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Research Article

A PROSPECTIVE STUDY ON ANTIMICROBIAL RESISTANCE PATTERN IN INPATIENTS OF GENERAL MEDICINE AND SURGERY DEPARTMENT

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ABSTRACT

Wide reports in literatures from different parts of the world revealed that antibiotics resistance is a serious and growing phenol menon in contemporary medicine and has emerged as one of the pre-eminent public health concerns of the 21st century. The purpose of the study is to compare the pattern of antibiotic resistance and to determine whether irrational use of antibiotics is a reason for antibiotic resistance. It was a Prospective observational study conducted multi-disciplinary super specialty tertiary care hospital in South India. All inpatients with either sex admitted to General Medicine and surgery department, including age groups of 18-70 and whose medication profile contains a culture sensitivity test report were included in the study. The outcome of the study was as follows: Klebsiella (25.49%) was the major organism isolated during the Pilot scale study, followed by E. Coli (22.5%), Pseudomonas(12.7%) and Staph. Aureus (19.6%). Amoxicillin showed the best resistance in Klebsiella (52.1%), E. Coli(21.7%), Pseudomonas(13.04%), Staph. Aureus (13.04%). During the prospective study, Klebsiella was the major organism identified in 71.42% of the isolated specimen- sputum. The resistance pattern data of the prospective study revealed that Klebsiella was highly resistant to Amoxicillin (52.1%) followed by E. Coli to Ampicillin (40.05%). Clinical pharmacists have to play an important role in promoting optimal antibiotic prescribing practice among physicians, during their routine visit to wards, which will enable to minimize resistance to antibiotics by the microorganisms.

Keywords: Antibiotics, Rational Drug Therapy, Resistance.

INTRODUCTION

Infections are very common and responsible for a large number of diseases adversely affecting human health. Most of the infectious diseases are caused by bacteria can be prevented, managed and treated through antibiotics. Antibiotics can be defined as the variety of substances derived from bacterial sources that control the growth of or kill other bacteria. Antibiotics do not kill viruses and are not effective in treating viral infections. Antibiotics operate by inhibiting crucial life sustaining processes in the organism: the synthesis of cell wall material, the synthesis of DNA, RNA, ribosomes and proteins. Judicious use of antibiotics is essential considering the growth of antimicrobial resistance and escalating costs in health care.

DEVELOPMENT OF ANTIMICROBIAL RESISTANCE

The recent problem in the antimicrobial therapy is the development of multidrug resistance. They adversely affect our ability to control the spread of infections.[1] The major reason for developing resistance may be the irrational use of antibiotics. [6]

EMERGENCE OF RESISTANCE

The use of antibiotics whether appropriate or not will produce an effect on microbial population. If the therapy with multiple antimicrobials result in emergence of resistance, it may lead to treatment failure. The host defense environmental factors and the properties of the drug used influence the development of bacterial resistance to the drugs.[7]

Bacterial resistance are either:

- Natural
- Acquired

In Natural Resistance, the drug sensitive enzyme reaction may be absent. In Acquired resistance,it can be demonstrated in vitro by serially culturing the organism in increasing concentration of antimicrobial drugs.[8]

MECHANISM OF ANTIMICROBIAL RESISTANCE

Natural drug resistance:
Due to lack of a suitable cell wall target site, lack of penetration of drug through the cell wall and susceptibility to naturally produced drug that destroying enzymes. E.g: S. Pyrogens resistant to Neomycin.

Acquired drug resistance:
Two mechanisms involved are: Intrinsic type of resistance and Drug destroying enzymes. Eg: Methicillin resistant S.aureus strains due to an altered penicillin binding protein in the cell wall.

Adaptation (Tolerance):
Loss of affinity of the target biomolecule of the micro organism for a particular antimicrobial agent. Eg: Resistant Staph. Aureus and E. coli develop an RNA polymerase that does not bind Rifampin.

Chromosomal mutations:
Any sensitive population of a microbe contains a few mutant cells which require higher concentration of the antimicrobial agent for inhibition. Eg: Enterococci to Streptomycin

Transmissible drug resistance:
Plasmids are extra chromosomal packets of DNA which may code for antibiotic resistance which will transferred to a sensitive strain from an antibiotic resistant strain, which makes the sensitive strain to become an antibiotic resistant. Most of the clinically important acquired drug resistances in antibiotic resistance strains of gram-negative bacilli are R factor (plasmid) mediated.
There are mainly three mechanisms; Conjugation, Transduction, and Transformation are involved in gene transfer in bacteria.[5]

IMPORTANCE OF CULTURE AND SENSITIVITY IN ANTIBIOTIC THERAPY

In modern laboratories characterization of genome is the basic step for identification of bacteria. This method is also used to identify the characteristics of the DNA and RNA of the sample species. When the bacterial infection is suspected and poses a sufficient health risk to demand immediate treatment empirical therapy should be given.e.g.; UTI, Tuberculosis. It is obvious to determining the type and sensitivity of causative organism for the better therapy. So accurate identification of the resistant pathogens by culture and sensitivity method are the primary concern of the clinicians to improve the treatment.[2]

ROLE OF PHARMACIST IN COMBATING RESISTANCE

Over the last 60 years, bacteria and other microorganisms have evolved towards microbial drug resistance. The evolution of the antimicrobial drug resistance has mainly two key steps, Emergence and Dissemination of resistance. All healthcare professionals especially clinicians should be aware of importance of susceptibility test which will helps to minimize the or prevent the occurrence of antibiotic resistance.[3] They should also insist on laboratory to follow these procedures to generate antibiotic susceptibility. Assurance of the quality of the test reports are essential to minimize the problems related with resistance. A consistent, reproducible and comparable data between different laboratories irrespective of outcomes regarding the antimicrobial susceptibility details necessary for developing region wise antibiograms.[9] clinicians should share sharing of experience and ideas about antibiotic therapy which is important to optimize the use of antibiotics and also for the management of infectious diseases.[10]

As a pharmacist, it is important to promote nationwide education, accreditation and training for antibiotic pharmacists. They have to perform major role in reviewing of antibiotic orders, drug selection and duration of therapy, designing and promotion of clinical practice guidelines, implementation of antibiotic switch programmes, and documentation of the effectiveness of interventions.[11] In many European countries it will be necessary to study the effect of the role of these specialists on improving and reducing antibiotic prescribing. This method will encourage the establishment of such posts.[4]

AIM AND OBJECTIVES

The main aim of the study is to evaluate the antimicrobial resistance in inpatients of General medicine and surgery department. The objectives include:

- To compare the pattern of antibiotic resistance;
- To determine whether irrational use of antibiotics is a reason for antibiotic resistance;

METHODOLOGY

STUDY SITE

The study was conducted at a 500- bedded multi-specialty hospital. The hospital is unique and people from different parts of the state come and avail its facilities.

DEPARTMENT SELECTED FOR STUDY

The study was conducted in the department of General Medicine and surgery. The reason for the selection of the department of General Medicine was that the pilot study revealed more scope for the study in the Department of General Medicine as the prevalence of antimicrobial prescription is more. When prescribing antibiotics, the knowledge on the organisms prevailing and the resistance pattern of antibiotics in the study hospital will help the health care professionals to select the appropriate antimicrobial agents to ensure rational therapy.

The study was conducted with expert guidance of the Clinical Pharmacy Professionals and Senior Physician of the General Medicine Department of the study hospital. Prior permission was also obtained from the Hospital and Institutional Ethical Committee.

LITERATURE SURVEY

An extensive literature survey was carried out regarding the use of antibiotics and its resistance patterns. The literatures were collected from various sources including journals

PATIENT SELECTION

Inclusion criteria: All inpatients with either sex admitted to General Medicine and surgery department, including age groups of 18-70 and whose medication profile contains a culture sensitivity test report.

Exclusion criteria: Patients who are not admitted in General Medicine and surgery department; Inpatients who are not willing to participate.

DATA ENTRY FORMAT

A specially designed data entry format was used to enter all patient's details like patient name, age, sex, weight, inpatient number, date of admission, date of discharge, reason for admission, past medical history, past medication history, social history, known allergies, previous ADRs, vital signs like temperature, BP and pulse. Provision is given in the format to enter laboratory investigations, specimen collected, organisms identified, and resistance to various antibiotics, diagnostics made, number of drugs prescribed and category of antibiotics.

STUDY DESIGN

A study design was carried out in the Department of General Medicine and surgery to find the scope of the study in this department. All the cases containing antibiotic prescriptions were monitored to know the frequency and extend of antibiotics use and also for conditions in which it was prescribed. The study protocol was designed and the necessity of the study and the study protocol was explained to the chief physician of the general medicine department of the study hospital.

The consent from the hospital authority was obtained during this phase. Literatures, which supports the study were collected and

reviewed the importance of antibiotic prescribing patterns. A standard data entry format for collecting patient details was designed and, during the ward rounds the entire patient data with special reference to the antibiotics prescribed and their resistance patterns were recorded in the data entry form.

RESULTS AND DISCUSSIONS

The study was carried out in a 500 bedded multi- specialty private hospital in South India. The study was performed in three phases to know the resistance pattern of microorganisms prevailing to various antibiotics in patients admitted to General Medicine and Surgery Department. Phase I of the study was a pilot scale study to know the scope of the study in the hospital. All the documented records, regarding the specimen tested, organism isolated, and also their resistance to various antibiotics were noted down in a specially designed data entry format and were analyzed. A total of 100 records were analyzed during the pilot scale study. The major organisms identified were E.coli (25.9%), Klebsiella species (22.5%), Pseudomonas species(12.7%), Staph. Aureus (19.6%), Acenobacter(9.8%), Betahemolytic Streptococci (9.8%)

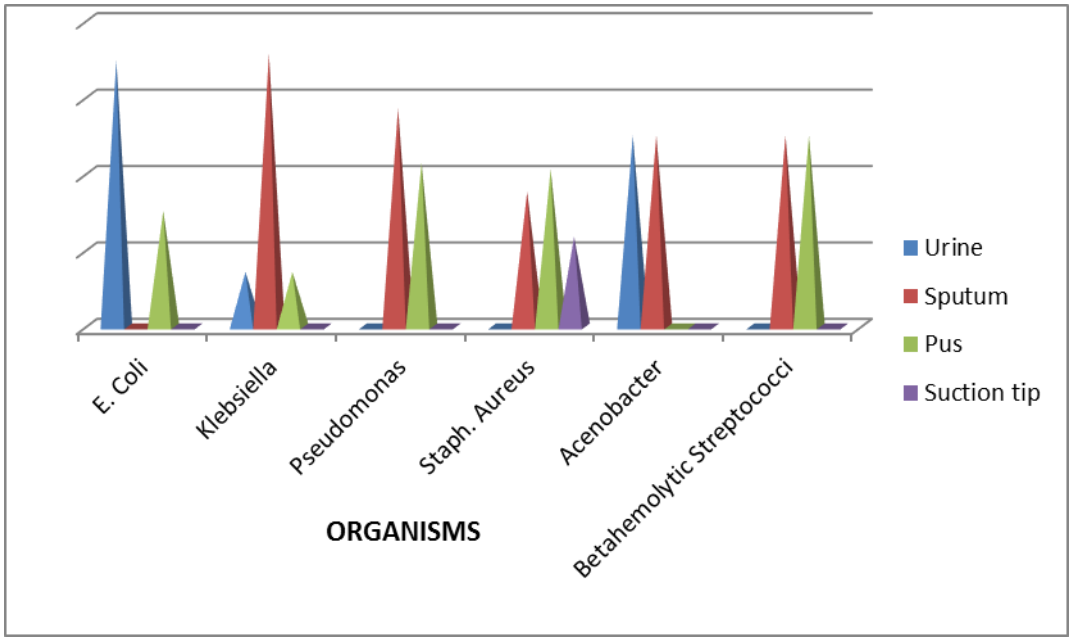


FIGURE 1: DISTRIBUTION OF ORGANISM IN DIFFERENT SPECIMEN

E.coli was highly prevalent in urine sample (69.6%).Klebsiella species were common in sputum (71.4%) and urine (14.2%). Pseudomonas was present more in sputum (57.1%), staphylococcus aureus was highly distributed in in pus (41.1%), Acenobacter was equally distributed in urine and sputum(50%), beta hemolytic also distributed equally in sputum an pus(50%).

TABLE 1: MAJOR ORGANISMS ISOLATED (n = 100)

ORGANISM	NUMBER OF PATIENTS	PERCENTAGE
E. Coli	23	25.49
Klebsiella	26	22.5
Pseudomonas	13	12.74
Staph. Aureus	20	19.60
Acenobacter	10	9.80
Betahemolytic Streptococci	10	9.80

Phase II of the study was a prospective analysis of the resistance pattern of micro organisms was carried out for a period of six months from December 2015- May 2016. During phase II a total of 100 documented records were analyzed. E.coli was the major organism identified in 25.49% of the isolated specimens followed by Klebsiella sp. (22.55%), Pseudomonas (2.74%),Acenobacter and Betahemolytic streptococci (9.8%). Urine, sputum, pus and suction tip were the major specimens samples collected.E.coli was isolated more in urine (69.6%),Klebsiella sp. in sputum (71.4%), Pseudomonas in sputum (57.14%),Staph. Aureus in pus (41.1), Acenobacter and Betahemolytic Streptococci were found equally in urine and sputum(50%) and sputum and pus(50%) respectively.

The resistance pattern data of the prospective study revealed that E.coli was highly resistant to Ampicillin (49%), Klebsiella to ciprofloxacin (37.9%), Pseudomonas to Nitrofurantoin (41.6%), staph aureusto Norfloxacin (32.5%), Acenobacter to Cefotaxime (10.3%) and Betahemolytic Streptococci to Gentamycin (7.5%)

Phase III of the study was to compare the data obtained from the pilot scale prospective study. The comparative phase showed that few organisms had developed resistance to certain antibiotics. In general Ampicillin, Cefuroxime, Gentamycin, Cotrimoxazole, Nalidixic acid and Cefoperazone were resistant to almost all the organisms.

The study conducted in a total of 100 patients in which 28 are UTI, 37 are LRTI and gastroenteritis and infected wound patients are 5 and 30 respectively. Out of the 100 patients 57 are females and 43 are males.

The patients were grouped based on their age. The most prominent age groups admitted in the hospital with UTI and LRTI

are 61-80. 38% of the patients fall under the age group of 41-60 and 9% fall under 21-40 age group.

40% of the patients hospitalized had a length of stay between 10-14 days, 22% had 3-5 days, and 19% had less than 3 days as the length of stay.

41% of the prescriptions had 6-10 drugs, 40 % had more than 10 drugs and the other 19% had less than 5 drugs in their prescription. Single antibiotic was prescribed for 30% of the total patients, 39% had two antibiotics, 18% had three antibiotics and 11% had four antibiotics respectively. Only 2% had more than five antibiotics.

There are mainly five classes of antibiotics are prescribed for the patients in the hospital, that includes Cephalosporins (36.27%), Aminoglycosides (28.43%), Flouroquinolones (9.8%), Penicillins (11.76%), others (13.72%). The antibiotic combinations that were commonly prescribed were Cefoperazone + Sulbactam (32%), Piperacillin+ Tazobactam(29%), Ceftriaxone+ Sulbactam (39%).

The major concomitant illness that was seen are Diabetes mellitus(33%), followed by Hypertension (29%), Dyslipidemia (18.86%).

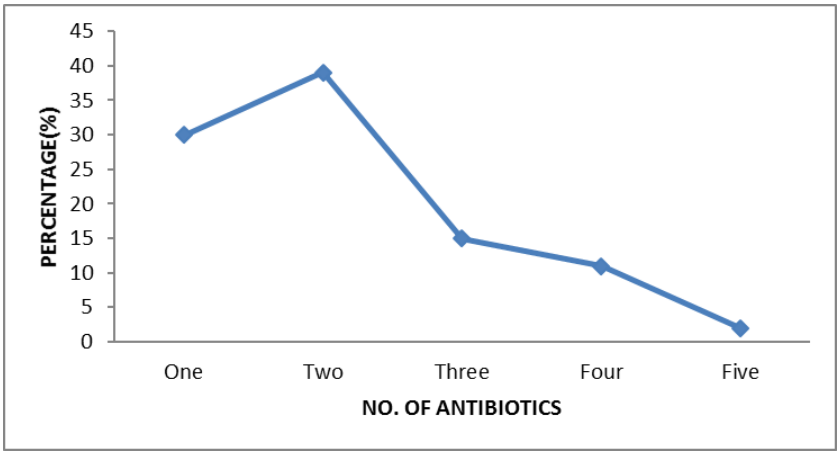


FIGURE 2: NO OF ANTIBIOTICS PER PRESCRIPTIONS (n = 100)

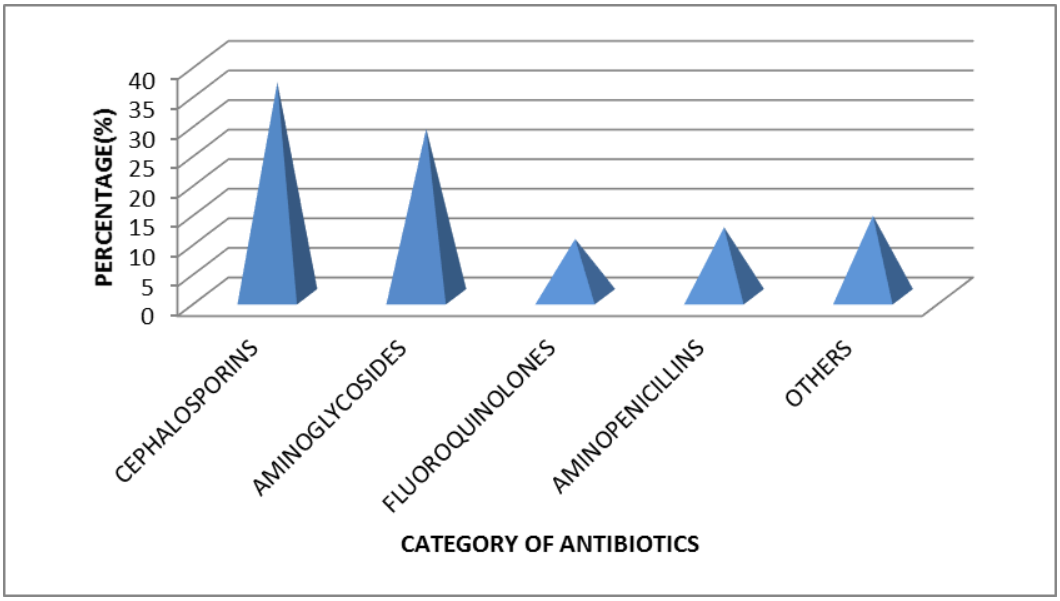


FIGURE 3: CATEGORY OF ANTIBIOTICS PRESCRIBED

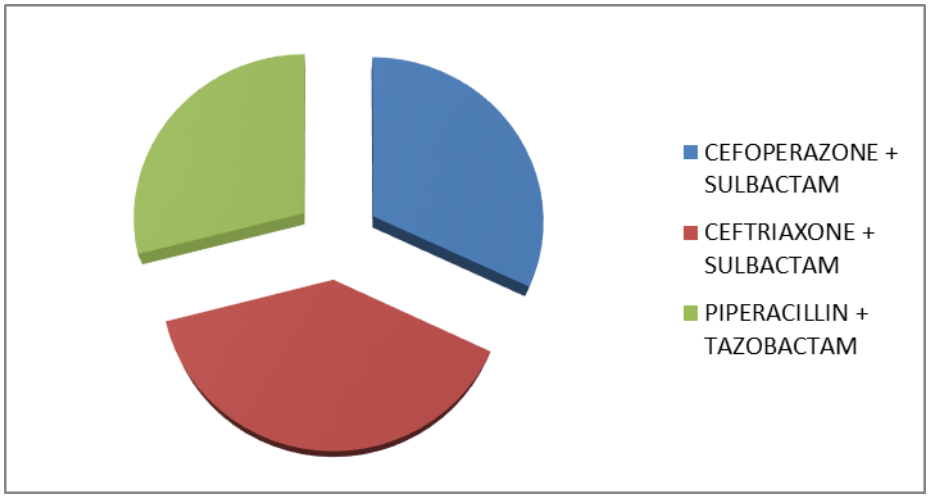


FIGURE 4: ANTIBIOTIC COMBINATIONS

TABLE 2: RESISTANCE PATTERN STUDIES (%)

ORGANISM	Ampicillin	Cephalexin	Cefuroxime	Gentamycin	Cotrimoxazole	Cefotaxime	Nalidixic Acid	Norfloxacin	Cefoperazone	Ciprofloxacin	Nitrofurantoin	Amoxicillin	Others
E. Coli	49.05	43.4	38.8	27.5	25.5	37.9	40.3	32.5	31.4	31.0	25	21.7	25.2
Klebsiella	11.3	30.4	16.6	27.5	25.5	31	19.2	20.9	25.71	37.9	33.3	52.1	32.2
Pseudomonas	16.9	19.5	30.5	15	20.9	20.6	10.5	13.9	17.1	0	41.6	13.04	12.2
Staph. Aureus	11.3	0	5.5	22.5	20.9	0	24.5	32.5	17.1	31.0	0	13.04	25.2
Acenobacter	5.6	6.5	8.33	0	6.9	10.3	0	0	8.5	0	0	0	5.2
Betahemolytic Streptococci	5.6	0	0	7.5	0	0	5.2	0	0	0	0	0	0

An extensive survey was conducted to identify the reasons of resistance mainly based on the self-medication. 33% of the patients were taking antibiotics themselves. For 39% of patients the major reason for their self medication is convenience. Common indications for self medication were Runny nose(24.4%),Cough(48.4%) and Sore Throat(18.8%) . Major reasons for the selection of antibiotics was based on previous doctor's prescription and it accounts for 57.7%.

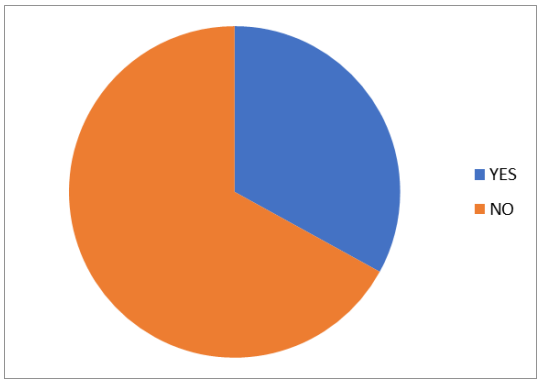


FIGURE 5: SELF MEDICATION PATTERN

TABLE 3: REASONS FOR SELF MEDICATION

REASONS	NO. OF PATIENTS	PERCENTAGE(%)
Cost Saving	10	30.30
Convenience	13	39.39
Lack of trust	4	12.12
Others	6	18.18

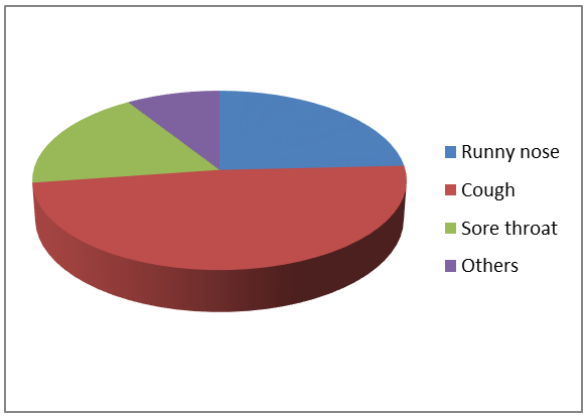


FIGURE 6: COMMON INSTANCES OF SELF MEDICATION

TABLE 4: REASONS FOR SELECTION OF ANTIBIOTICS

ANTIBIOTIC SELECTION	NO. OF PATIENTS	PERCENTAGE(%)
Recommendation by Community Pharmacist	2	6.06
Opinion of others	2	6.06
My own experience	10	30.30
Previous Doctor's Prescription	19	57.57

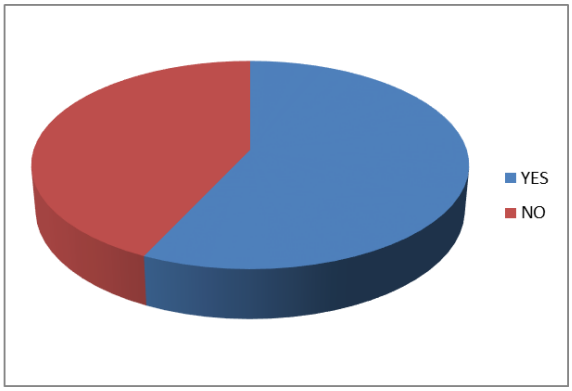


FIGURE 7: SELF-CHANGING OF DOSE OF ANTIBIOTICS

TABLE 5: REASONS FOR CHANGING DOSE OF ANTIBIOTICS

REASONS FOR CHANGING DOSE OF ANTIBIOTICS	NO. OF PATIENTS	PERCENTAGE
Improving conditions	38	66.66
Worsening conditions	7	12.28
To reduce adverse reactions	10	17.54
Others	2	3.50

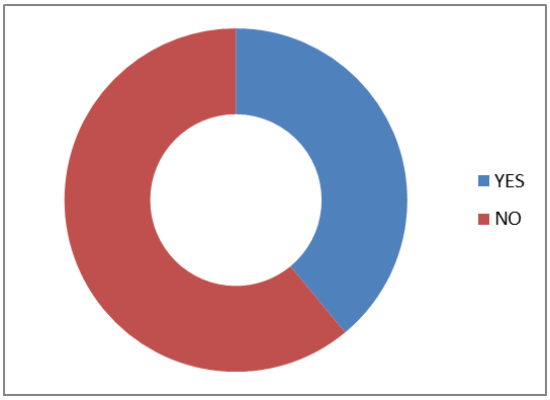


FIGURE 8: SWITCH OVER OF ANTIBIOTICS DURING THE COURSE OF TREATMENT

TABLE 6: REASONS FOR SWITCHING OVER OF ANTIBIOTICS

REASONS FOR SWITCHING OVER OF ANTIBIOTICS	NO.OF PATIENTS	PERCENTAGE
The former antibiotics did not work	23	58.97
The latter one was cheaper	3	7.69
To reduce adverse reactions	11	28.20
Others	2	5.12

TABLE 7: REASONS FOR SELF STOPPAGE OF ANTIBIOTICS

REASONS FOR SELF STOPPAGE OF ANTIBIOTICS	NO.OF PATIENTS	PERCENTAGE
After symptoms disappeared	45	45
At the completion of the course	50	50
After consulting a doctor/pharmacist	3	3
Others	2	2

CONCLUSION

As antibiotics share a very high percentage in most of the prescriptions, study on appropriate use of antibiotics and its resistance pattern in a hospital set up is necessary to be conducted in periodic intervals. The study had many limitations due to various reasons. The study was carried out over a period of six months and seasonal variations in the disease pattern and drug utilization were not considered. The prescriber should be alert regarding the condition of the patients and also be aware of the cost of drugs they are prescribing. Hospitals should encourage the practitioners to review their own prescriptions and to compare the cost effectiveness of alternative therapeutic regimens. Educate the public that antibiotics are potent drugs having various interactions and side effects and to avoid its abuse.

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