Journal of Advances and Scholarly Researches in Allied Education
Vol. 16, Issue No. 5, April-2019, ISSN 2230-7540

Emergence of Empirical Antibiotic Therapy and Its Outcomes against Common Infectious Diseases: A Prospective Study Using General Practice Research Database

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Abstract – Background: *In India, Antibiotic use has been increasing steadily in recent years. Increasing use of antibiotics is not categorized as problem indicative, but evidence from research works related to Drug utilization gave a statement that antibiotics are very routinely used in different inappropriate ways. Therefore, it is important to evaluate antibiotics usage to reduce prevalence of antimicrobial resistance which could be a major problem in mere future.*

Objective: *The documentary target of the present research is to assess the use of Antibiotics (Rational / Irrational) in a private multi-specialty hospital, its positive and negative outcomes also, to interpose scheme from pharmacist view to encourage rational use of antibiotics to improve favorable outcomes and caliber of patients.*

Method: *It was a single centered, prospective observational study. Subjects of both genders who were indicated with antibiotic therapy and patients with comorbid pathological conditions were taken into consideration. Pediatrics, Pregnant women and surgical cases were excluded of the study.*

Results: *On assessing the results of study it was found that out of 500 cases studied which accounted for 100%, ceftriaxone was highly prescribed drug followed by Pipercillin + Tazobactum. On assessing rationality, it was found that 76% of prescriptions were rationality prescribed and 24% had irrationality. Amikacin was found to be the major resistant Antibiotic.*

Conclusion: *After evaluation of above results, Rational use of antibiotic for management of infection cause by microorganisms can be achieved by performing culture sensitivity testing and is very necessary to recognizes the organism to select the appropriate antibiotic leads to decrease development of resistance, decrease cost of the therapy and decrease hospital stay. By providing awareness programs, one should minimize those problems which are common at ward level such as irrational use. Counseling should be done at ward level. Awareness programs should be launched and seminars should be conducted. Monthly News sheets and Drug brief reports about the intelligent use of antibiotics should be released through publication formats. Cost effective prescription should also be encouraged. All these facts are possible when Clinical Pharmacist work along with the physician at ward level.*

Key Words: *Empiric Treatment, Antibiotic Resistance, Culture Sensitivity Test, Therapeutic Outcomes, Schedule H1, Pilot Study.*

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INTRODUCTION

Rational use of chemical constituents is defined as: Patients receive medicinal remedies appropriate to their clinical conditions, in correct doses that meet individual requirements, for a specific time period at lowest cost to patients and community.[1]. An antibiotic is an agent that inhibits bacterial growth or kills bacteria it is a substance produced by a micro-organism or synthetically that is antagonistic to the ontogenesis of strange or unusual or some other microorganisms that produces diseases in superior dilution. The unusual antibacterial therapy and inappropriate use of antibiotics have contributed to the issue or egression of developing anti-bacterial-resistant. Antibiotic resistance is defined as the resistance developed by microorganisms to anti-microbial agents, when bacteria modifies or alliterate to protect itself from antibiotics [2]. The egression or issue of antimicrobial resistance (AMR) is a major concern in public health and antibiotic usage is being ever more identified as the main discriminatory pressure driving this resistance. Antimicrobial resistance is a broader term, encompassing resistance to drugs to treat infections caused by other microbes, as a result of resistance infections fail to respond to standard treatment, so as result prolonged illness and increase risk of death anti-microbial resistance lead to decrease effect of effective antibiotic and infection remains for prolonged period of time and communicate to other. When microorganisms become resistance to first line antibiotics more expensive antibiotics are prescribed which increase cost of the therapy and increase hospital stay [3]. This problem cannot be prevented but its prevalence can be decreased Irrational use of medicines is a global problem. Irrational or inappropriate use of antibiotics is harmful for both patients and society people. The irrational antibiotics are one of the magnificent engender of mortality and morbidity around the world wide[4]. Rational use of a drug means when the patients receive the drug which is appropriate, in doses that meet their individual requirement, for an adequate period of time at the lowest cost both to them and the community and irrational use of Medicine is that when one or more of the above condition is not met. Joint commission International and Institute for Health Care Improvement estimated that about half of all medicinal products are prescribed, dispensed or sold without following precautionary steps and less than half of all patients take their medicinal products as prescribed or dispensed. An increased or high level or greater extent of antibiotic resistance has major consequences for society, and specifically for parameters on the margins who had decreased access to health care settings. It has been estimated that about half of all medicines are prescribed, dispensed or sold inappropriately and that less than half of all patients take their medicines as prescribed or dispensed. It is important to predict the factors for medication discrepancies to develop effective strategies to identify the presence of infectious diseases. Medication reconciliation on hospital admission at patient transition points is an important element to prevent and minimize adverse drug events. Irrational use of medicines can harm patients in terms of poor patient outcome un-necessary adverse reactions and wastage of resources, often out of pocket payment by patient. Irrational use of antibiotic is particularly serious because it is contributing to antimicrobial resistance that is increasing rapid worldwide and it is causing significant morbidity and mortality [5]. A high level of antibiotic resistance has major consequences for society, and especially for those on the margins who have the least access to health care. Delaying treatment with the right antibiotic increases the chance of severity and complications and forces the use of more potent and costlier antibiotics. Simple infections may need to be treated with antibiotics that need hospitalization and that increases the pressure on the overburdened hospital system. It is therefore important to look at what could be promoting the rise of antibiotic resistance. One of the possible causes of this phenomenon is the inappropriate use of antibiotics. Community studies have indicated that for illnesses such as diarrhea and fever, which are predominantly viral in etiology, approximately 70 percent of patients going to health facilities are given antibiotics. This is an inappropriate use of antibiotics (since antibiotics have little effect on viruses) and has resulted in increased resistance [6]. Streptococcus pneumonia resistance to beta lactam antibiotic involve alteration one or more of the penicillin binding proteins, result of which decrease binding of antibiotics to binding site. Enzymatic inactivation. The beta lactamase producing bacteria inactivate the beta lactam antibiotic these enzymes hydrolysis the beta lactam ring result of which loss of it activity. It is necessary for antibiotic to diffuse inside to microorganism and perform its function. In resistance organism such as bacteria the antibiotics is not concentrated inside bacteria and does not produce its action. In quinolones the DNA gyrase enzymes is mutated and result quinolones is not attach to such specific protein responsible for it mechanism of action so does not show it effect. In amino glycoside the plasmid mediated acetyl Transferase inactivate the amino glycoside and which result loss of its effect. Cause of this irrational use it leaded towards development of strains of bacteria like super-bugs & MDR-TB for which the treatment has become complex an uneasy [7]. Previous research and review Literature states that, In India antibiotic use has been become greater and enhanced eroded steadily in present years. Between 2004 and 2008, the units of antibiotics sold to a greater amount by about 37 percent. Increased sales of Cephalosporins were particularly striking, with sales (in units sold) increasing by 48 per cent over that seven-year period, but some increase was

seen in most antibiotic classes. In comparison, a pilot survey conducted at private retail pharmacies in 2009 and a survey in the same areas in 2010 & 2015 found increased use of Cephalosporins, but minimized or weakened or shrunken use of macrolides. The fact that antibiotic use is increasing is not, itself, indicative of a problem, but evidence from studies of prescribing patterns suggests that antibiotics are often used in inappropriate ways [8]. In order to shortlist the misuse of antibiotics and to improve therapeutic outcomes in patients so that prevalence of antimicrobial resistance(AMR) could be decreased which have become a major global cause in present era. The concept of rational drug use is very old and this confirms true with the evidence given by Alexandrian physician, Herophilus 300 B.C stated that "Medicines are nothing but they are the hands of god if employed with reason & prudence." In simplest words rational use means "prescribing right drug, in adequate dose for the sufficient duration& appropriate to the clinical needs of the patient at lowest cost. Rational uses of drugs have attained more significance in present days in terms of medical, socio economical and legal aspects. The following factors are responsible for the sudden realization of rational drug use [9].

1) **Drug explosion:** Greater extent due to presence of number of available drugs made terrifically complicated to select best and appropriate drug for specific or particular indication.

2) **Efforts to prevent the ongoing resistance mechanisms**: Irrational or improper use of drugs may lead to premature decline of highly efficient lifesaving new antimicrobial drugs due to development of unknown i.e., idiopathic cause underlined resistance.

3) **Growing awareness**: Now a day, current information about drug development, it's indications, therapeutic uses and untoward effects travel from one planet to the other planet with greater speed through various media.

4) **Increased cost of the treatment**: Increase in cost of the drug proportionally increases economic burden on the public as well as on the government. This can be reduced by prescribing all drugs or at least 70% of drugs rationally.

5) **Consumer protection Act (CPA):** Extension of CPA in medical profession may restrict the irrational use of drugs [10].

Measures to Enhance Rational Drug Usages: Medicines (drugs) cannot be used rationally unless all health care professionals involved in the pharmaceutical supply chain has access to know the complete information and in particularly, therapeutic indications of the drugs. Knowledge and ideas about drugs are constantly changing, so a physician is expected to know about the new development in drug therapy. The pre-requisites of rational drug use include Critical assessment & evaluation of benefits and risks of used drug; Compare the advantages, disadvantages, safety & cost of the drug with existing drug for some indication [11]. Various obstacles in rational drug use are as follows;

A) Lack of information about further education and training in pharmacology.

B) Lack of well-organized drug regulatory authorities and supply of drugs.

C) Presence of large number of drugs in the market and the lucrative methods of promotion of drugs employed by pharmaceutical industries.

D) The prevalent belief that "Every ill has a Pill."

Pharmacist's contribution: Pharmacists play a vital role in promoting the rational use of medicines. From the provision of pharmaceutical care and unbiased drug information to the selection, procurement and dispensing of essential medicines, pharmacist should be in a position to make a major difference to the manner in which medicines are prescribed [12]. However, the full potential of pharmacists can only be realized within a well – regulated, rule – based healthcare systems. Until then, it will be the efforts and commitment of individual pharmacists to contribute rational drug use (RDU). Activities in which pharmacists play an important role are Member of Pharmacy and Therapeutic Committee (PTC), Drug Procurement, Drug storage, Dispensing, Patient education, Pharmacovigilance, Drug information service and Pharmaceutical care [13].

RESEARCH METHODOLOGY:

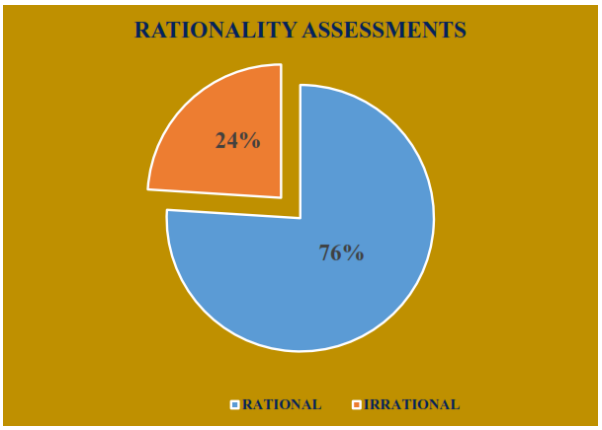
The Aim of the work is to determine the use of antibiotic (rational / irrational) in a tertiary care hospital and its beneficial and adverse outcomes. The objective of the study is to document an and analyze the rational use of antibiotics, to detect the spread of antimicrobial resistance among the selected group of subjects, to evaluate the safety, and effectiveness of treatment implemented on subjects indicated with antibiotics for treatment of infection and to intervene strategies from pharmacist perspective to promote rational use of antibiotics in order to improve therapeutic outcomes in patients in order to improve quality of life of patient. Justification of this study includes, due to abuse of antibiotics during the last decade, antibiotics resistance is on the rise, which not only affected the therapy but also increased the cost of antibiotic therapy. Misuse of antibiotics have

impacted immensely in declining the quality of life of patients. To overcome the above listed problems and to assure safety and effectiveness of therapy drug utilization and evaluation must be carried out and changes should be intervened to perfectionate the therapy. A pilot study was carried out for a period of six months to find the usage of antibiotics and prevalence of antibiotic resistance in population. All the prescriptions containing antibiotics were monitored and documented to know the frequency and extent to which antibiotics were indicated. The study protocol was designed on basis of necessity of study and was explained to the institutional ethical committee an approval was procured to carry out the study as per the designed protocol, literature which supported the study were reviewed for the need for rational use of antibiotics and common prescribing patterns. A standard data entry form was designed to document patient`s profile and during the ward rounds entire patient data were collected with special reference to those cases in which antibiotics were indicated and the whole data was documented in the format. This study was conducted in General medicine department, Shadan Institute of Medical Sciences, Shadan Hospital, Hyderabad, which is 750 bedded multi-specialty hospital. The hospital is one of private runned hospital, managed by senior professionals, highly experienced in respective specialty. The hospital operates all surgical cases especially cardiology, neurology and emergency medicine. A hospital based prospective, observational study was carried out on 500 patients in general ward. Demographic data of patient was documented which included (age, sex, occupation, date of admission, date of discharge, history of present illness, past medical history, family history, diagnosis, therapy indicated which listed all medicines which were given to the subject. Along with it data pertaining to culture test and its sensitivity was also taken into concern. A total of 500 patients (in-patients as well out-patients) in department of general medicine of Osmania general hospital, who were prescribed with antibiotics and one`s who fulfilled the inclusion and exclusion criteria were selected for the study. The study was carried out for a period of six months from December 2016 to June 2017. Subjects of either sexes who were indicated with antibiotic therapy in general medicine department and patients with comorbid pathological conditions are included. Neonates and pediatrics, Pregnant women and patients admitted for surgical procedures were excluded. Permission for collecting the patient data was approved by Institutional Ethical Committee, superintendent of hospital and head of department of general medicine. The authors were permitted to utilize the hospital facilities to make a follow up of the prescription in the department.

RESULTS:

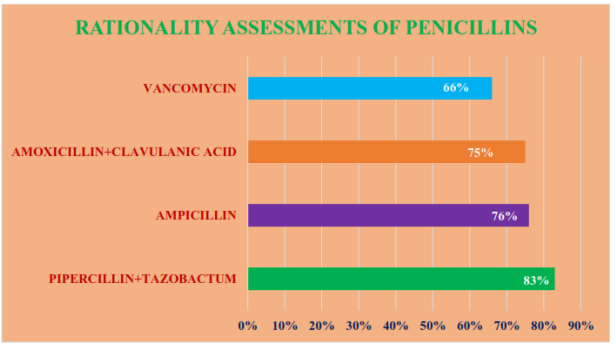
Rationality Assessments:

Rationality assessment for all prescriptions was carried out using WHO assessment criteria, it was found that 382 cases (76%) were treated rationally whereas remaining 118 cases (24%) had irrationality.



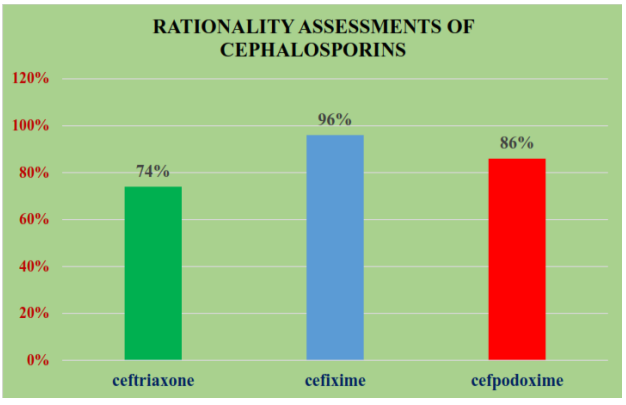
RATIONALITY ASSESSMENTS OF PENICILLINS:

On assessing the results among penicillin category, it was found that, Rationality percentages for Piperacillin+Tazobactam was 83%, Ampicillin was 76%, Amoxicillin+Clavulanic acid was 75% and Vancomycin was 66%.



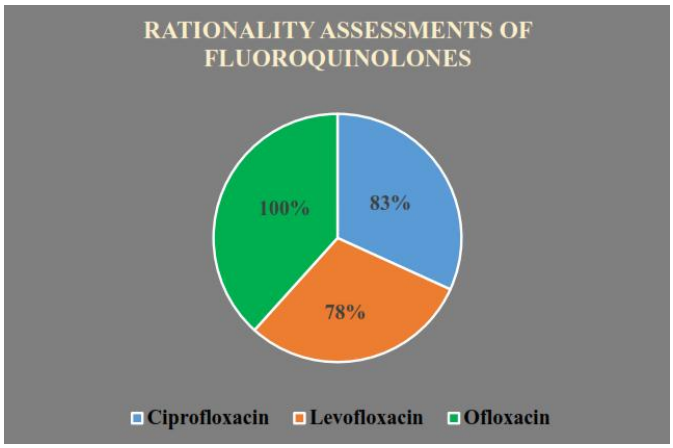
RATIONALITY ASSESSMENTS OF CEPHALOSPORINS:

On assessing the results among Cephalosporin category, it was found that, Rationality percentages for Ceftriaxone was 74%, Cefixime was 96%, and Cefpodoxime was 86%.



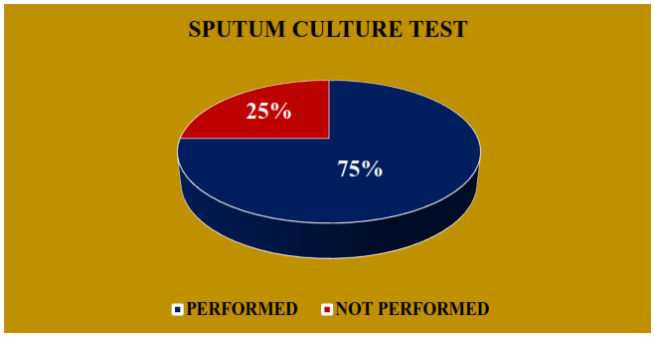
RATIONALITY ASSESSMENTS OF FLUOROQUINOLONES:

On assessing the results among Fluoroquinolones category, it was found that, Rationality percentages for Ciprofloxacin was 83%, Levofloxacin was 78%, and Ofloxacin was 100%.



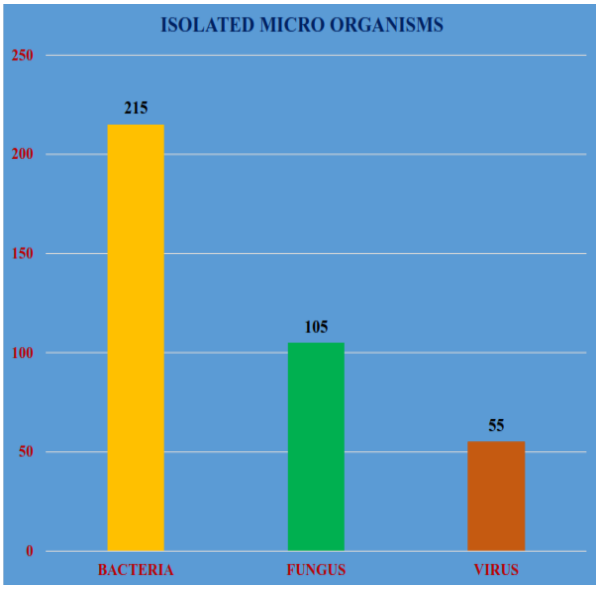
SPUTUM CULTURE TEST

In a total of 500 patients, 375 patients had undergone sputum culture test constituted for 75% and remaining 125 patients did not undergo sputum culture tests constituted for 25%.



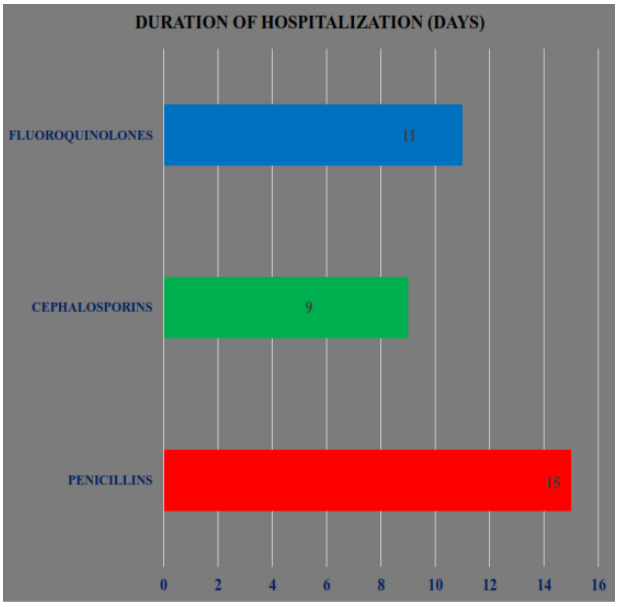
ISOLATED MICRO ORGANISMS

A total of 500 patients with clinical diagnosis of Bacterial infections were selected. Of 500 patients, 375 subjects had undergone sputum culture tests. Of 375 subjects, Bacteria was isolated in 215 patients constituted for 58%, Fungus was isolated in 105 patients constituted for 28% and Virus was isolated in 55 patients constituted for 14%



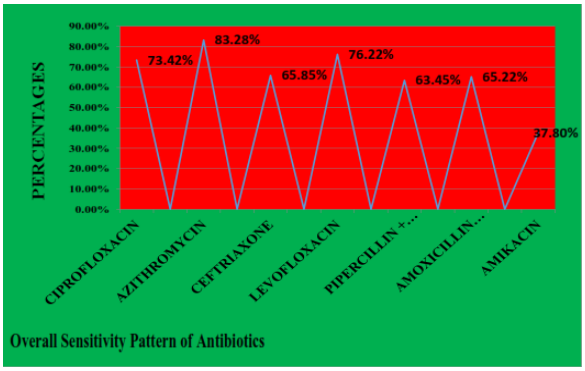
LENGTH OF HOSPITAL STAY (IN-PATIENTS):

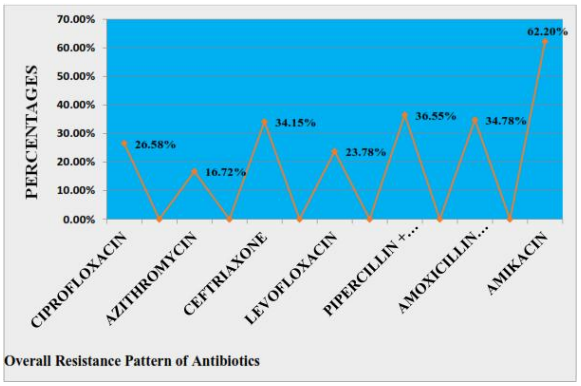
It is a time period that exists between Date of Admission (DOA) into the hospital and Date of Discharge (DOD) from the hospital. Mean Hospitalization days of patients on treatment with Penicillins was 15 days, Cephalosporins was 9 days and Fluoroquinolones was 11 days.



OVERALL SUSCEPTIBILITY PATTERN OF ANTIBIOTICS

The overall sensitivity and resistance of Ciprofloxacin was 73.42% and 26.58% respectively. Similarly, Azithromycin was 83.28% and 16.72%, Ceftriaxone was 65.85% and 34.15%, Levofloxacin was 76.22% and 23.78%, Piperacillin + Tazobactam was 63.45% and 36.55%, Amoxicillin Clavulanate was 65.22% and 34.78%, Amikacin was 37.80% and 62.20%.





DISCUSSION:

Antimicrobials are the most frequently prescribed drugs among hospitalized patients. The present study was a prospective observational study to monitor the antibiotic usage in a private hospital. In a total of 500 patients who were considered for the study, Male predominance was seen more when compared to Females. Respiratory infections were found to be common in present study about 45% of cases were reported. Antimicrobials were extensively used in general medicine to treat infectious cases. Irrational prescriptions and poly pharmacy of antimicrobials lead to emergence of drug resistance and therapy failure and increased patient`s morbidity and mortality. General Practioners were among the top three Health Care Professionals who prescribed the most antibiotics, corticosteroids and injection form of drugs. Frequent prescription of above-mentioned categories may suggest an increasing risk of inappropriate use of medicines. According to our findings, there is a significant difference between prescribing behavior of physicians depending on their specialties. Not using the antibiotic at the right time, stopping taking antibiotics before course completion may leads to antibiotic resistance development and is an emerging problem worldwide [14]. Among all the prescribed drugs Cephalosporins were extensively prescribed when compared to other group of antibiotics such as penicillin and fluoroquinolones. Among Cephalosporins majorly prescribed drug was ceftriaxone. Among second line antibiotics, penicillin derivative Piperacillin+Tazobactam combination was prescribed reason for choosing the above drug is that its wide spectrum activity and it is active against organisms which has shown resistance to Cephalosporins. It is preferable to keep the number of drugs per prescription as low as possible so as to minimize the risk of drug interactions, development of bacterial resistance and hospital costs. Two or more antibiotics were prescribed to patients due to lack of improvement in the clinical condition and were started together in serious ill patients [15]. Physicians were prescribing broad spectrum antibiotics rather than narrow spectrum antibiotics, though several antibiotic guidelines recommend to use narrow spectrum antibiotics. Irrational prescriptions of antibiotics is the major health care problem and burden to the society which lead to development of resistance and increase in health care costs. Previous study has shown that some physicians also prescribed antibiotics for non-infectious conditions. similar result was also seen in our study, that antibiotics were prescribed for conditions where antimicrobials in not required.

CONCLUSION

A wide spectrum of clinical dosing and variety of drugs were utilized from various drugs classes results showed that Cephalosporins were extensively used, among Cephalosporins, ceftriaxone was mostly prescribed followed by Piperacillin + Tazobactam combination was prescribed as secondly. On assessing the rationality of prescriptions it was found that majority of prescriptions were found to be rationally prescribed but rest had irrationality to some extent. Fewer cases were assessed for culture sensitivity test of which hardly very few cases were indicated with sensitive antibiotic treatments. The choice of Antibiotics for different infectious diseases is differed at different Indian hospitals by physician's choice and preference. This study also reveals that many standard treatment guidelines are available from various state government agencies. The study concludes that treatment implemented without culture sensitivity in most of cases may lead to irrational therapy which would lead to resistance as in many cases it has been seen that multiple antibiotics have been indicated on basis of prophylaxis and empirical treatment. After evaluation of above results, Rational use of antibiotic for management of infections caused by microorganisms can be achieved by performing culture sensitivity testing and is very necessary to recognizes the organism and select the appropriate antibiotic that leads to decrease in resistance development, decrease cost of the therapy and decrease hospital stay. Government of India might be able to ensure both rational and restricted use of Antibiotics with the implementation of Schedule H1 from 1st March, 2014. Along with physicians, other health care professionals should also take part in promoting Rational use of Antibiotics for their professional betterment.

ACKNOWLEDGEMENT:

Corresponding Author (Shaik Kareemulla), would like to express special thanks of gratitude to Dr. Vasanth Prasad, HOD, Dept. of General Medicine, Shadan Hospital, for giving fruitful guidance and providing all the facilities that were required to do Research work smoothly. By doing this study, I got enriched with much useful information that helps me in future endeavors.

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