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DRUG UTILIZATION STUDY IN MEDICAL INTENSIVE CARE UNIT IN A TERTIARY CARE TEACHING HOSPITAL IN SOUTH INDIA

Pharmacology

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ABSTRACT

Aim: This study aims to evaluate the drug utilization pattern in the medical intensive care unit. **Materials And Methods:** Case papers of patients admitted to MICU between December 2022 to November 2023 were analyzed for demographic variables; indications; duration of MICU stay; and proportion of common drugs used. The use of antimicrobials was evaluated based on the culture report and empirical regimen used. A defined daily dose (DDD)/100 bed-days was calculated. The cost of drugs was calculated from Indian Drug Review (2023). **Results:** A total of 253 cases were admitted to MICU during the study period with a mean age of 44.62 years (95% confidence interval [CI]: 42.56-46.69). The average duration of MICU stay was 5.12 days (95% CI: 3.79-5.51). The average number of drugs prescribed per patient was 13.04 (95% CI: 12.05-14.04). Total drug utilization in terms of DDD/100 bed-days was 225.27. Metronidazole, cefotaxime, atropine, adrenaline, dopamine, dobutamine, metoclopramide, and furosemide were prescribed in more than 40% of cases. Number of antimicrobials prescribed per patient was 2.60 (95% CI: 2.37-2.66). Cefotaxime + metronidazole (27.50%) was the most common empirical regimen used. Average cost of treatment per patient was Rs. 3315.70 (95% CI: Rs. 2749.8-Rs. 3701.6) **Conclusion:** In a teaching hospital, it is imperative to have robust prescribing guidelines which is indispensable to rational prescription and ultimate patient safety. Such types of studies when done periodically and regularly will provide continuous and regular data on prescribing practices in the hospital and help in formulating the guidelines for the same that will eventually lead to better patient care.

KEYWORDS

Antimicrobial resistance, critical care unit, drug utilization research, pharmacoeconomic, pharmacoepidemiology

INTRODUCTION:

A drug utilization study is defined as "The marketing, distribution, prescription, and use of drugs in a society, with special emphasis on resulting medical, social, and economic consequences".[1] Drug utilization evaluation studies reflect the clinical use and also help in assessing its impact on the health-care system.[2] in a setup like the Intensive care unit (ICU) multiple medications are prescribed to patients of varying diseases where often similar kinds or classes of drugs are prescribed to different times of patients. The patients admitted to ICU are often critically ill and end up using higher resources both medically and financially.[3] The drugs used in ICU are often drugs of high cost such as the latest antimicrobials, targeted drugs, immunoglobulins, etc, or the drugs of last resort which are usually highly-priced. In such conditions, especially in developing countries where it is inevitable to overlook these difficulties, it is important to realize the role of rational prescription as it will help in developing strategies to lessen the number of medications that patients will need and also reduce the cost of treatment.[4] Use of multiple medications which is also known as polypharmacy has many disadvantages such as drug interactions which can result in adverse drug reactions, increased cost of treatment, resistance to antimicrobials, and ultimately treatment failure. Therefore, it is important to conduct such studies periodically to keep a check on prescribing patterns and growing antimicrobial resistance which will lead to better patient outcomes. These studies will also help in optimizing the healthcare system and the proper use of resources.[5]

In this study, we aim to study the drug utilization pattern of the medical intensive care unit MICU of our hospital. This is done by calculating DDD which is the "Daily Defined Dose" for the drugs used in MICU. DDD is defined as "The assumed average maintenance dose per day for a drug used for its main indication in adults".[6,7] An important tool to compare drug utilization among different clinical setups within a country and between different countries is DDD. A rough estimate of drug consumption in hospital inpatients is DDD/100 bed-days. It is a fixed unit of measurement independent of formulation and price. An important aim of drug utilization is to monitor rational as well as irrational drug use as an important step in improving the quality of drug use.

MATERIALS AND METHODS.

We carried out a retrospective study of the past year i.e. from December 2022 to November 2023 in our hospital after taking ethical committee clearance for the same. The data was collected from the medical records section of the MICU department. The data was manually extracted and entered into the Microsoft Excel sheet for tabulation and analysis. The details that were taken down were age, gender, diagnosis, duration of stay in MICU, treatment provided, and lab investigations done. The data that was specifically looked for were adverse drug reactions and antimicrobial sensitivity reports if any.

The data that was analysed were; The demographic variables of the patients, indication of admission in MICU, duration of MICU stay, total number of drugs prescribed per patient, particulars of each drug prescribed (group and indication), the total number and types of antimicrobials used and use of life saving emergency drugs such as inotropes, used per patient, use of fixed dose combinations (FDCs), no of drugs prescribed by generic and brand names, No. of oral and parenteral formulations used, a list of three costliest drugs used; organisms isolated and their antimicrobial sensitivity, and the outcome of the patient. The total cost of drugs per patient was calculated from the Indian Drug Review (2023). The total cost of laboratory investigations per patient was calculated according to the price list of our hospital. The drugs were classified according to the Anatomical Therapeutic Chemical classification based on their chemical, pharmacological, and therapeutic properties. The drug utilization was measured in DDD/100 bed-days.[7] A bed day is a day during which a person is confined to a bed and in which the patient stays overnight in a hospital. With access to drug utilization statistics based on the ATC/DDD system, it is possible to construct simple indicators reflecting the quality of prescribing or drug use.

DDD/100 bed-days were calculated using the following equation:

$$\text{DDD/100 bed-days} = \frac{\text{No. of units administered in a given period} \times 10}{\text{DDD} \times \text{number of days} \times \text{number of beds} \times \text{occupancy index}}$$

$$\text{where Occupancy index} = \frac{\text{Total inpatient service days for a period} \times 100}{\text{Total inpatient bed count} \times \text{number of days in the period}}$$

In our MICU, bed strength was 20, and the average bed occupancy index was 0.8 during the study period.

Statistical Analysis

The descriptive statistics were used for data that were expressed as

proportions and mean (95% confidence interval [CI]), Comparisons of the total number of drugs prescribed per patient, duration of MICU stay, cost of total treatment, antimicrobials, inotropes and other drugs used per patient were performed using the Kruskal-Wallis test followed by Dunn's multiple comparison tests between patients admitted in MICU. The same parameters were compared between survived and expired patients using the Mann-Whitney *U*-test. Statistical comparison was performed by using SPSS version 20. $P < 0.05$ was considered to be statistically significant.

RESULTS:

A total of 253 case files of patients admitted to MICU were extracted and scrutinized for the required data after screening the files for appropriateness and completeness of data. Out of these 105 (41.50%) patients were between 18 and 49 years and 148 (58.49%) patients were above 49 years of age group. The mean age of admitted patients was 44.62 years (95% CI: 42.56-46.69 years). A total of 151 (59.68%) patients were male and 102 (40.31%) were female. The common indications for admission were chronic kidney disease (12.21%), COPD with respiratory failure (14.26%), gastrointestinal complications (14.08%), cardiovascular emergencies (40.23%), and organophosphate poisoning (15.03%). A total of 110 (43.47%), 86 (33.99%) and 57 (22.52%) patients had one, two, and more than two system involvement respectively. Cardiovascular (40.23%) was the most commonly involved system followed by respiratory failure (14.26%), gastrointestinal (14.08%), and renal (12.21%). Other diagnoses include hematology and endocrine disorders.

The average duration of MICU stay was 5.12 days (95% CI: 3.79-5.51 days). A total of 4927 drugs (87.98% parenteral and 12.02% oral formulations) were prescribed in all patients. A total of 218 different drugs were prescribed out of which only 53% of drugs were prescribed by their generic names. fixed drug combinations were prescribed in 9 % of patients. A minimum of 4 drugs were prescribed to any patient and the maximum number went up to 25 by the time patients were discharged or expired. The average number of drugs prescribed per patient was 13.04 (95% CI: 12.05-14.04). Total drug utilization in MICU during the study period in terms of DDD/100 bed-days was 225.27. Metronidazole, cefotaxime, ceftriaxone, atropine, adrenaline, dopamine, dobutamine, etofylline + theophylline hydrate, pantoprazole, metoclopramide, and furosemide were prescribed in more than 40% of patients. Amoxicillin, ciprofloxacin, noradrenaline, hydrocortisone, Sorbitrate, nitroglycerin, aspirin and were used in 10-30% of patients. The utilization pattern of various drugs and DDD/100 bed-days is shown in Table 1. The most commonly prescribed FDCs are shown in Table 2. The antimicrobials were prescribed to 245 (96.83%) patients and inotropes were used in 226 (89.32%). The average number of antimicrobials prescribed per patient was 2.60 (95% CI: 2.37-2.66). The average number of antimicrobials prescribed was significantly higher in expired than survived patients (2.70 [95% CI: 2.61-2.30] vs. 1.85 [95% CI: 1.7-2.06]; $P < 0.05$). The average number of inotropes prescribed per patient was 1.63 (95% CI: 1.49-1.75). 49 different antimicrobials were used. Cefotaxime with metronidazole (27.50%), ceftriaxone with metronidazole (18.98%), cefotaxime with gentamicin (9.78%) and ceftriaxone with gentamicin (4.63%) were the commonly used empirical regimens. The antibiotic sensitivity testing was performed in 52 (20.55%) patients. A total of 20 organisms were isolated in 18 (34.61%) patients. Change in antibiotic was performed in 12 cases (66.66%) based on isolated organisms and their sensitivity pattern. Isolated organisms were *Klebsiella* (35%), *Pseudomonas* (23%), *Escherichia coli* (14%), *Staphylococcus aureus* (8%), *Candida* (10%), *Proteus vulgaris* (6%) and *Acinobactum* (4%). Among 50% of cases, S. aureus was sensitive to penicillin, oxacillin, cefazoline, ciprofloxacin, roxithromycin, tobramycin, amoxicillin + clavulanic acid, chloramphenicol and rifampicin.

Table 1: Utilization Pattern Of Various Drugs In MICU, DDD/100 Bed Days, And ATC Code

Drugs	Total (n=396)	DDD/100-bed days	ATC Code
Antimicrobials (total DDD/100bed days=36.54)			
Metronidazole	220 (55.68)	10.95	J01XD01
Cefotaxime	189(47.84)	5.52	J01DD01
Ceftriaxone	102(25.54)	7.43	J01DD04
Ampicillin	35(9.29)	1.40(p), 0.45 (o)	J01CA01
Cloxacillin	08 (2.21)	0.60 (p), 0.03) (o)	J01CF02
Ciprofloxacin	55(14.10)	5.64	J01MA02
Gentamicin	54(13.28)	1.29	J01GB03
Anticholinergic drugs (total DD/100 bed days=32.80)			
Atropine	292 (74.05)	68.64	N04AC01
Inotropes (total DD/100 bed days=32.80)			
Adrenaline	245 (61.80)	21.44	C01CA24
Dopamine	196 (49.90)	8.20	C01CA04
Dobutamoine	157 (40.01)	5.23	C01CA07
Nor adrenaline	67 (18.06)	2.09	C01CA03
Corticosteroids (total DDD/100 bed days=16.86)			
Hydrocortisone	65 (18.87)	18.90	H02AB09
Respiratory drugs (total DD/100 bed days=32.80)			
Etofylline+theophylline hydrate	145 (37.23)	11.02	R03DA54
Cardiovascular drugs ((total DD/100 bed days=32.80)			
Furosemide	145 (38.34)	15.26	C03CA01
Aspirin	46 (11.90)	2.23	B01AC06
Atorvastatin	26 (7.21)	1.89	C10AA05
Sorbitrate	23 (6.01)	1.78	C01DA08
Clopidogrel	17 (3.99)	1.22	B01AC04
Amiodarone	14 (3.30)	0.67	C01BD01
Amlodipine	13 (3.04)	0.72	C08CA01
Metoprolol	11 (2.54)	0.11	C07AB02
Digoxin	08 (2.13)	0.29	C01AA05
Gastrointestinal drugs (total DD/100 bed days=32.80)			
Metoclopramide	135 (34.15)	5.47	A03FA01
Pantoprazole	68 (16.98)	6.23	A02BC02
Ondansetron	35 (8.59)	0.86	A04AA01
Omeprazole	24 (5.81)	0.11 (p), 2.49 (o)	A02BC01

Table 2: Most Commonly Prescribed FDCs

FDC	No. of patients (%)
Piperacillin + tazobactum	125 (49.40)
Multivitamin injection	46 (18.10)
Cefoperazone + Sulbactam	25 (9.88)
Folic acid + niacinamide +vitamin B12+vitamin C	35 (13.83)
Amoxicillin + clavulanic acid	75 (29.64)

The average total cost of treatment per patient was Rs. 3315.70 (95% CI: Rs. 2749.8-Rs. 3701.6). The average total cost of antimicrobial drugs per patient was Rs. 1452.92 (95% CI: Rs. 1056.3-Rs. 1671.6). The average total cost of inotropes per patient was Rs. 271.62 (95% CI: Rs. 223.32-Rs. 301.30). Human-albumin, meropenem, imipenem+cilastin, piperacillin + tazobactum and enoxaparin sodium were the costliest drugs used in MICU. The average total cost of laboratory investigations per patient was Rs. 1498.39 (95% CI: Rs. 1379.3-Rs. 1663.5). Total 274 (69%) patients were expired. The mortality rate for patients admitted to MICU was 71.58%. The most common cause of mortality was septicemia (21.91%).

DISCUSSION:

We evaluated 253 cases admitted in the 20-bed MICU of our hospital. Male preponderance (59.68%) is observed and male: female is in accordance with the previous reports. The average age is lesser than the previous reporting.[1,4,5] The most common indication for admission was complications of cardiovascular diseases whereas previous studies had reported more admissions in Intensive care due to cancer, septicemia, and chronic obstructive pulmonary disease.[1,4,8] Complicated cases of acute abdomen (25.35%), and chronic kidney disease were the other causes that were recorded in previous studies.[1,8]. A total of 43.47% of patients were having more than one illness, which is similar to other published reports.[4] The average duration of MICU stay (5.12 days) is similar to Shankar *et al*. (2005).[4] and Yamashita *et al*. (2000).[9] and lower than the Shankar *et al*. (2010),[1] and Curcio *et al*. (2011)[5] Use of brand names (45.77%) and FDCs (7.21%) are comparatively lower in our study.[1,3] However, the use of parenteral drugs (86.57%) is higher than previous studies.[1,4,8]

The average total number of drugs prescribed per patient is higher than the reported in other studies.[1,3,4,8] However the use of a total number of drugs and parenteral preparations may be proportionate to the condition and diagnosis of patients admitted under different scenarios. Antimicrobial drugs (94.45%), anti-peptic ulcer drugs (89.67%), and

inotropes (71.79%) were the commonly utilized groups similar to John *et al*.[3] However, cardiovascular drugs were the most commonly used therapeutic class in our study also as in the other previous studies.[8,10,11] Aggressive use of anti-peptic ulcer drugs was to prevent stress-induced ulcers. Atropine was used in patients of organophosphate poisoning, as a premedication and for bradycardia in late stages of septic shock to counter bradycardia, cardiac hypo-oxygenation, and hypoperfusion.[12] Adrenaline was mainly used for cardiac resuscitation. Dopamine, dobutamine, and noradrenaline were used in combination with intravenous fluids for the patients of septic and cardiogenic shock. They were used to restore cardiac output, tissue perfusion, and oxygenation. The selection of individual inotropes was mainly empirical.

Cephalosporins (73.30%), metronidazole (55.67%), and penicillins were the most commonly prescribed antimicrobials similar to previous studies.[3,4,8,9,10] However, aminoglycosides, meropenom, fluoroquinolones, and piperacillin + tazobactum were also commonly utilized antimicrobials in other studies.[1,5] In our study, linezolid, meropenem, vancomycin, netilmicin, and tobramycin were used as second-line antimicrobials. The most common isolated organism in our study is *Klebsiella*. Other studies had reported *Pseudomonas*,[13,14,15] *E. coli* [1,4,16]and *S. aureus*.[9] Our study showed lower utilization of antibiotic sensitivity testing than Shalini *et al*.[17]. And this also reflected in the difficulty to suggest the empirical antimicrobials for admitted patients due to underutilization of antibiotic sensitivity testing. The antimicrobial combination forms the different classes that should be considered for septicemia due to high mortality. The selection of an initial appropriate antibiotic regimen is important for reducing mortality. The empirical combination antibiotic regimen directed against Gram-negative bacteria (carbapenem plus aminoglycoside or fluoroquinolone) reduces the initial inappropriate selection as compared to monotherapy alone. Aminoglycosides offer broader coverage than fluoroquinolones as combination agents for patients with this serious infection.[18] The combination of carbapenems and aminoglycosides can be preferred in patients with severe sepsis and septic shock.[19] There is an urgent need to enhance the utilization of antibiotic sensitivity testing for the better selection of antimicrobials and reduction of mortality. Avoiding the use of unnecessary antibiotics helps to improve patient outcomes.[20] In the present study, patients had spent approximately 40% of the total cost on antimicrobials. Preparation of an antibiotic use policy helps in the reduction of nosocomial infections and has a positive impact in the form of cost reductions.[21,22] The average cost of treatment prescribed per patient [Rs. 3558.09] is higher in comparison with two studies by Shankar *et al*.[1,4] However, the cost of treatment was lower than Biswal *et al*. from India and Inan *et al*. from Turkey.[10,13] Biswal *et al*. performed a study in the advanced referral center of India. Differences in the mean cost of treatment in our study than other studies may be due to variations in the type and severity of the admitted patient, indications for the admission, different prescribing patterns, or changes in currency differences of various countries. Patients with medical + surgical indications have spent more money on the overall treatment. This is because of the use of higher-expenditure medications. They have also spent more money on antimicrobials. The cost for the treatment, antimicrobials, and inotropes are higher in expired patients.

This study has certain limitations. Being a retrospective nature it was not possible to assess the rationality and quality of prescriptions. However, it helps to create a drug utilization database in a tertiary care teaching hospital in a developing country lacking separate medical and surgical intensive care units. These data provide no direct link with the outcomes associated with the use of the various categories of drugs. The line of treatment and selection of drugs varied from physician to physician and it provided no data for the same.

CONCLUSION:

In conclusion, in our study, we found that antimicrobial drugs were the most commonly prescribed drugs in the MICU followed by inotropes and other supportive drugs. In a teaching hospital, it is imperative to have robust prescribing guidelines which is indispensable to rational prescription and ultimate patient safety. Such types of studies when done periodically and regularly will provide continuous and regular data on prescribing practices in the hospital and help in formulating the guidelines for the same that will eventually lead to better patient care.

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