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Study the Existing Prescription Pattern of Antimicrobial Agents and Data for Improvement of Intensive Care Unit at Tertiary Heath Care Centre

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ABSTRACT
Antibiotics are the most commonly prescribed drugs by various health care professionals. The use of antimicrobials has reduced the incidence of deaths due to various critical infectious diseases. Use of antimicrobial agents (AMAs) forms an important aspect of intensive care units. Infections caused by antimicrobial-resistant micro-organisms, Irrational use of antibiotics, high cost and less availability of antimicrobials in ICUs in hospital are the various factors which affect the patient's outcomes in government hospitals. The study was conducted in Intensive Care Units of a tertiary health care centre for a period of 18 months. Relevant data of 400 patients was collected from the intensive care units. Drugs prescribing data of antimicrobials was collected. All the data collected was entered in a pre-approved case record form and tabulated using Microsoft Office Excel Software. The frequency of age distribution of the study subjects. Majority of patients were in the age group of 50 years. 306 (76.5%) were prescribed more than 5 drugs, 94 (23.3%) were prescribed less than 5 drugs for the treatment. 68.3% of the patients (n = 273) received a single AMA, whereas 31.8% of subjects (n = 127) required concurrent use of two or more antimicrobials during management in Intensive care units. Most frequently used drugs include Cefotaxime 69.0% (n = 276), metronidazole 29.0% (n = 116), ceftriaxone 7.0% (28), gentamycin 7.0% (28) and ciprofloxacin 5% (n = 20). Empirical therapy with appropriate combinations of commonly used AMAs can be very effective in preventing or controlling various nosocomial infections and significantly contribute in reducing the mortality and improving the survival without producing serious adverse effects or interactions.

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Key Words
Antimicrobial, ICU, Antibiotics, AMA's, infections

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INTRODUCTION

The discovery of antibiotics is one of the greatest milestones in the 20th century. Antimicrobials are useful in control and cure of many infectious diseases[1]. These are the most commonly prescribed drugs by various health care professionals. Nowadays antimicrobials have been recognized as double-edged sword, on one side being the appropriate use and availability of antimicrobials which allows the improvement of infectious disease while on the other hand excess use/misuse can cause adverse drug reactions (ADRs), antimicrobial resistance[2]. Use of antimicrobial agents (AMAs) forms an important aspect of intensive care units, either for prevention or control of infections, as critically ill patients are more susceptible for infections due to immobilization, invasive procedures, (i.e., tapping, catheters, intubation etc.), compromised immune status, and exposure to cross infections. The widespread consumption of antimicrobial agents especially broad-spectrum ones may reflect the physician's concern and the need for effective therapy for severely ill patients. Additionally, it cannot be dissociated from the worldwide problem of antimicrobial resistance (AMR)[3-5]. The incidence and prevalence of multidrug-resistant (MDR) organisms are so high in the hospital settings that even very effective drugs like fluoroquinolones, cephalosporins, aminoglycosides, etc., are fast losing their utility in covering hospital pathogens, thus strictly restricting the choice of AMAs for treating serious infections.

Intensive care units in hospitals are crowded with many patients like severe critical illnesses, which necessitate the use of broad spectrum antimicrobials (empirical therapy) immediately. This can be achieved by either de-escalation or escalation, or targeted therapy with culture and Sensitivity reports. The study of prescribing patterns seeks to monitor, evaluate and suggest modifications in practitioner's prescribing habits so as to make the prescriptions more rational and cost effective. The inappropriate use of antimicrobial agents (AMAs) has been noticed all over the world. Even for trivial infections of viral etiology, an increasing trend is noticed for use of combinations, broad spectrum and newer generation antimicrobial[6-8]. Rational use of a drug means the appropriate drug receive by patients, in doses that meet individual requirements, for an adequate period of time at the lowest cost[9]. Irrational drug use has been found to have definite impact on the quality of care, cost of therapy and incidence of adverse drug reaction[10]. In developing countries, the cost of health care is a matter of major concern[11]. Infections caused by antimicrobial-resistant micro-organisms, Irrational use of antibiotics, high cost and less availability of antimicrobials in ICUs in hospital are the various factors which affect the patient's outcomes in government hospitals. Despite the constructive guidelines from regulatory and professional bodies, very few hospitals have implemented antimicrobial policies, therefore warranting extensive studies for further evaluation and critical appraisal of the existing situation. In view of emerging worldwide threat of bacterial resistance, there is increasing need to identify determinants and patterns of antimicrobial prescribing. Hence, the above study was undertaken to study the existing prescription pattern of antimicrobial agents and data for improvement of Intensive care unit at tertiary heath care centre.

MATERIALS AND METHODS

Study place: The study was conducted in Intensive Care Units of Brims teaching hospital, Bidar for a period of 18 months (January 2022 to June 2023).

Study design: Prospective observational study.
Inclusion criteria-Patients age >18 years, belonging to both the genders, admitted in intensive care units receiving one or more antibiotics and ready to give informed consent.

Exclusion criteria: Patients age <18 years, pregnant and lactating women, Patients with systemic and local malignancy and patients who refuse to give informed consent for participation.

Sample size: 400 patients.

Data analysis: All the data collected was entered in a pre-approved case record form and tabulated using Microsoft Office Excel Software. Data was analyzed using the SPSS version 26 for windows (SPSS Inc., Chicago, Illinois). Results will be statistically analyzed by using descriptive statistics the quantitative data are presented as mean and standard deviation (mean±sd), qualitative variables are described in terms of percentages and graphs, significance is assessed by using Chi square test.

Ethical considerations: Institutional Ethics Committee approval was taken before beginning the study. Written informed consent was taken from the patients in their local language.

All the relevant data was collected in regards to age, gender, admission and discharge date, death of the patients. Data pertaining to drugs such as dose, frequency, route of administration, duration was also noted. Drugs prescribing data of antimicrobials was also collected and noted.

RESULT

Majority of the patients (152) were found to be in the age group >50.

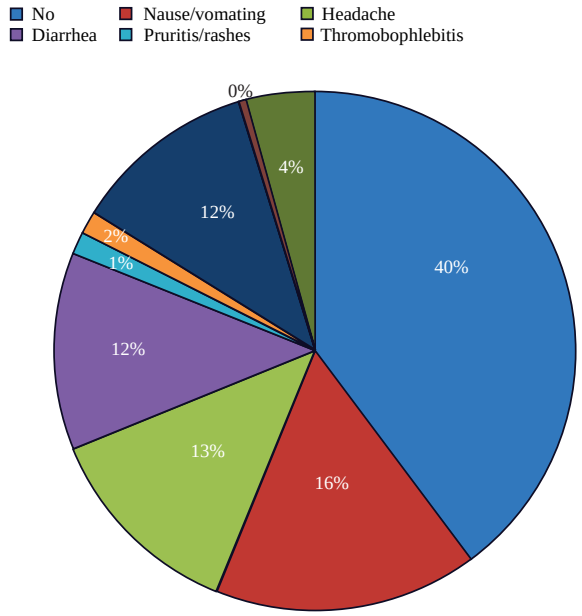

Fig. 1: Adverse Drug Reaction

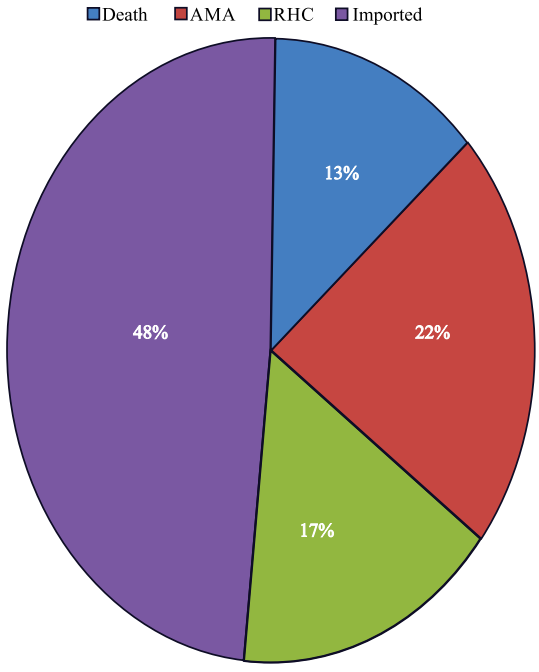

Fig. 2: Outcome of antimicrobial therapy

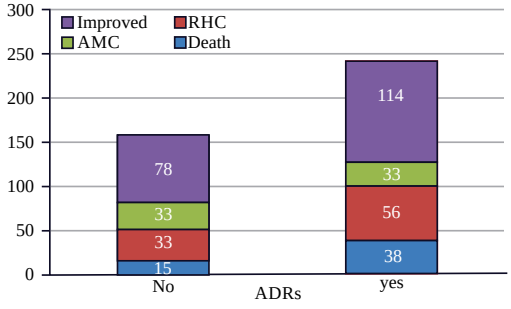

Fig. 3: Comparison of ADR's with outcome

DISCUSSIONS

In the present study, majority of patients (38) were in the age group of 50 years (n = 152) probably because of the higher incidence of serious illnesses requiring medical care in aging population. The least no was in the age group of 21 years (n=39) i.e. 9.8%.

Since, the patients admitted in ICUs have various terminal illness along with co-morbid conditions which require treatment with more number of drugs, 306 (76.5%) were prescribed more than 5 drugs,94 (23.3%) were prescribed less than 5 drugs for the treatment.

68.3% of the patients (n = 273) received a single AMA, whereas 31.8% of subjects (n = 127) required concurrent use of two or more antimicrobials during management in Intensive care units. Such combinations were intended for wider antimicrobial coverage, synergistic effect and also to prevent anticipated emergence of antimicrobial resistance.

Most of the subjects (99.25%, n = 397) received the AMAs by IV route and 2 patients received AMAs by oral route and 1 patient received AMAs by both iv and oral route. Since patients under ICUs were critically ill, parenteral routes were preferred, particularly IV, to ensure high concentration in the plasma and infected tissues/sites.

In the duration of antimicrobial therapy. 10.50% of subjects (n = 42) were under antimicrobial therapy for 7 days and 21.75% of subjects (n = 87) received AMAs for 5 days due to non-availability of higher facilities in the hospital many patients have been referred to higher centre after the giving the initial dose of antimicrobial agents i.e. 21.75 (n = 86) and 19.50% (n = 78) received AMAs for 3 days.

Adverse drug reactions noticed during antimicrobial therapy were nausea and vomiting seen in 16.5%(n = 66) subjects, headache in 12,8% (n = 51) subjects and diarrhea in 12.0% (n = 48) subjects, altered taste sensation was noted in 11.5% (n = 46) subjects, anorexia and photosensitivity in 4.3%(n = 17) subjects were noted, as these were the expected adverse effects of the drugs antimicrobial therapy has not been altered, Rest 39.5% (n = 159) subjects tolerated AMAs well.

The most frequently used antimicrobial group includes cephalosporins and penicillins fallowed by nitroimidazoles and aminoglycosides. Most frequently used drugs include cefotaxime 69.0% (n = 276), metronidazole 29.0%(n = 116), ceftriaxone 7.0% (28), gentamycin 7.0% (28) and ciprofloxacin 5% (n = 20), most commonly used combination drug include piperacillin+tazobactam, followed by amoxicillin+clavulanic acid, cefoperazone+sulbactam. Drug use pattern study from ICUs of north India, 70% of patients received 2 or less antibiotics,[12] and 60% received 2 AMAs, 26% received 3 AMAs, and 14% received 4 or more AMAs in Caribbean ICU,[13] Our study also evaluated for number of antimicrobials used and found that 68.3% (n = 273) patients were

Table 1: Age distribution of study subjects/patients

AGE	Frequency	Percentage
<21	39	9.8
21-30	90	22.5
31-40	65	16.3
41-50	54	13.5
>50	152	38.0
Total	400	100.0

Table 2: Total number of drugs prescribed

Total number of drugs prescribed	Frequency	Percentage
<5	94	23.5
≥5	306	76.5
Total	400	100.00

Table 3: Antimicrobial therapy monotherapy/multitherapy

MO/MU	Frequency	Percentage
Monotherapy	273	68.3
Multitherapy	127	31.8
Total	400	100.0

Table 4: Route of administration of AMAs

Route	Frequency	Percentage
IV	397	99.25
IV, oral	1	0.25
Oral	2	0.50
Total	400	100.0

Table 5: Duration of antimicrobial therapy

Duration of antibiotics	Frequency	Percentage
1 Days	86	21.75
2 Days	72	18.00
3 Days	78	19.50
4 Days	15	3.75
5 Days	87	21.75
6 Days	4	1.00
7 Days	42	10.50
8 Days	4	1.00
9 Days	2	0.50
10 Days	5	1.25
13 Days	2	0.50
14 Days	1	0.25
30 Days	1	0.25
Total	400	100.0

prescribed with single AMA and about 31.8% (n = 127) were prescribed in combinations, cefotaxime, was the most common single AMA's prescribed. Fallowed by ceftriaxone, and ciprofloxacin either metronidazole or gentamycin in combinations and for most of the AMA's were prescribed, culture and sensitivity was seldom performed which was in comparison with other study[14]. In a study by Gupta *et al.*, they found that single antibiotic Single antimicrobial treatment was maximum, over all prescribing of cephalosporins and penicillins was higher and that culture and sensitivity was seldom performed[15]. Average number of the drugs per prescription is an important index of the scope for review and educational intervention in prescribing practices. It is preferable to keep the mean number of drug per prescription as low as possible, since highest figures always leads to increased risk of drug-drug interaction.

Most of the infections were effectively prevented or controlled in most of the patients with the selected AMAs and their combinations. The antimicrobials used were well tolerated without serious adverse drug reactions or drug interactions. 16.5% had nausea/vomiting and 12.8% headache, 12.05% had diarrhea which were managed by giving medical therapy.

The duration of antimicrobial administration for most of the patients was less than one week. This strategy may help in reducing the rate of nosocomial infections, as longer duration of antimicrobial therapy predisposes the patient to infection with resistant bacteria[16,17]. Very few subjects were administered antimicrobials for more than three weeks, particularly including those who developed nosocomial infections, or those who responded inadequately to initial empirical therapy. Similar observations were made in other studies. In our study (n = 384) subjects received AMAs for up to 7 days few were continued more than 7 days.

The route of administration of AMAs is generally determined by the site and severity of infection; parenteral route being preferred in ICU as the patients are critically ill[18]. In our study, majority of antimicrobials were administered parenterally, predominantly intra-venous route and in a very few patients were given orally.

The initial empirical antimicrobial therapy was continued in 97.8% of subjects, but changed in 2.3% based on laboratory report, or due to inadequate clinical improvement or both. Similar pattern was observed in another study[19]. Infections were effectively prevented or controlled in 48% of the patients (n = 192) who also showed a favorable outcome with medical management. The effectiveness of AMA therapy could not be assessed in patients who got discharged against medical advice and in patients who were referred to higher centre. Other studies have not clearly reported the efficacy of antimicrobial therapy in preventing or controlling intensive care units[18-21]. During the course of antimicrobial therapy in medical ward, no serious adverse drug reactions or drug interactions were encountered, and some of the AMAs were administered only after test dose. No serious adverse drug reactions or drug interactions were reported in otherstudies[18-23].

A study in Karnataka includes Cephalosporins are most commonly used drugs in ICUs fallowed by Nitroimidazoles, Penicillins, Aminoglycosides and Fluoroquinolones. Ceftriaxone, Cefixime, Metronidazole are individual agents, Piperacilline+Tazobactum and Amoxicilline+Sulbactum are fixed drug combinations (FDCs)[24]. Another study conducted in Bengaluru Karnataka says most commonly used groups of AMAs are Cephalosporins, Aminoglycosides, and Penicillins, then Cefperazone, Ceftriaxone, Amikacin and Metronidazole are commonly used drugs and Cefperazone+Sulbactum, Amoxicillin+Clavulanic acid are the FDCs[26].

In our study Cefotaxime 69.0% is most commonly prescribed cephalosporin fallowed by ceftriaxone, similar to study in Gujrat in which 22.53% were prescribed cefotaxim[9].

In our study the most common groups of AMAs include Cephalosporins and penicillins fallowed by

Table 6: Class and individual antimicrobials used

	Male		Female		Total	
Antimicrobials use	No	Percentage	No	Percentage	No	percentage
Penicillins and monobactums						
Amoxicillin 1g + clavulanic acid 0.2g IV BD	12	5.2	8	4.7	20	5.0
Piperacillin 4g + tazobactum 0.5 g IV TID	32	14.0	17	9.9	43	10.8
Meropenem 1g IV BD	3	1.3	0	0.0	3	0.8
Total	47	20.5	25	14.6	66	16.5
Cephalosporins						
Cefotaxime 1g IV BD	154	67.2	122	71.3	276	69.0
Ceftriaxone 1g IV BD	15	6.6	13	7.6	28	7.0
Cefaperazone 1g +sulfbactam 0.5g IV BD	6	2.6	1	0.6	7	1.8
Total	175	76.4	136	79.5	311	77.8
Macrolides						
Azithromycin 0.5 g oral OD	2	0.9	0	0.0	2	0.5
Total	2	0.9	0	0.0	2	0.5
Aminoglycosides						
Amikacin 0.5 g IV BD	3	1.3	0	0.0	3	0.8
Gentamycin 0.08 g IV BD	5	2.2	23	13.5	28	7.0
Total	8	3.5	23	13.5	31	7.8
Nitroimidazoles						
Metronidazole 0.5 g IV BD	58	25.3	58	33.9	116	29.0
Total	58	25.3		0.0	116	29.0
Fluroquinolones						
Ciprofloxacin 0.2 g IV BD	8	3.5	12	7.0	20	5.0
Levofloxacin 0.5 g IV BD	0	0.0	1	0.6	1	0.3
Total	8	3.5	13	7.6	21	5.3
Others						
Fluconazole 150 mg weekly once	0	0.0	1	0.6	1	0.3
Total	0	0.0	1	0.6	1	0.3
Total no of patients	229	100	171	100	400	100

nitroimidazoles and aminoglycosides, similar to study carried Chandigarh hospital reported that, penicillin and cephalosporins were prescribed more frequently followed by quinolones, aminoglycosides and metronidazole[15] most commonly used FDCs include piperacillin+tazobactam, amoxicillin+clavulanic acid and cefoperazone+sulbactam similar to Karnataka study[25]. These drugs were preferred because of their broad-spectrum of activity which cover a large number of commonly occurring pathogens. Metronidazole and gentamycin are used along with penicillins or cephalosporins, fluroquinolones wherever infections with gram-negative bacteria and anaerobes are suspected.

CONCLUSION

Based on the observations from the present study, it may be reasonable to conclude that empirical therapy with appropriate combinations of commonly used AMAs can be very effective in preventing or controlling various nosocomial infections and significantly contribute in reducing the mortality and improving the survival without producing serious adverse effects or interactions. Supplementing with specific antimicrobials may be necessary in resistant infections or unusual pathogens.

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