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A CROSS-SECTIONAL STUDY ON ANTIMICROBIAL STEWARDSHIP AMONG IN-PATIENTS AT TERTIARY CARE TEACHING HOSPITAL

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ABSTRACT

The appropriate use of antimicrobials has the potential to improve the efficacy, reduce the treatment-related costs, minimize drug related adverse events, and limit the potential for emergence of antimicrobial resistance. The objective of the study is to pursue knowledge about antimicrobial drugs used in the management and treatment of patients with various infectious diseases. Thus, review the emergence and evolution of the term 'antimicrobial stewardship'. Within the sample size the most number of antimicrobial were prescribed among 31 to 50 years age group (35.56%). About 63 cases that account for 32.47% where observed in age group of 51 to 70 years of age. Among the prescribed antimicrobial drug the most commonly prescribed drug was Ceftriaxone which belongs to the class of drugs called as Cephalosporin antibiotics. Out of 136 total PDDI found from our study 30 were major, 68 were moderate and 38 were minor in severity. Antimicrobial stewardship programs (ASPs) have the capability to decrease antimicrobial resistance, lower healthcare expenses, and minimize drug-related adverse effects, all while enhancing clinical outcomes. All these rapidly growing consequences implies the fact that there is an urgent need of implementation of antimicrobial stewardship programme to ensure the safe and efficient disease management to the patient. Most of the prescriptions were observed to be rational in accordance with the Indian Council of Medical Research (ICMR) treatment guidelines for common syndromes and National Formulary of India (NFI). Highest number of drugs were prescribed from Cephalosporin (Ceftriaxone) and nitroimidazole (Metronidazole) class of

drugs.

KEYWORDS: *Antibiotics, antimicrobial resistance, antimicrobial stewardship program, global health.*

INTRODUCTION

In India the infectious disease burden is among the highest in the world and the recent report showed inappropriate and irrational use of anti-microbial agent against these diseases, which lead to increase in development of anti-microbial resistance.[1] A recent study highlighted the importance of rationing antibiotic use to limit antibiotic resistance in India by introduction of anti-microbial stewardship program.[2] Anti-microbial resistance will result in difficulty in controlling the diseases in the community and in effective delivery of health care services.

There is increasing concern on the quality of antibiotic prescription in hospital medicine as well as community, since numerous authors report that 30-50% of antibiotic prescriptions are inappropriate.[3] more than 3 million kilograms of anti-microbial were administered to humans in United States in 2009. Although the benefits of appropriate antimicrobial prescribing are indisputable, major harms are associated with use and misuse, and antimicrobial resistance is compounding.[4]

Stewardship is defined as "the careful and responsible management of something entrusted to one's care".[5] It was originally applied in the health-care setting as a tool for optimizing antimicrobial use, termed "antimicrobial stewardship".[6] Anti-microbial stewardship programme is an organizational or system health care strategy to promote appropriate use of antimicrobials through the implementation of evidence based intervention.[7]

Antimicrobial stewardship programs (ASPs) are focused efforts by healthcare organizations or sections of organizations (e.g., intensive care units) to optimize antimicrobial use and thus to improve patient outcomes, reduce adverse consequences (emergence of resistance, selection of pathogenic organisms, or toxicity), and deliver cost-effective therapy. The emphasis is on appropriate selection, dosing, route, and duration of antimicrobial therapy Despite recognition of the growing problem of antimicrobial resistance, a 2008 survey estimated that only 48% of hospitals in the United States had an ASP.[4]

In fact, the concept of stewardship was first introduced in 1970s. Hospitals use antimicrobial stewardship activities to ensure "the optimal selection, dose, and duration of an antimicrobial

that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patients and minimal impact on subsequent resistance".[8]

Core features of antimicrobial stewardship

- Improving infection, prevention and control programme.
- Minimizing the source of infection.
- Prescribing anti-microbial only when indicated.
- Selecting anti-microbial rationally with precise dosage schedule.
- Anti-microbial prescribing for a brief period on evidence.
- Reassessment of prescribed anti-microbial after culture and sensitivity reports.
- Upholding surveillance of anti-microbial resistance.
- Monitoring anti-microbial consumption.
- Regular education intervention among health professional.
- Promoting interdisciplinary strategy.

In the 1940s, Sir Alexander Fleming alerted the public to the dangers of antibiotic resistance, a concern materialized within a decade due to the improper use of these medications. Since that time, various educational programs, quality management systems, and clinical guidelines have been created by organizations focused on infectious diseases to address and mitigate this issue; however, these measures have largely proven to be ineffective.

In a recent study, 50 % of antimicrobial were prescribed or misused improperly (CDC, 2013), this could to lead a major problem that we know as Antimicrobial resistance. Anti-microbial resistance happens when germs like bacteria and fungi develop the ability to defeat the drugs designed to kill them. AMR could kill 10 million people every year and cost the global economy up to $100 trillion by 2050.[9]

Antimicrobial Resistance (AMR) poses one of the gravest threats to public health in the 21st century. The growing resistance to antimicrobial medications has emerged as a significant contributor to illness and death on a global scale.

MATERIAL AND METHODS

Study site: The study was conducted at the General Medicine Inpatient department of Chigateri district hospital Davangere over a duration of six months.

Study design: It is a cross section study.

Sample size: The study was conducted over 194 inpatients of general medicine department.

Study criteria Inclusion criteria

- All inpatients admitted in general medicine department during the period of study.
- All inpatients of general medicine who have been prescribed with minimum one antimicrobial agents.

Exclusion criteria

- Outpatients
- Lactating and pregnant women
- Patients below 18 years of age.
- Patients showing unwillingness to study procedures.

Study procedure

A cross sectional study was conducted among 194 patients admitted to general medicine department of Chigateri district hospital Davangere over a period of six months. The study received approval from the Institutional Ethical Committee of S C S College of Pharmacy, and written consent was obtained from all residents. A specifically designed data collection form was created to gather information, which encompasses the patient's demographic details, medical history, personal history, comorbid conditions, social and family history, as well as the medications prescribed for each individual.

RESULTS

This research involved the participation of 194 patients. The demographic details and patterns of drug prescriptions were gathered using an appropriate data collection form. The completed forms were examined for potential drug-drug interactions in individuals admitted to the general medicine department. The results obtained were analyzed utilizing Microsoft Excel.

1. AGE STRUCTURE OF THE STUDY POPULATION

Within the sample size 194 of patients, the utmost number of antimicrobial were prescribed within the age group of 31-50 which was 69 (35.56%) in number. Cases 63 (32.47%) were observed in the age group of 51-70, which was second highest. Followed by 43 (22.16%) cases in age group below 30. The least number of cases where found among the age group above 80 which was 5 (2.57%) cases.

Table 1: Age structure of the study population.

AGE (in years)	FREQUENCY	PERCENTAGE
BELOW 30	43	22.16%
31-50	69	35.56%
51-70	63	32.47%
71-80	14	7.21%
80 ABOVE	5	2.57%

2. GENDER WISE CATEGORIZATION

Out of 194 patients in study population, 106 males with percentage of 54.63% and 88 were females that account for 45.36% in the sample size.

Table 2: Gender wise Categorization.

GENDER	FREQUENCY	PERCENTAGE
MALE	106	54.63%
FEMALE	88	45.36%

3. CATEGORY OF ANTIMICROBIAL PRESCRIBED

The study reports that Cephalosporins (35.56%) class of drugs as the commonly prescribed drug class followed by Nitroimidazoles class of antimicrobial with percentage of 13.36%.

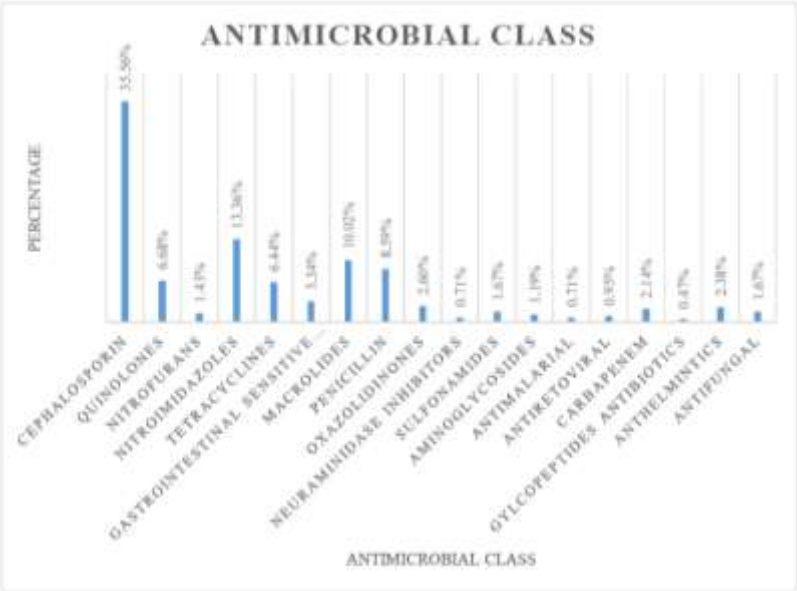

Figure 1: Distribution of antimicrobial category.

4. NUMBER OF TIMES ANTIMICROBIAL PRESCRIBED

The study reports that 35.32 percent of prescriptions were prescribed by the drug Ceftriaxone which comes under the class of drugs called as Cephalosporin antibiotics. Metronidazole that

belongs to class of drug called as Nitroimidazole antimicrobials comes under the second highest prescribed drug among other antimicrobial with a percentage of 12.64%.7.39% of prescription were prescribed by the drug Piperacillin/Tazobactum which is a combination drug belongs to class of drug called as Penicillin like antibiotics.

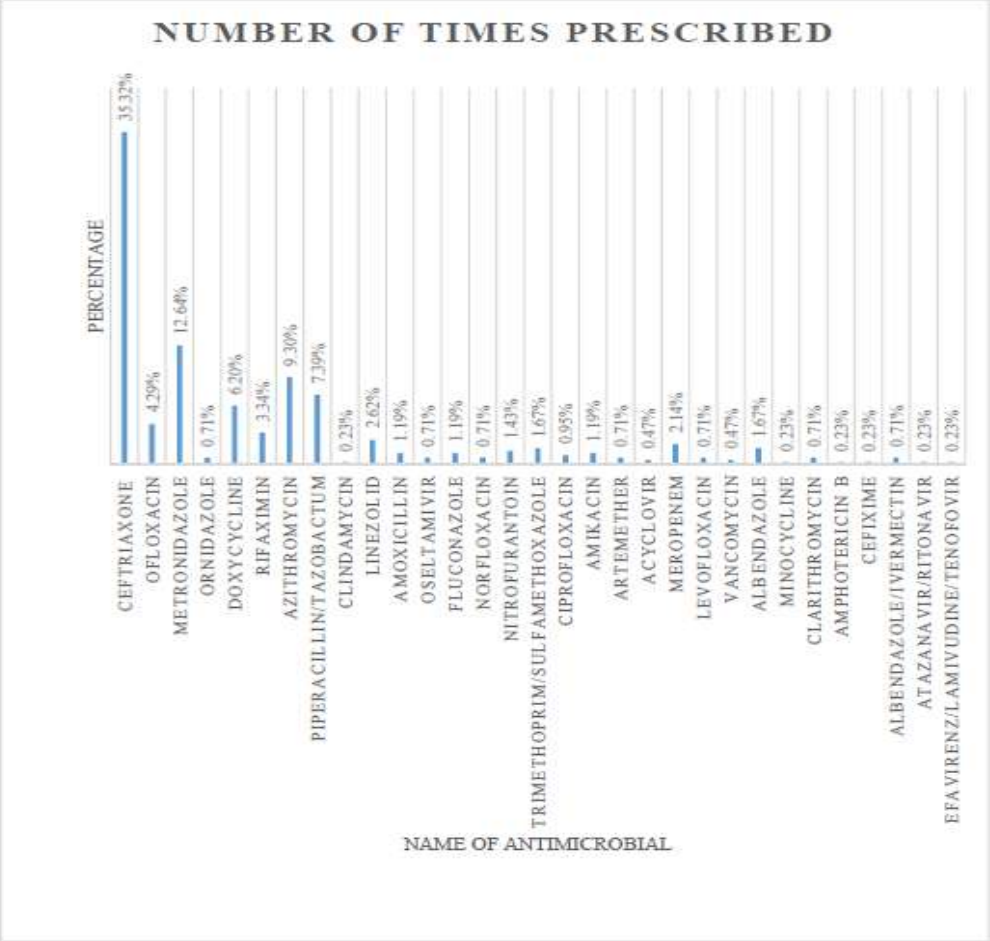

Figure 2: Distribution based on number of times antimicrobial prescribed.

5. USE OF ANTIMICROBIAL IN PRESCRIPTION

In the study on analysing it was found that among 194 study population 141 (72.68%) cases were showing rational use of antimicrobial with respect to particular indication and appropriate dose were given. Whereas 53 (27.31%) cases were showing irrational use of antimicrobial prescribing pattern.

Table 3: Distribution of use of antimicrobials.

USE OF ANTIMICROBIAL	FREQUENCY	PERCENTAGE
RATIONAL USE	141	72.68%
IRRATIONAL USE	53	27.31%

6. POTENTIAL DRUG-DRUG INTERACTION

Out of 194 cases 136 drug interactions were found from the study. In 30 (22.05%) cases, major interaction were noted. Moderate interaction were found in 68 (50%) cases and minor interaction in 38 (27.94%) cases.

Table 4: Frequency distribution table for severity of drug interaction.

SEVERITY	FREQUENCY	PERCENTAGE
MAJOR	30	22.05%
MODERATE	68	50.00%
MINOR	38	27.94%

7. ANTIMICROBIAL EXHIBITING SYNERGISTIC ACTION

Out of 23 antimicrobial combinations, 21.84% drug combinations were capable of exhibiting additive increase in risk of nephrotoxicity followed by 13.44% drug combinations with a capability of inducing an additive QT interval prolongation.

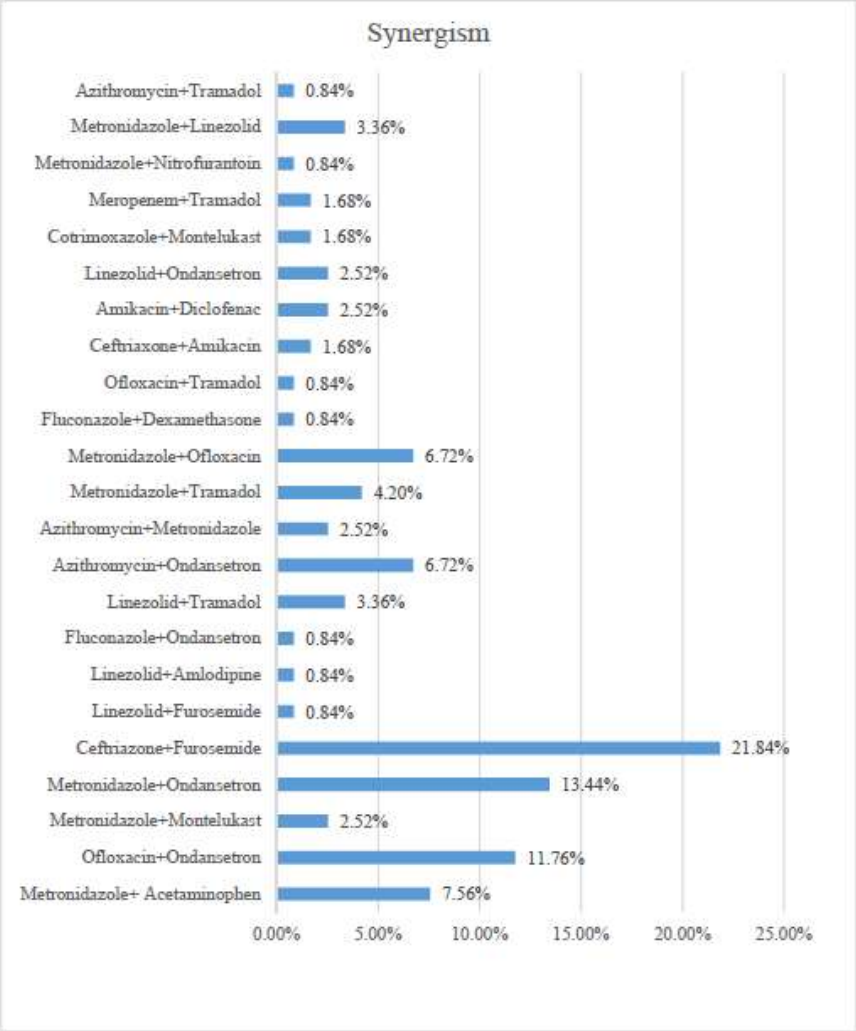

Figure 3: Antimicrobial combination exhibiting synergism.

8. ANTIMICROBIAL COMBINATION EXHIBITING ANTAGONISTIC EFFECTS

In the study out of 8 combination of drugs exhibiting antagonistic effects 33.33% drug combination shows pharmacodynamic antagonism by decreasing the ceftriaxone concentration and 23.80% drugs shows reduced effects of piperacillin.

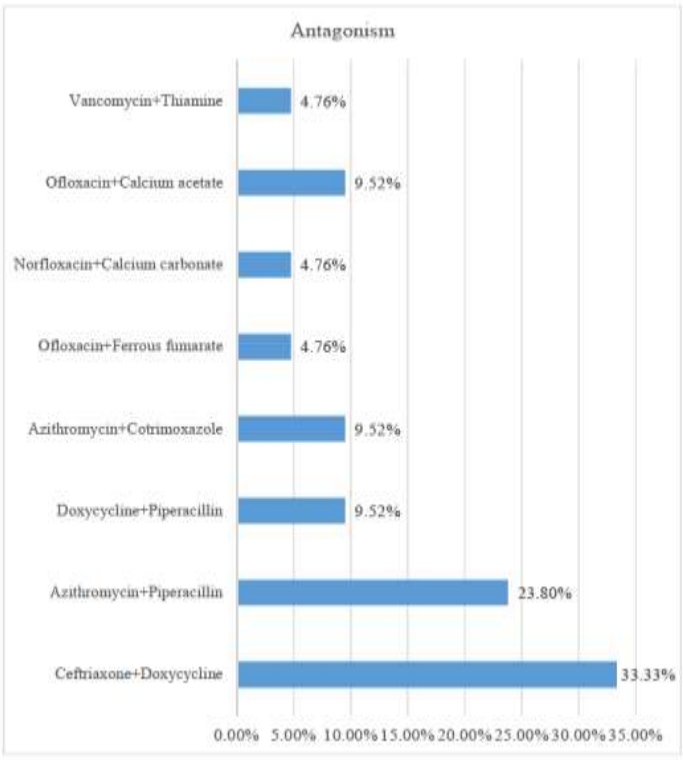

Figure 4: Antimicrobial combination exhibiting antagonism.

9. ANTIMICROBIALS PRESCRIBED PER TREATMENT CHART

The study reports that 58.76% (114) of prescriptions were prescribed by two antimicrobial followed by 22.16% (43) of prescription with 3 antimicrobial. Out of 194 cases 12.88% (25) of prescription were prescribed with only 1 antimicrobial and 6.18% (12) prescription with more than 3 antimicrobials were prescribed.

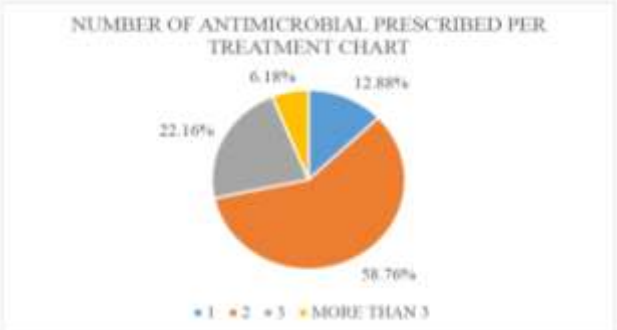

Figure 5: Distribution of number of antimicrobial prescribed per treatment.

DISCUSSION

Antimicrobial stewardship plays a crucial role in averting AMR and thus makes the management of infectious disease a trouble-free process improving patient outcome as well as preventing the spreading of multidrug resistant microorganism to a greater extent by rationalizing the antimicrobial prescription. AMS programs help the patients and healthcare professionals to change their prescribing practices that improve the patient care and also reduces unnecessary use of antimicrobials. The implementation of national guidelines or hospital or local antimicrobial policies demonstrates a responsibility to use Antimicrobial wisely.

Similar study was conducted by Md. Anwarul Azim et al., on antimicrobial stewardship: fighting antimicrobial resistance and protecting Global public health which states the importance of conducting antimicrobial stewardship as a crucial step in rationalizing antimicrobial treatment.[10]

Studies conducted by Dilip Nathwani et al., on value of hospital antimicrobial stewardship programs: A systemic review which also states the importance of antimicrobial stewardship.[11]

Within the sample size the greatest number of antimicrobials were prescribed among 31 to 50 years age group (35.56%). Similar results were obtained by Ryngkatbor Marbaniang et al., in their study on antimicrobial stewardship which was conducted in Bangalore.[12] About 63 cases that account for 32.47% were observed in age group of 51 to 70 years of age. Among the prescribed antimicrobial drug, the most commonly prescribed drug was Ceftriaxone which belongs to the class of drugs called as Cephalosporin antibiotics. Followed by Metronidazole which belongs to class of drugs called as nitroimidazole antibiotics which was second highest prescribed antimicrobial.

Studies conducted over Lagos university teaching hospital Nigeria by Oshun et al., shows similar results that the commonly prescribed antimicrobial was ceftriaxone and metronidazole in year 2015 and 2018.[13]

About 9.30% of prescriptions were prescribed by Azithromycin which belongs to the class of drug called Macrolide antibiotics. 7.39% of prescription were prescribed by the drug Piperacillin/Tazobactum which is a combination drug belongs to class of drug called as

Penicillin like antibiotics.

Out of total prescribed drugs, about 419 were antimicrobial, which means more than a quarter half of the total drugs prescribed where antimicrobial which suggests the importance of conduction of antimicrobial stewardship in hospitals for improving the rational use of prescribing antimicrobials.

Rationality of antimicrobial use were analyzed using ICMR and NFI guidelines along with Medscape and Drugs.com for determining potential drug-drug interaction, synergism and antagonistic effects of prescribed antimicrobial drugs. Out of 136 total PDDI found from our study 30 were major, 68 were moderate and 38 were minor in severity. The interaction between Ceftriaxone and Furosemide were predominant as is other studies with percentage 21.84%. Moreover, these two drugs show synergistic effect by increasing the risk for nephrotoxicity which is highlighted the fact that it should not be given as a combination in patients especially with kidney related disorders. The combination of Ondansetron and Metronidazole synergistic effects was seen second highest, capable of inducing an additive QT interval prolongation. Hence this combination should not be prescribed to patients with cardiovascular disease.

Similar results were obtained in the studies conducted in Bangalore by Ryngkatbor Marbaniang et al., in their study on antimicrobial stewardship in tertiary teaching hospital.[12]

The drug combination of Doxycycline and Ceftriaxone shows pharmacodynamics antagonism by reducing the effects of Ceftriaxone. Similar antagonistic effects are seen in combination of Azithromycin and Piperacillin.

On analyzing the number of antimicrobials per treatment chart 114 prescription contained two antimicrobial drugs, 43 prescriptions with 3 antimicrobials, 25 prescriptions with only one antimicrobial and 12 prescriptions contained more than 3 antimicrobial agents. Increasing time gap between two doses without taking it together can avoid the potential side effects.

CONCLUSION

The irrational use of antimicrobials is certainly a complex and multifactorial problem in developing countries, and a proper understanding of problem is necessary for effective control policies. Overuse or misuse of antibiotics and other antimicrobials for hospital inpatients is relatively common and can be associated with several unintended negative

consequences.

All these lead the way to irrational prescribing of antimicrobial. All these rapidly growing consequences implies the fact that there is an urgent need of implementation of antimicrobial stewardship programme to ensure a safe and efficient disease management to the patient. Thus, it is very crucial to preserve the sensitivity of existing antimicrobial agents and steer clear of disclosure of antimicrobial resistance.

The study conducted by us included those patients in the inclusion criteria to which at least single antimicrobial agent was prescribed in their treatment chart. Most of the prescriptions were observed to be rational in accordance with the Indian Council of Medical Research (ICMR) treatment guidelines for common syndromes and National Formulary of India (NFI). Highest number of drugs were prescribed from Cephalosporin (Ceftriaxone) and nitroimidazole (Metronidazole) class of drugs. From our prospective study we concluded that majority of prescriptions were rational and all potential drug interactions, additive actions and contraindications were found to be theoretically. Thus, Antimicrobial stewardship is a crucial step towards rational use of antimicrobial, improving the antimicrobial therapy and preventing AMR.

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AUTHOR'S CONTRIBUTION

All the authors have contributed equally.

CONFLICT OF INTEREST

All authors declare that there are no conflicts of interest.

ETHICS DECLARATION

The Institutional Ethics Committee at SCS College of Pharmacy approved the protocol. All residents in the hospital provided informed consent.

CONSENT FOR PUBLICATION

All authors have consented to the publication of their work.

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS FUNDING

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