

“Antimicrobial Stewardship in Inpatients in General Medicine in a Secondary Care Teaching Hospital.”

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ABSTRACT:

Antimicrobial resistance happens when microbes like bacteria, fungi, virus and parasites alter the ways medications used to treat infections caused by them. Possible solution of antimicrobial misuse which may lead to antimicrobial resistance includes prescription or consumption of antimicrobials when necessary. Antimicrobial stewardship program (ASP) is one of the approach to address improper antimicrobial use and antimicrobial resistance. It is an effective method to restrict overuse of antimicrobials if implemented properly. It will also provide an outlook to improve clinical outcomes and reduce adverse drug reactions due to their use. This cross sectional study was conducted for 6 months and 260 were included in this study. The prescription with at least one antimicrobial was considered and the rationality of antimicrobial prescribing was analysed using NFI 2016. The overall appropriateness of antimicrobials on rational use prescribed was found to be 89.76%. It was found that, 91.86% antimicrobials were appropriate especially with reference to indication, 91.60 with dose, 87.92% with frequency, 87.66% with duration. According to the prescription assessed in this study Ceftriaxone was most commonly prescribed followed by Ciprofloxacin and Cefotaxime respectively. Also through the data collected, 124 drug interactions were identified. The most common major drug interaction was between ciprofloxacin and metronidazole and the effect was found to be QT prolongation. During this study period ceftriaxone induced SJS was also observed and it was assessed by Naranjo ADR Probability scale. The study concluded that majority of the prescriptions were rational, and the drug interaction were found to be theoretical. Thus, antimicrobial stewardship is a major factor for rationalizing a drug

KEYWORDS: Antibiotic, Antimicrobial resistance, Stewardship, Rational use, Adverse drug reaction, Drug interaction

I. INTRODUCTION

The objectivity of antimicrobials are the most widely recognized dubious and discussed issue in the present clinical practice^[1]. Rational utilization of antimicrobials might be characterized as: "Patients get prescriptions suitable for their clinical requirements, in dosages that meet their own demands, for a satisfactory timespan, at minimum expenditure to them and their community"^[2]. According to WHO (World Health Organization), it was accounted for that around the world, over half of all meds are recommended, apportioned or sold improperly, while 50% of patients neglect to take them accurately. Basic instances of unreasonable medication use are overprescribing, multi-episode endorsing, and utilization of superfluous costly medications, self-drug and over utilization of anti-infection agents and infusions have begun. In this way, drugs are beginning to be misused^[2]. The effect of nonsensical prescriptions use can differ broadly. When meds are utilized improperly, the dangers of unfavorable medication reactions (ADRs) is expanded, particularly in geriatric patients or in co-dismal people who may have undermined physiologic functions^[3].

Antibiotic resistance circumstance which happens when the smaller scale life form is impervious to an anti-infection range.^[4,5] The antimicrobial opposition is a significant general medical issue for some reasons such as it decreases the specialist's decisions of treatment, constraining explicit anti-microbial appropriate for that contamination. Hence, the doctor is compelled to pick an anti-infection which might be costly or maybe increasingly harmful and possibly limited pharmacokinetic properties for a specific disease. It

expands rate of mortality.^[6] Also, it results in human agony, obstinate contaminations, longer stays in medical clinics or constrained emergency clinics, since it is important to utilize parenteral therapy^[7,8]The event of obstruction in emergency clinics is viewed as a marker of low quality consideration administrations and numerous patients resort to claims for harms.^[9,10]

Stewardship is characterized as "the cautious and capable administration of something depended to one's care".^[11] It was initially applied in the medicinal services setting as a device for improving antimicrobial use, named "Antimicrobial Stewardship" (AMS).^[12]These programs centralize at guaranteeing the right utilization of antimicrobials to give better patient results, minimize the danger of unfriendly effects, advance cost-viability, and diminish degrees of opposition. The objective of antimicrobial stewardship is 3-fold. The first objective is to work with human services professionals to enable every patient to get the most suitable antimicrobial with the right portion and length. The subsequent objective is to forestall antimicrobial abuse. The third objective is to limit the improvement of opposition.^[15]These 3 creases of ASPs are to improve understanding results and wellbeing and to decrease AMR and human services costs by advancing wise utilization of antibiotics. Joseph and Rodvold expounded on the "4 D's of ideal antimicrobial treatment": right Drug, right Dose, De-acceleration to pathogen-coordinated treatment, and right Duration of treatment.^[14]

According to World Health Organization (WHO) characterize an ADR defined as 'a medication related occasion that is poisonous and unintended and happens at portions utilized in people for prophylaxis, conclusion or treatment of infection or for the change of physiological capacity. ADR can cause due to Overdose (counting recommending or organization mistakes), Therapeutic disappointment, Drug interactions and Drug withdrawal.^[13] Drug interaction happen when the impact of a medication is changed by the organization of any of the accompanying by another medication, food and drink. It can be brought about by pharmacokinetic instruments or pharmacodynamics components.

II. MATERIALS AND METHODS:

This cross sectional study was conducted at inpatient department of general medicine in K.C. General Hospital. The duration of the study was 6 months, from September 2019 to February 2020.

Asper the department of General Medicine, K.C. General Hospital, Bengaluru, sample size is 260 patients. Using prevalence from previous literature (19.61%) Using formula, $N = \frac{4PQ}{L^2} = \frac{4 * 19.69 * (100 - 19.69)}{25} = 253$; rounding off to 260 where, P= Prevalence, Q=(100-P), L=allowable errors (5%), N= Total sample size. Inclusion criteria: All the inpatients in general medicine in the study duration who were prescribed with at least one antibiotic and expressed willingness to participate in the study. Exclusion criteria: Outpatients, inpatients below 18 years, pregnant or lactating women, patients in ICU or surgical department, unwillingness to participate in the study.

The study was approved by the Institutional Ethics Committee. Patients falling under the inclusion requirements were enrolled in the study and, after presenting sufficient details, written consent forms were obtained. In the explicitly prepared data collection forms, patient medical data containing information such as demographics, past medical and medication history, social and family history, medication map, laboratory data, etc., are documented when obtaining ICD. Assessment of rationality was done by using NFI guidelines. Drug interactions and ADR were identified using MICROMEDEX and NARANJO SCALE. Later, obtained data was subjected for suitable statistical method.

III. RESULT:

A total of 260 patient's data were collected and analyzed, patients who were prescribed with at least one antibiotic were taken into the study. Their median age was 36-50 years (Table 1) and 168 were males (64.61%) (Table 2). The overall appropriateness of antimicrobials on rational use prescribed was found to be 89.76%. It was found that, 91.86% antimicrobials were appropriate especially with reference to indication, 91.60 with dose, 87.92% with frequency, 87.66% with duration. (Table 3). When irrationality was checked, 10.23% of antimicrobials prescribed was found to be inappropriate. It was found that 8.13% was inappropriate with indication, 8.39 % with dose, 12.07 with frequency, 12.33% with duration. (Table 4). Cephalosporins (53.01%) are commonly prescribed antimicrobials followed by Fluoroquinolones (14.21%) (Figure 1). Ceftriaxone (180) is more often drug followed by Ciprofloxacin (42) and Cefotaxime (21) (Figure 2).

Drug interactions were found in 124 cases. Out of 124 cases, 102 major interactions were found followed by 15 moderate and 7 minor interactions (Table 5). In our study we have found a Ceftriaxone induced Steven's-Johnson syndrome in a male patient of 75 years. Patient was diagnosed with Pneumonia and was prescribed with Inj. Ceftriaxone 1g BD but

developed rashes and inflammation of mucous membrane all over the body. We have reported this ADR in a Suspected Adverse Drug Reaction Reporting Form and the causality of the ADR was assessed with Naranjo Adverse Drug Reaction Probability Scale, based on which the total score was found to be 7.

TABLES & FIGURES:

AGE GROUP	FREQUENCY	PERCENTAGE(%)
Early adulthood (19-35)	67	25.76
Adulthood (36-50)	81	31.15
Late adulthood (51-65)	74	28.46
Young old (66-74)	21	8.07
Old (75-84)	17	6.53

Table 1: Age distribution

GENDER	FREQUENCY	PERCENTAGE(%)
Male	168	64.61
Female	92	35.38

Table 2: Gender distribution

RATIONAL USE	FREQUENCY	PERCENTAGE(%)
Indication	350	91.86
Dose	349	91.60
Frequency	335	87.92
Duration	334	87.66

Table 3: Distribution for rational use of antimicrobials

IRRATIONAL USE	FREQUENCY	PERCENTAGE(%)
Indication	31	8.13
Dose	32	8.39
Frequency	46	12.07
Duration	47	12.33

Table 4: Distribution for irrational use of antimicrobials

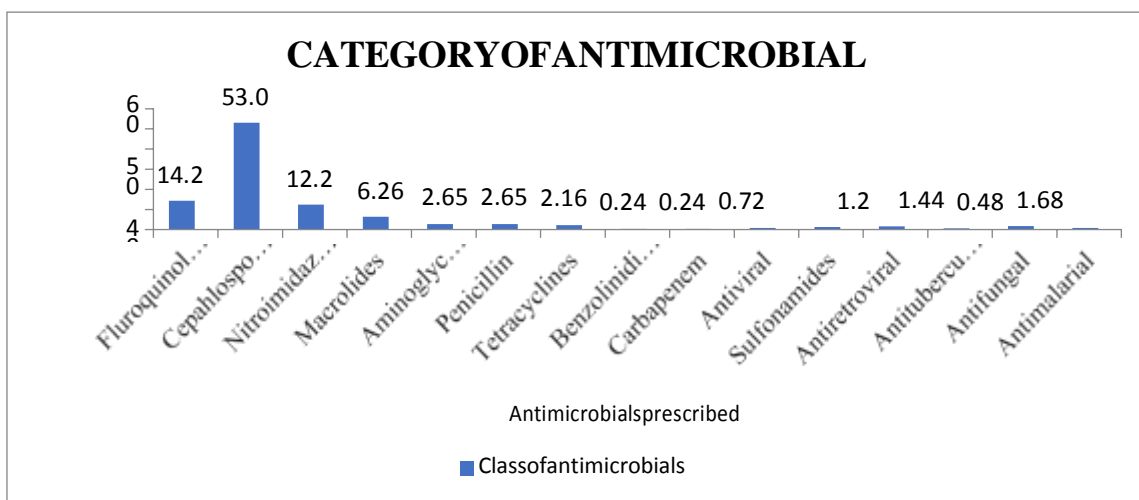


Figure 1: Frequency distribution of category of antimicrobials

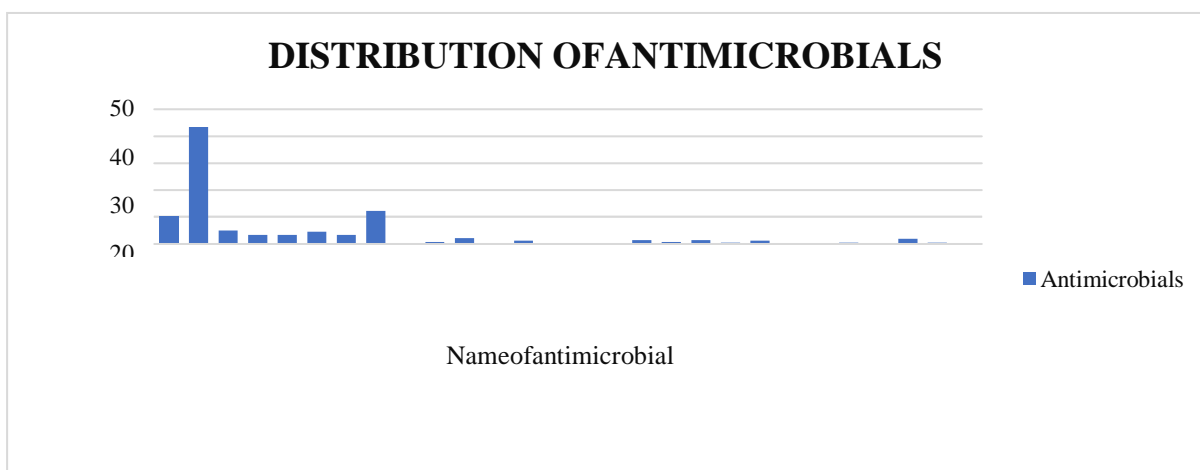


Figure 2: Frequency distribution of number of times antimicrobials prescribed

SEVERITY OF INTERACTION	FREQUENCY	PERCENTAGE (%)
Major	102	82.25
Moderate	15	12.09
Minor	7	5.64

Table 5: Distribution of potential drug-drug interactions

IV. DISCUSSION:

As a way to rationalise the use of antimicrobials to avoid the rise in resistance and enhance patient therapy outcomes, antimicrobial

stewardship is of vital importance^[16] Antimicrobial stewardship is a concerted attempt to inform and convince antimicrobial prescribers to adopt evidence based prescribing in order to avoid

overuse of antibiotics and therefore antimicrobial resistance.

A total of 260 patients were enrolled in the study, male patients were predominant 168(64.61%) and the age of the patients ranged between 36-50 years i.e., 80 cases (31.15%) was found to be high. In a study conducted by Noreen Sultana et al^[17] 102 study subjects were enrolled in the study. Out of 102 study subjects, 46% were females and 54% were males which is similar to our study. In the study conducted by S Rajiniet al^[18], out of 170 patient's case studies, 101 patients (59.46%) were male and 69 patients (40.54%) were female. Also, a demographic detail concedes that prescription of antimicrobials in age group of 31-40 years, 45 cases (17.61%) and 41-50 years, 40 cases (26.47%) was found to be high which is similar to our result. In our study a total of 1182 drugs were prescribed, out of which 413 drugs were antimicrobials. This shows that over quarter half of the drugs prescribed are antimicrobials indicating an immediate need in the rational prescribing of antimicrobials.

Out of 260 prescriptions, 153 (58.84%) prescription contain 1 antimicrobial, 79(30.38%) prescription contain 2 antimicrobials, 17(6.53%) prescription contain 3 antimicrobials, 10(3.84%) prescriptions were prescribed with 4 antimicrobials and only 1(0.38%) prescription with more than 4 antimicrobials. These results were similar with the findings of Duo-shuang Xie et al^[19] and Hanmant Amaneet al^[20] except for the prescription contain 2 antimicrobials which was found to be higher in their results. However, these findings were contrary to the study of Admaneet al^[21] in which single antimicrobial was prescribed in 68.32% patients, two antimicrobials in 25.6% and 6.08% in 3 or >3 antimicrobials.

Out of 16 antimicrobials prescribed in the hospital, the mostly preferred antimicrobials were Cephalosporins 220(53.01%) than other classes of antimicrobials such as Fluroquinolones 59(14.21%), Nitroimidazole 51 (12.28%), Macrolides 26 (6.26%), Penicillin 11 (2.65%), Aminoglycosides 11(2.65%) and Tetracyclines 9 (2.16%). Our results were relevant with the findings of Dr. Merin Titus et al^[22] and P. Maheshwari et al^[23] in which cephalosporins were mostly prescribed drug, which is prescribed 180 times (43.37%) followed by Metronidazole 51(12.28%) and ciprofloxacin 42(10.12%).

In a study conducted by Remesh A et al^[24] among 93 patients most predominant class of

antibiotic were cephalosporins 59 (63%), fluroquinolones 29 (31%), penicillins 15(16%) which is similar to our study. Among cephalosporins, ceftriaxone is the most commonly prescribed in our study 180 (43.37%) and also these results are relevant with the study conducted by Remesh A et al in which among 93 patients, higher rate of prescription were of ceftriaxone 46 (49%), levofloxacin 24(26%), azithromycin 14 (15%). These findings are also relevant to Rajopadhye B. D et al^[25] in which total 60 antimicrobials were prescribed or the 30 study participants. The most commonly prescribed were cephalosporins - (70%), of which ceftriaxone was maximally used (63.3%). Next in line were metronidazole (26.6%), azithromycin (23.3%) and quinolones (20%). Fixed dose combinations (FDCs) contributed 36.6% of antibiotics prescribed. Amongst FDCs, penicillins were most commonly used (40%), of which piperacilin -tazobactam contributed 23.3%, followed by amoxicillin-clavulanic acid (13.3%).

The rationality of antimicrobials were analysed with the guidelines prepared from MICROMEDEX and NFI 2016. The dose, indication, route and duration of antibiotics were verified from MICROMEDEX. When rationality was checked for overall appropriateness of antimicrobials prescribed were analysed and was found to be 89.76%. It was found that 91.86% antimicrobials were appropriate specially with reference to indication, 8.39% with dose, 12.07% with frequency and 12.33% with duration. These results in our study are similar to the study conducted by B. Rajalingamet al^[26] Our findings were contrary to the study conducted by Rajopadhye B.D et al. As far as rationality of selection of AMAs was concerned, 42% prescriptions were found to be rational. Almost equal, i.e. 40%, were irrational, while for 18% of antibiotics prescribed, rationality could not be assessed due to inadequate information.

In our study, while cephalosporins and carbapenems were the most commonly prescribed antimicrobials, we did not detect any Potential drug-drug interaction (PDDIs) with these antimicrobials. Cephalosporins and carbapenems are generally safe antimicrobials for PDDIs and should usually be preferred to quinolones, macrolides, or linezolid. In our study we found that the number of antimicrobials and number of other drugs used are associated with higher risk of PDDIs. Prescriptions were subjected for finding potential drug interactions. The results showed that only 47.69 % had at least 1 drug interaction and

remaining 52.30 % did not have any drug interaction at all. The number of drug interactions from 260 prescriptions were counted to 124. Out of 260 prescriptions, majority of interactions were caused by antimicrobials. Incidence of drug interactions are Major 102 (82.25%), Moderate 15 (12.09%) and Minor 7 (5.64%). In our study, cephalosporins are the commonly prescribed antimicrobials as well as metronidazole and macrolides, these are generally safe antimicrobials for PDDIs. The results obtained in our study was relevant with the findings of F Kuscu et al.^[27] in which among 150 major interactions, 61 (38%) were with antimicrobials. Quinolones, triazoles, metronidazole, linezolid, and clarithromycin alleged for 173 (25.7%) of 673 prescribed antimicrobials, but were accounted for 141 (92.1%) of 153 interactions.

Adverse Drug reactions are defined as unwanted effect of drugs which may occur due to administration of either single or prolonged dose of a drug or both combined. In our study we have found an ADR cause by ceftriaxone which belongs to the class of cephalosporins, the patient was diagnosed with Pneumonia and was prescribed with Inj. Ceftriaxone 1g BD but developed rashes and inflammation of mucous membrane all over the body. This is comparable to the study conducted by Liberopoulos EN et al.^[28]

V. LIMITATIONS:

Firstly Even though antimicrobial resistance patterns were collected, evaluation of AMS not included due to difficulty in capturing antimicrobial sensitivity data. Secondly although most commonly found drug interactions were QT prolongation but we could not calculate the risk of cardiac abnormalities, since most of the patients ECG procedure was not done.

VI. CONCLUSION:

Irrational use of medicine is a major problem worldwide. Inappropriate use of antimicrobial for non bacterial infection and failure to prescribe in accordance with clinical guideline which leads to major problem for irrational prescribing. The gap between rational and irrational use of antimicrobial agent indicate an urgent need for rigorous implementation of antimicrobial stewardship program in order to avoid the emergence of resistance and conserve the sensitivity of available antimicrobial agents.

We conducted a cross sectional study which include patients with at least one antibiotic in a prescription. Most of the prescription were rational as per

the guidelines (NFI, MICROMEDEX). Commonly prescribed antimicrobials were cephalosporins (Ceftriaxone) and fluoroquinolones (Ciprofloxacin). The major drug interactions were found between Fluoroquinolones-Nitroimidazole and 5-HT₃ antagonist-Nitroimidazole class of drug which resulted in QT prolongation that should be avoided in high risk patient (specifically, Cardiovascular patients).

From the study we concluded that majority of the prescriptions were rational, and the drug interaction were found to be theoretical. Thus, antimicrobial stewardship is a major factor for rationalizing a drug.

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