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Patterns of antimicrobial prescribing, utilization, and cost of in patients attending a tertiary care hospital's general medicine ward: A retrospective study

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***Abstract*---**BACKGROUND: Antibiotic overuse is of great public health concern.Multiple studies performed globally have demonstrated a strong association between antibiotic use and antibiotic resistance (AMR), at both individual and community levels and they also shown that Antimicrobials are most commonly prescribed medications in acute care settings with 80% of its usedeemed inappropriate. OBJECTIVES: The primary aim of this study was to determine the possible impact of appropriate prescribing of antibiotics in General medicine ward of tertiary health centre on treatment outcomes and costs related to treatment. METHODOLOGY: This retrospective study

looked at antimicrobial prescribing data in patients admitted to general medicine.Patients data was retrieved from Medical record section and the records of discharged patients were reviewed. The demographic data, disease related data and utilization of antibiotics were noted in specially designed proforma and analyzed. The documented data evaluated for use, safety outcomes and cost for the treatment associated with the use of antibiotics. RESULTS: Female patients 60.2 %(n=759)aremore hospitalized when compared to males, Average length of stay in hospital was 8 days. Majority of hospitalized patients had HTN & DM as primary comorbidities. The widely prescribed antibiotics among all classes as prophylaxis were third generationcephalosporins in parenteral form. The drugs are mostly prescribed by combination of brand and generic (68.5%). The total cost incurred on patients for drugs given by parenteral route was Rs.8,49,754/- (83%), Beta lactams (Cephalosporins being major and next to it is Piperacillin followed by Carbapenems) accounted for the maximal cost of the antimicrobials. CONCLUSION: Patterns of antibiotic prescribing among patients admitted to general medicine ward in a tertiary care hospital revealed that more than 82% of patients received inappropriate antimicrobial therapy. This study would be best articulated through preparation and circulation of STG and establishing the antimicrobial stewardship programs to measure and improve the use of antimicrobials to achieve optimal clinical outcomes and reduce bacterial resistance, reduction in treatment costs, which is the ultimate goal of our study.

***Keywords*---**STG-standard treatment guidelines, AMR- anti microbial resistance, stewardship programs, antibiotics.

Introduction

The development of antibiotics, which have been called “miracle” drugs, represented a huge step forward in human medicine since the 1940s and became pillars of public health in the 21st century as most important tools in modern medicine. Antibiotics effectively stop dangerous bacterial infections in their tracks by eliminating the growth of bacteria or by killing the bacteria directly and ineffective in treating infections caused by viruses and others[1]. Antibiotics are the most rapidly expanding class of drugs and most frequently prescribed drugs worldwide (Ozkurtet al.,2005)(Fadare et al.,2011)which are used to treat both life threatening and trivial infections (Sharma etal.,2012)[2].In spite of their advantages in treatment, the problems that occur from the irrational use of antibiotics (IUA) have put them in the health agendas ofthe countries as a common issue of consideration(Holloway et al.,2011;WHO,2001) as their overuse contributes directly to the selection pressure that results in the emergence of resistant pathogens (Roberts et al.,2008) leading to “ANTI MICROBIAL RESISTANCE”**.** Antimicrobial resistance (AMR) is considered acritical public health concern, leading to higher mortality and greater morbidity(Aaerestrup et al.,2012) and has become an international health threat.

The role of antibiotic stewardship programmes is to strikea balance between the potent ability of antibiotics forindividual patients and their potentially hazardous effects. Initiatives to support appropriate antibiotic use arerelevant because of its effects on bacterial resistance,clinical outcome, and costs[3]. The decision to prescribe an antibiotic is complex, based not only on an assessment of the likely risk of complications, but also on the doctor–patient relationship, the patient's psychosocial history, and the time constraints of the consultation. A number of approaches have been evaluated with the aim of reducing consultations and prescribing for minor infections. These mainly focus on either reducing diagnostic uncertainty or altering physician and patient behaviour. In a multicentre trial in six European countries, point-of-caretesting using C-reactive protein (CRP) or communication training led to a marked reduction in antibiotic prescribing for acuterespiratory tract infection in primary care (Little et al., 2013). However, the greatest effect was seen by combining these interventions, which led to a 62% reduction in antibiotic prescriptions. Scoring systems such as the Centor criteria and latterly the Fever, pain score have beenused to try to target antibiotic treatment, but they are poorly predictive of bacterial infection and outcome (Little et al., 2013)[4].

In patients who have commenced empirical broad-spectrum antimicrobial therapy, the results of microbiological investigations should prompt a re-evaluation of therapy. If the cultures are negative and the patient has clinically improved, early cessation of antimicrobial therapy should be considered. If the cultures are positive, then the use of narrower-spectrum antimicrobial agents should be encouraged wherever possible. Patients who receive a prolonged course of broad-spectrum antimicrobials areat increased risk of later infective episodes caused by resistantpathogens[5]. The development of local antimicrobial guidance for clinicians initiating empirical antibiotic therapy not only serves to guide the clinician in making the appropriate antibiotic choice but also serves to restrict the inappropriate use of broader-spectrum antimicrobial agents. Along with these we should aim at:

- Reducing the need for antibiotics;
- Lowering resistance-enhancing drug pressure through improved antibiotic targeting, andeliminating antibiotic use for growth promotion in agriculture. The highest priority needs to be given to[6]
    - national surveillance of antibiotic resistance and antibiotic use better information to underpin decisions on standard treatment guidelines, education and other actions, as well as to monitor changes over time[8];
    - increasing the use of diagnostic tests, which necessitates behavioural changes and improvements in microbiology laboratory capacity;
    - setting up and/or strengthening infection control committees in hospitals; and
    - restricting the use of antibiotics for non-therapeutic uses in agriculture. These interventions should help to reduce the spread of antibiotic resistance, improve public health directly, benefit the populace and reduce pressure on the healthcare system.

The objectives of the study are:

- To evaluateand analyzethe rationality of the prevalent prescribing practices of antibiotics in general medicine ward based on National evidence-based guidelines (National Treatment Guidelines for Antimicrobial Use in Infectious Diseases, India)
- To assess
  - Overall frequencies of infections
  - The pathogens involved and their antibiotics sensitivities
  - Antibiotic's utilization and costs for most common infections in general medicine ward.
- To assess prophylactic measures to prevent infectious diseases[7].
- To assess antibiotic related problems and to improve overall patient care.

Methodology

The study protocol was prepared and submitted to the ethics committee for ethical clearance. This study was approved by Institutional Ethics Committee. It was a retrospective study and study was conducted for a period of six monthsin Dr.Pinnamaneni Siddhartha Institute Of Medical Sciences & Research Foundation, Gannavaram, Andhra Pradesh.759 Patient Recordswere enrolled into the study as per the inclusion and exclusion criteria stated in the study protocol.

Inclusion criteria

- Case records of patients who are admitted to general medicine ward during JANUARY 2015 –DECEMBER 2015 are included.
- Patients > 12 years old, of either gender.
- Case record with at least one antimicrobial agent in the medication chart.

Exclusion criteria

- Incomplete case records are excluded.
- Accidental and intentional poisoning case records are excluded.
- Pregnant patients.

A separate data collection form was designed. It includes patient demographic details, chief complaints, past medication history, objective evidence, final diagnosis, treatment chart, culture sensitivity form, prescription analysis form. It will be converted using electronic database and appropriate statistical analysis will be done. The demographic data collected includes the patient's age, sex and weight. The past medical and medication history data collected includes the patient's previous allergies, co-morbidities and the drugs received previously. Treatment regimen was collected for antimicrobial appropriateness (selection, route of administration, dosage, duration, frequency, and indications), allergy, and adverse events,drug-drug interactions observed due to Antibiotics.

Then the prescriptions were analyzed for the average number of antibiotics per encounter, percentage of encounters with an antibiotic prescribed, route of

administration based prescription pattern, group wise prescription of antibiotics, percentage of antibiotics prescribed by generic name, percentage of antibiotics prescribed from the WHO essential drug list, prescription adherence to guidelines, outcome and cost analysis. The data was pooled and descriptive analysis done. The results were presented as mean and percentages[9]. Evidence based National Guidelines- "National Treatment Guidelines For Antimicrobial Use In Infectious Diseases" Produced By National Centre For Disease Control, Government of India, were used to analyze the adherence of prescribing patterns to guidelines.The Micromedex Solutions and Textbook of applied pharmacotherapeuticsby kodakimble were used as the reference to check Drug-Drug interactions, Drug and dosage related problems.World Health Organization (WHO) Indicators and some other authorized recommendations were used as reference[10]. Statistical analysis was carried out using Graph pad prism software version 5.0 , SPSS software version 19.0.

Results

Table 1
Frequency distribution of co-morbidities observed in patients attended to general medicine ward

Co-morbidities	Frequency	Percentage
Hypertension	181	23.84%
Type 2 Diabetes Mellitus	75	9.88%
Hypothyroidism	31	4.08%
Bronchial Asthma	22	2.89%
Rheumatoid Arthritis	10	1.31%
COPD	10	1.31%
Pulmonary Tuberculosis	07	0.92%
Old Cardiovascular Accident	06	0.79%
Epilepsy	04	0.52%
Parkinson's Disease	03	0.39%
Chronic Kidney Disease	03	0.39%
Systemic Lupus Erythematosus	02	0.2%
Congestive Cardiac Failure	02	0.2%

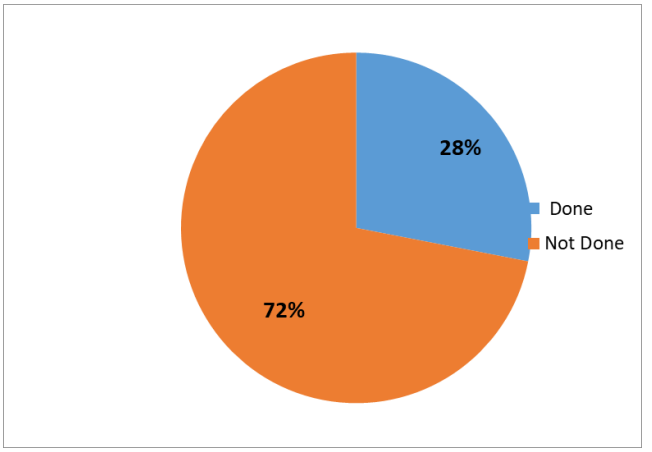

Figure 1. Frequency of prescription with and without culture sensitivity tests

Results from Figure 1 indicate that, Number of cases for which culture sensitivity was done found to be 213(28.06%) and number of cases without the culture sensitivity tests were 546(71.93%).

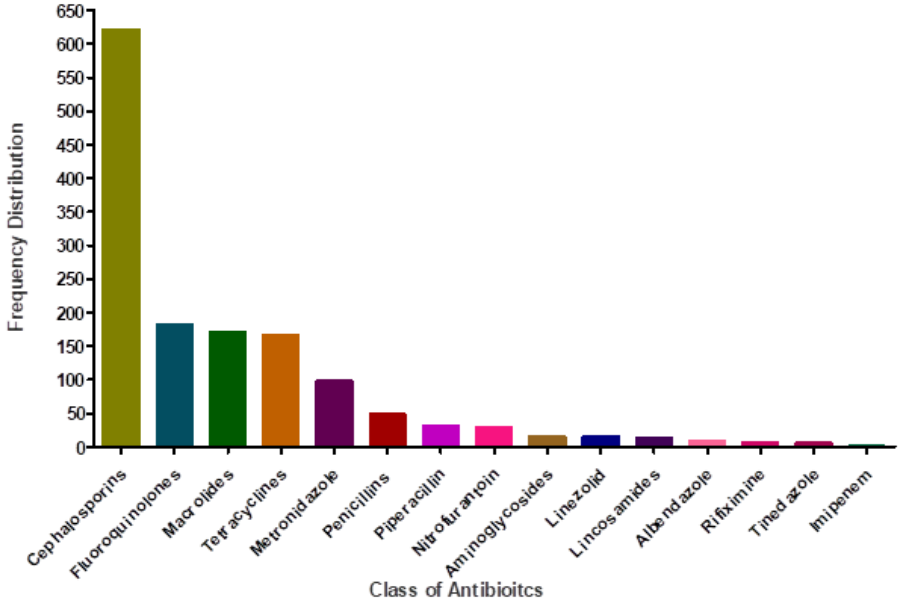

Figure 2. Frequency of Prescription Based on Antibiotic Class

The results from Figure 2 indicate that frequency of prescribing Cephalosporins were found to be highest 622(n=759) where percentage frequency of prescription was found to be 81.94%. The results from Figure 3 indicate that frequency of Antimicrobial therapy was found to be highest between 2-4 days.

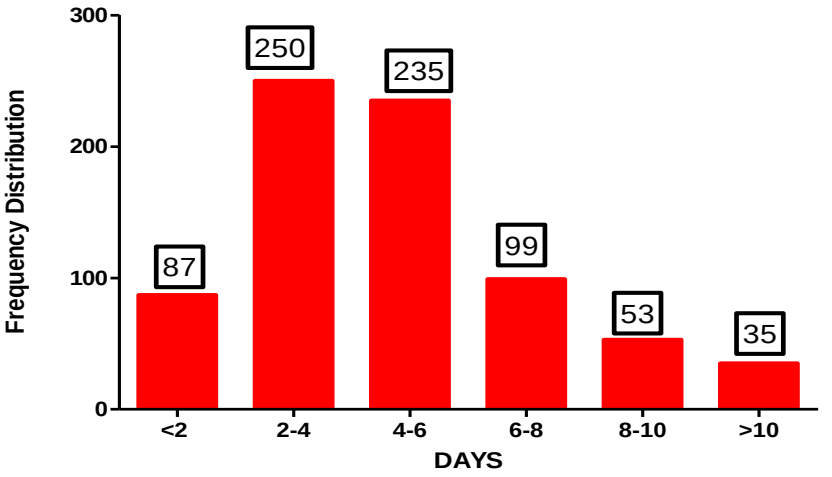

Figure 3. Duration of Antimicrobial Therapy

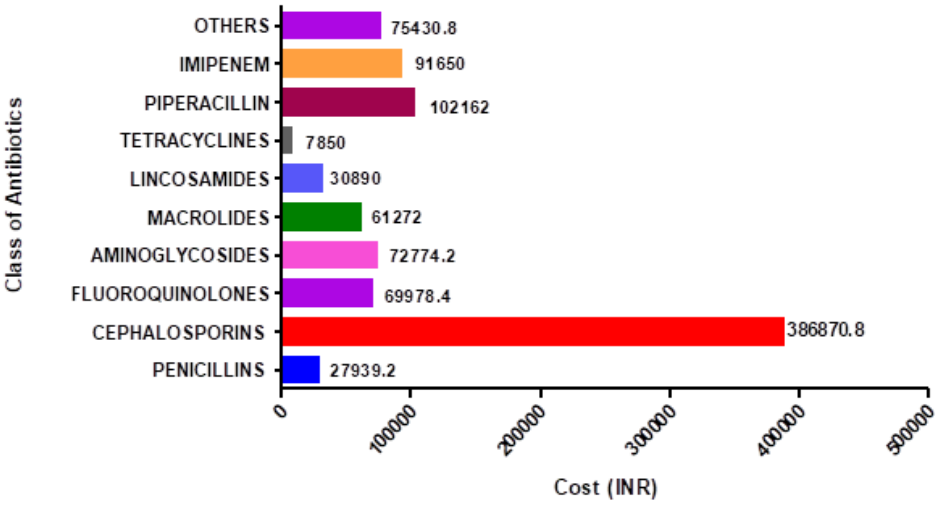

Figure 4. Cost Wise Prescription Based on Antibiotic Class

Results from Figure 4 indicate that the cost of Cephalosporins is comparitively more than other class of Antibiotics.

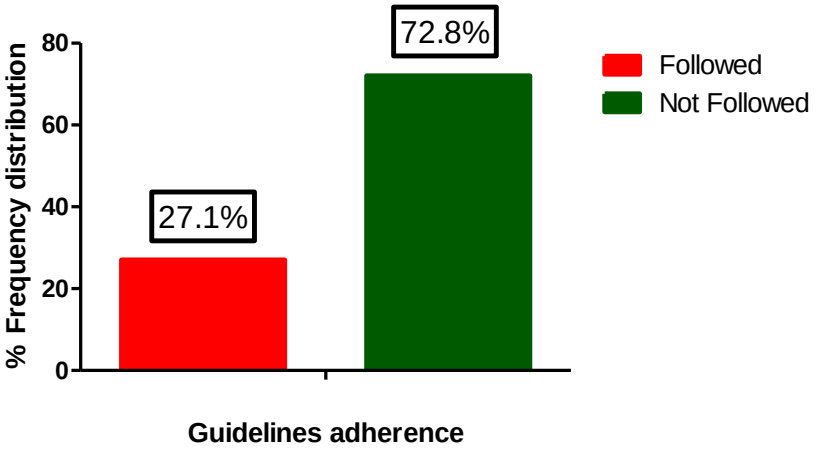

Figure 5. % Frequency distribution for guidelines adherence

Results from Figure 5 indicates that the prescription 82.8% are not adhere to guidelines

WHO drug indicators
Frequency of antibiotics encounter per prescription

Number	Frequency	Percentage
1	232	30.5%
2	326	42.9%
3	104	13.7%
4	46	6.06%
5	21	2.76%
6	30	3.95%

Discussion

The present study provides us with an overall pattern of antibiotic use profile in patients admitted in General Medicine wards in a tertiary care hospital. Majority of the patients were females 60.21%.This can be attributed to the prevalence of gender inequality as a result of which females are preferentially taken to tertiary care institutes for treatment as compared to males with a similar severity of illness.Majority of the patients (69.4%) were prescribed at least one antibiotic which is many times more than what was found in another study. As already mentioned, total antibiotic usage included both intravenous and oral antibiotics, of which beta-lactams (Cephalosporins the most) were maximally prescribed followed by Macrolides. Third generation cephalosporins were prescribed more frequently, which may be because ours is a tertiary care hospital and patients would have already been administered and probably developed resistance to lower generation antibiotics like co-trimoxazole, chloramphenicol, penicillinase resistant penicillins (methicillin, Oxacillin, Cloxacillin) etc.,

Culture sensitivity was not done in most of the patients(72%) and was done 28% patients but due to prior exposure to antibiotics (before reaching the hospital), the cultures are negative most of the times. Antimicrobials were prescribed empirically prior to the availability of culture results, and once the results were obtainedthe antimicrobials were modified in only 12% patients. This prescribing behavior was possibly related to the attitudes of health care professionals toward antimicrobial use in patients' management. An antibiotic utilization study in Saudi Arabia, carried out in a tertiary care center over a 12 month period, also found similar prescribing behavior in termsof failure to modify antimicrobial agents based on available cultures results. Fifty-two positive blood cultures were found in 43 patients (1.2 infections per patient), and initial antimicrobial selection was appropriate in around 63% of all encountered antimicrobial agents.

Majority of the drugs were given by intravenous route (55.9%) followed by the oral route (44%) and intravenous route is mostly preferred for the prophylactic use(55.9%). According to our study, there were a fairly good percentage of prescriptions by combination of brand and generic(68.5%),brand names(29.7%), followed by generics(1.84%).There is a very long way to achieve and inculcate the habit of prescribing generic drugs which will help in reducing the cost. Thus, more information about generic drugs and more research in the field of clinical pharmacology are needed for increasing generic medicine prescription rate. The total cost incurred on patients for drugs given by parenteral route was Rs.8,49,754/- (83%) and drugs given by oral route was Rs.1,69,617/- (16.6%).

Beta-lactams (Cephalosporins being major, Piperacillin) followed by Carbapenems accounted for the maximal cost of the antimicrobials.Fluoroquinolones, Aminoglycosides, Macrolides,Tetracyclines, lincosamides, penicillins and Miscellaneous antibiotics also contributed to a significant extent to the total cost of AMAs. Patients reach tertiary care hospital (like ours) in advanced stage with prior appropriate/inappropriate exposure to antibiotics and it becomes an absolute necessity to use higher generations of antibiotics. This leads to increased cost of therapy. Newer generation of antibiotics are more commonly prescribed leading to increased cost of therapy. Moreover, due to feasibility purpose, we are mentioning only the direct cost of the antibiotics, whereas there are various indirect expenses involved in a patient's hospital stay which cost the patient many times more.

Conclusion

This retrospective study addressing the patterns of antibiotic prescribing among patients admitted to general medicine ward in a tertiary care hospital revealed that more than 82% of patients received inappropriate antimicrobial therapy. There is indiscriminate and excessive use of antibiotic therapy. The study identified a need for local or hospital based guidelines for the management of common infections to reduce overuse and misuse of antimicrobial agents in tertiary care hospitals. Although our study has been conducted using a reasonably good sample size making various parameters quite trustworthy but the limitation of our study could be the smaller sample size. The robustness of our findings could have been increased by an even larger sample size had the

duration of study been longer. Another limitation is that it is a single centre study, hence the validity of findings would increase if it is a multi-centre study.

Though the number of Antimicrobial drug utilization studies is adequate, still we must seek ways and means to rationalize and prioritize which antibiotics must be prescribed in general practice to the patients. This would be best articulated through preparation and circulation of standard treatment guidelines (STG) and establishing the Antimicrobial stewardship programs to measure andimprove the use of antimicrobials to achieve optimal clinical outcomes and reducebacterial resistance, reduction in treatment costs, which is the ultimate goal of our study.

Major Findings of our Study

- Females are found to be mostly hospitalized than males.
- Cephalosporins are the most commonly prescribed class of antibiotics.
- Among Cephalosporins, third-generation drug Ceftriaxone is mostly prescribed.
- Parenteral antibiotics are mostly prescribed.
- Maximum number of prescriptions was found to be the combinations of brands and generics followed by brands and generics respectively.
- Low frequency of Generic drug prescriptions were observed in our study.
- Beta-lactams, Cephalosporins being the major and next to it is Piperacillinfollowed by Carbapenems accounted for the maximal cost of the antimicrobials.
- The total cost incurred on patients for drugs given by parenteral route was found to be more (83%).
- Newer generation of antibiotics are more commonly prescribed leading to increased cost of therapy.
- More than 70% of the prescriptions were prescribed with more than one antimicrobial agent.
- Adherence to National guidelines was very poor accounting 17.1% of antimicrobial prescription.
- 82.8% of the prescriptions were not adhered to guidelines and were found to be inappropriate.

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