polypeptide	11.04	3.73
Nitroimidazoles	5.63	7.65
Aminoglycoside	4.34	7.37
Fluoroquinolonees	3.16	4.90
Oxazolidinones	1.08	0.56
Nitrofurans	0.19	0.46
Macrolides	5.03	2.52
Azoles and other antifungal agents	6.92	2.89
Nicotinic acid derivative	0.29	0.56
Diaminopyrimidines	0.69	0.28
Others	9.38	7.84
Total	100	100

infection in patients of ICUs (78) was twice the number in wards (36).

Prescribing pattern of antimicrobials

A total of 2083 AMDs were prescribed in 966 patients. AMDs prescribed in wards were 1071/2083 (51%) while in ICUs were 1012/2083 (49%).

Prescribing pattern was further analyzed for different classes of antimicrobials (Table 4). Most frequently prescribed antimicrobial class was beta-lactams (55%). Other common classes of antimicrobials prescribed were glycopeptides and polypeptides (6.8%) and nitroimidazoles (6.6%).

40% of patients were prescribed single antibiotic, while 31%, 15%, 7% and 6% had two, three, four and five or more antibiotics prescribed, respectively.

Within beta-lactams, the most commonly prescribed were cephalosporins followed by penicillins and carbapenems. Within cephalosporins, cefuroxime and ceftriaxone accounted for 58.7% and 27.7% of total times cephalosporins were prescribed, respectively.

Beta-lactams were also most commonly prescribed class in both sub-groups i.e. ICUs (50%) as well as wards (59.4%). In ICUs, second most commonly prescribed class after beta-lactams was glycopeptides and polypeptides (11%), followed by azoles and antifungals (6.9%), nitroimidazoles (5.6%) and macrolides (5%). In the wards, nitroimidazole group (7.6%) was the second most commonly prescribed class, closely followed by aminoglycosides (7.3%) and fluoroquinolones (4.9%).

Cefuroxime was prescribed twice the number in wards (287) when compared to ICUs (124). Use of last line antibiotics such as colistin, teicoplanin, polymixin B and colistimethate was found more than twice in ICUs than wards. More admissions of patients with infectious and critical conditions in ICUs can be the reason for it.

The most commonly prescribed fixed dose combination was piperacillin and tazobactam (7.05%), followed by amoxicillin and clavulanate (5.04%) and cefoperazone and sulbactum (1%).

DISCUSSION

The results of present study are based on data of 966 patients. The proportion of male patients in the study has been higher (1.32:1); however, the authors do not relate this to any findings reported here.

In this study, the average number of AMDs prescribed was found to be 2.10±1.40. In similar studies, Chippa *et al.* Tiwari *et al.* Randad *et al.* and Singha *et al.* reported 2.73, 3.1, 3.5 and 1.26 as average number of AMDs prescribed, respectively.[4-7] Tiwari *et al.* reported it nearly in the same population size as this study, while Chippa *et al.* Randad *et al.* and Singha *et al.* reported it nearly in one fourth of sample size compared to this study.[4-7]

The average number of medications prescribed per hospitalization was 11.75±5.48 in this study. More than half of patients were elderly patients (≥61 yrs). Use of multiple medication increases the risk of polypharmacy along with occurrence of adverse drug event, especially in elderly population.[8-10] Further, polypharmacy has number of drawbacks like high health care costs, prescribing cascades and poor patient compliance.[11,12] Singha *et al.*,[7] Meher *et al.*,[13] Mittal *et al.*[14] and Ahmad *et al.*[15] reported 2.9, 4.2, 3.6 and 2.74 as average number of medications in sample sizes that were one fourth of this study. This was reported to be 12.26±0.83 and 15.68±1.44 in CCU and MICU of a private tertiary care hospital by Tiwari *et al.*[5]

In this study, average number of AMDs and medications per hospitalization were found to be higher in ICUs than wards. More number of critical patients with high comorbidities in ICUs as compared to wards could be the reason for it.

Half of the antimicrobials prescribed in this study were found to be consistent with NLEM 2015, which is less when compared to the study of Mittal *et al.* (78.4%) which had a sample size of one fourth of this study.[14] While, it is comparable to findings of Tiwari *et al.* in private hospital setting, which reported 56.3% and 70% adherence of AMDs with NLEM 2015 in CCU and MICU, respectively in sample size half of this study.[5] Drugs listed in the NLEM offer high quality care with the effective utilization of health resources. Thus, this is advisable to promote adherence of the prescription to the NLEM.

A statistically significant difference was found in adherence of the antimicrobials to the NLEM 2015 in between ICUs and wards.

Total 75% of prescribed antimicrobials were parenteral in this study. The results of a similar study by Dharmshaktu *et al.*[16] (71.9%) are in concurrence with this study while Gowthami *et al.*[17] (80.1%) and Singha *et al.*[7] (91%) reported higher use of parenteral antibiotics as compared to this study. Prescribing of parenteral AMDs were more in ICUs (76.5%) than wards (72.7%) to achieve immediate physiological response and it is also helpful in

unconscious, uncooperative and nauseous patients which were seen mostly in ICUs.

Prescription by generic name was found to be in 97% patients in this study. No significant difference was found for this indicator in between ICUs (96%) and wards (97%). Sharma *et al.*[18] (30%), Jain *et al.*[19] (28.8%), Meher*et al.*[13] (11%), Mittal *et al.*[4] (21.5%) and Singha *et al.*[7] (86.5%) reported low generic prescriptions. Generic prescription should be promoted as it helps in reducing cost related non-adherence along with prescription, dispensing and administration errors in the hospital.

In this study, AMDs prescription was 18% (2,083/ 11,346) of the total number of medicines prescribed in the hospital. Findings of Ahlawat *et al.*[19] (15%) are in concurrence with this, while Thiruthopu *et al.*[20] (33.29%), Tiwari *et al.*[5] (41.9%) and Mittal *et al.*[14] (60%) have reported higher prescription of AMDs with respect to current results.

The most commonly prescribed class was found to be beta-lactams (55%) followed by glycopeptides and polypeptides (6.8%) and nitroimidazoles (6.6%). Findings of Sharma *et al.* (51.4% beta-lactams) are also similar to this study.[18] Cephalosporins are known to be the drug of choice for empirical therapy of common infectious diseases and complications in ICUs. So, among beta-lactams, cephalosporins followed by penicillins were frequently prescribed subclasses, which was similar to findings of Singha *et al.*[7] Gowthami *et al.*[17] Ahmad *et al.*[15] and Prabahar *et al.*[21] studies.

In ICUs as well as wards, beta-lactams were most prescribed class and cefuroxime was most frequently prescribed AMD. Cefuroxime was mainly prescribed for surgical prophylaxis in knee replacement cases.

Total 40% of patients were prescribed with a single antibiotic whereas the remaining 60% were prescribed two or more antibiotics. Other studies like Mittal *et al.*[14] and Ghosh *et al.*[22] reported single antibiotic prescription as 45.7% and 33.17%, respectively.

CONCLUSION

The results have demonstrated a satisfactory generic name prescription in this study. Point of concern in this study is the high rate of number of medications prescribed along with high rate of parenteral AMDs. Adherence to NLEM 2015 also has scope to improve. Findings of this study could help in encouraging appropriate use of antimicrobials in future.

ACKNOWLEDGMENT

CONFLICT OF INTEREST

None.

ABBREVIATIONS

NLEM: National List of Essential Medicines; **ICU:** Intensive care unit; **WHO:** World Health Organization; **AMD:** Antimicrobial drugs; **SPSS:** Statistical Package for the Social Sciences; **RPM:** Rational Prescription Management; **CCU:** Coronary care unit; **MICU:** Medical intensive unit

SUMMARY

Surveillance of antimicrobial usage is primary step in combating antimicobial resistance. In this study, we evaluated and compared the utilization of antimicrobial drugs in between ICUs and wards using RPM plus indicators recommended by World Health Organization. Consumption of antimicrobials was more in ICUs when compared to wards. Beta-lactams were most frequently prescribed class, followed by glycopeptides and polypeptides. Within beta-lactams, the most commonly prescribed were cephalosporins followed by penicillins and carbapenems. The cultures were found resistant to *E. coli, Klebsiella pneumonia, Pseudomonas aeruginosa, Staphylococcus aureus, Acinetobacter baumanii and Enterococcus faecalis.* Appropriate use of antimicrobials is the best possible way to reduce the development of antimicrobial resistance.

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