International Journal of Allied Medical Sciences and Clinical Research (IJAMSCR)

ISSN:2347-6567

*IJAMSCR |Volume 6 | Issue 3 | July - Sep - 2018*
**www.ijamscr.com**

*Research Article* *Clinical Pharmacy*

# Comparative Study Analysis and Rationality Assessment of Antibiotics in General Medicine Department of a Tertiary Level Teaching Hospital in South India

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## ABSTRACT

Rational use of medicines requires that "patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community". Irrational use of medicines is a major problem worldwide. WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly? The overuse, underuse or misuse of medicines results in wastage of scarce resources and widespread health hazards. Examples of irrational use of medicines include: use of too many medicines per patient ("poly-pharmacy"); inappropriate use of antimicrobials, often in inadequate dosage, for non-bacterial infections; over-use of injections when oral formulations would be more appropriate; failure to prescribe in accordance with clinical guidelines. The aim of the research is to study the comparative study analysis and to determine the Rational / Irrational use of antibiotics in a tertiary care hospital along with its beneficial and adverse outcomes and to Intervene strategies from pharmacist perspective to promote rational use of antibiotics to improve therapeutic outcomes in patients thereby improving quality of life (QOL) of patients. The study was carried out for a period of 24-36 months in Shadan Institute of Medical Sciences, Shadan Hospital, Hyderabad. It is a single centered, prospective observational study. Subjects of both genders who indicated with antibiotic therapy are taken in our study. On assessment, in a total of 3685 patients, it was concluded that, 1565 cases were male, 2120 cases were female, 1425 patients were Literates, 2260 patients were Illiterates, 1060 patients belongs to Low class, 1645 patients belongs to Middle class and 980 patients belongs to High class. In a total of 3685 prescriptions, it was concluded that, 2594 prescriptions (71%) were rationally prescribed and 1091 prescriptions (29%) were prescribed irrationally. In a total of 4700 antibiotics, it was concluded that, Prescriptions with single antibiotic are 1856, accounted for 39%, Prescriptions with 2 antibiotics are 2004, accounted for 44% and Prescriptions with 3 antibiotics are 840, accounted for 17%. In a total of 4700

antibiotics, it was concluded that, Cephalosporins (1420 antibiotics) were found to be highly prescribed antibiotic category accounted for 30.21%. Aminoglycosides (548 antibiotics) accounted for 11.65%, Macrolides (1165 antibiotics) accounted for 24.78%. Quinolones (902 antibiotics) accounted for 19.19%. Penicillins (385 antibiotics) accounted for 8.19% and Tetracyclines (278 antibiotics) accounted for 5.91%. There is a need of educational programs to promote rational use of antibiotics.

**Keywords:** Rational Drug Use (RDU), Quality of life (QOL), Socio-Economic Status (SES), Multi-Disciplinary Framework (MDF), Health Care Professionals (HCP).

## RATIONAL DRUG USE (RDU)

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. [1]

- ***Drug explosion*:** Increase in the number of available drugs made incredibly complicated the choice of appropriate drug for particular indication.
- ***Efforts to prevent the development of resistance*:** Irrational use of drugs may lead to premature demise of highly efficacious lifesaving new antimicrobial drugs due to development of resistance.
- ***Growing awareness*:** Today, the information about drug development, its uses and adverse effects travel from one end of the planet to the other end with amazing speed through various media.
- ***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 rational drug use.
- ***Consumer protection Act (CPA):*** Extension of CPA in medical profession may restrict the irrational use of drugs. [2]

## REASONS FOR IRRATIONAL USE OF DRUGS

### Lack of information

Unlike many developed countries, India doesn't have regular facilities to provide updated unbiased information on the currently used drugs. Majority of Indian practitioners rely on medical representatives. There are differences between pharmaceutical concern with respect to drug regulatory authorities in the interpretation of the data related to indications and safety of drugs.

### Inadequate training & education of medical graduates

Lack of proper clinical training about prescription writing during training period, dependency on diagnostic aid, rather than clinical diagnosis in many health care professionals.

### Poor communication between health care professionals & patient

Medical practitioners & other healthcare professionals have less time for counseling patient results in not explaining basic information about the use of drugs.

### Lack of diagnostic facilities/Uncertainty of diagnosis

Correct diagnosis is an important step toward rational drug therapy. Doctors posted in remote areas have to face a lot of difficulty in reaching to a precise diagnosis due to non-availability of diagnostic facilities and it promotes to practice poly-pharmacy further.

### Demand from the patient

To satisfy the patient expectations and demand of quick relief, physician prescribe drug for every single complaint. Also, there is a belief that "every ill has a pill" that increase the tendency to practice poly-pharmacy.

### Defective drug supply system& ineffective drug regulation

Absence of well-organized drug regulatory authorities and presence of large number of drugs in the market leads to irrational use of drugs.

### Promotional activities of pharmaceutical industries

The lucrative (profitable) promotional programs of the various pharmaceutical industries influence the drug prescribing. [3]

## MEASURES TO PROMOTE RATIONAL DRUG USE

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 [4]. 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. 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." [5]

## STEPS TO IMPROVE RATIONAL DRUG PRESCRIBING

### Step I

Identify the patient's problem based on symptoms and recognize the need for action.

### Step II

Diagnosis of the disease. Identify underlying cause and motivating factors may be specific in diagnosing infectious disease.

### Step III

List out the possible interventions and treatment. This may be either non-pharmacological treatment or pharmacological treatment. Drug must be chosen from different alternatives based on efficacy, convenience and safety of drugs that involves drug interactions and high risk group of patients.

### Step IV

While treating the patient, write accurate and complete prescription that include Name of drugs with dosage forms, Dosage schedule and Total duration of the treatment. [6]

### Step V

Giving proper instruction and indications regarding the treatment such as side effects (ADR), dosage schedule and dangers/risk of stopping the therapy suddenly.

### Step VI

Monitor the treatment to check whether advised treatment solved the patient's problem. It may be:

### Passive monitoring

Done by the patient himself by explaining necessary steps to be taken if the treatment is not effective or if the treatment has serious ADR's.

### Active monitoring

Done by physician through consultations to check the response of the treatment. [7]

### NOTE

Indiscriminate use of drugs not only affects scarce resources but also leads to drug induced disease. The drug control authority, the teaching institutes, drug industries, N.G.O and the patient himself would have a significant role for rational drug use. Drug authority must circulate the list of essential drugs and should be updated from time to time [10]. It should monitor the safe & proper use of these drugs, also should enforce a uniform regulation for promotional literature. Teaching institutes may also participate in conducting regular research work, proper training of undergraduates and post graduates. Motivation of NGO to organize various programs:

- Availability of essential and lifesaving drugs and unbiased drug information with generic name.

- ❖ Adequate quality control and drug control.
- ❖ Withdrawal of hazardous and irrational drugs.
- ❖ Drug legislation reform. [8]

## PHARMACISTS 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. However, the full potential of pharmacists can only be realized within a well – regulated, rule – based healthcare systems. [9] 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 given below:

- ❖ Member of the Pharmacy and Therapeutics Committee (PTC)
- ❖ Drug Procurement
- ❖ Drug storage
- ❖ Dispensing
- ❖ Patient education
- ❖ Pharmacovigilance
- ❖ Drug information service
- ❖ Pharmaceutical care.[10]

## ANTIBIOTICS

Antibiotics are a group of medicines used to treat infections caused by germs (bacteria and certain parasites). A parasite is a type of germ live in another living being (host). Antibiotics are sometimes called antibacterial or antimicrobials. Antibiotics are available in the form of parental, oral, topical (creams, ointments, or lotions) to treat certain infections. It is important to remember that antibiotics only work against infections that are caused by bacteria and certain parasites. They do not work against infections that are caused by viruses (for example, the common cold or flu), or fungi (for example, thrush in the mouth or vagina), or fungal infections of the skin. There are various antibiotics available that exists in different brand names. Antibiotics are usually grouped together based on their mechanism of action [11].

The main categories of antibiotics include:

- ➢ **PENICILLINS**: Phenoxymethylpenicillin, Flucloxacillin, Amoxicillin.
- ➢ **CEPHALOSPORINS:** Cefaclor, Cefadroxil,Cefalexin, cefuroxime.
- ➢ **TETRACYCLINES:** Tetracycline, Doxycycline,Lymecycline.
- ➢ **AMINOGLYCOSIDES**: Gentamicin, Tobramycin.
- ➢ **MACROLIDES:** Erythromycin, Azithromycin, Clarithromycin, Clindamycin.
- ➢ **SULFAMETHOXAZOLE & TRIMETHOPRM**: Co-Trimoxazole
- ➢ **METRONIDAZOLE AND TINIDAZOLE**
- ➢ **QUINOLONES**: Ciprofloxacin, Levofloxacin, Norfloxacin

Certain antibiotics works by killing germs like bacteria or parasites by interfering with the structure of the cell wall of the bacterium or parasite, termed as ***Bactericidal*** and some other antibiotics inhibits the growth of germs, termed as ***Bacteriostatic***. The choice of antibiotic mainly depends on type of infection and the germ (bacterium or parasite) responsible in causing infection, because each antibiotic is effective only against certain bacteria and parasites. For example, if patient diagnosed as pneumonia, the doctor prescribes those antibiotics that relieves the symptoms of pneumonia by a specific mechanism of action acting on bacteria [12]. Other factors that influence the choice of an antibiotic include:

- Severity of the infection.
- Functioning of kidneys and liver.
- Dosing schedule.
- Other medications.
- Common side-effects.
- A history of allergy to a certain type of antibiotic.
- Pregnant or breast-feeding

Most of the antibiotics are to be taken immediately after food while drugs used to reduce gastric acidity are to be taken on an empty stomach. Not taking the antibiotics at the right time causes decrease in drug absorption and reducing drug efficacy. So, patients should follow the instructions as given by physician on the leaflet that contain prescribed antibiotics. Patients are also advised to take complete course of antibiotics even though,

patient got better health and relieved from illness. If an antibiotic is stopped in mid-course, germs (bacteria) may be partially treated, not completely killed and may develop resistance to respective antibiotics. Overuse of antibiotics changes the structure (mutating) and develops the resistance [13]. For example, Methicillin Resistant Staphylococcus Aureus (MRSA) is a bacterium develops resistance to many antibiotics and is difficult for further treatment. Antibiotics also kill normal defense bacteria that live inside the bowel and vagina. Many adverse drug events of antibiotics are not serious. Common side effects include soft stools (feces), diarrhea, mild stomach upset, feeling sick and nausea. Some patients may develop allergic reactions on taking antibiotics. Some antibiotics may interact with other medicines causing reactions or reducing the efficacy of drugs.

- Severe watery diarrhea and tummy (abdominal) cramps: ***Signs of a serious bacterial infection of gut occur due to Clostridium difficile bacteria.***
- Shortness of breath, hives, rash, swelling of lips, face, tongue and fainting: ***Signs of an allergic reaction.***
- Vaginal itching or discharge: ***signs of vaginal thrush.***
- White patches on the tongue: ***signs of oral thrush.***
- Being sick: ***Signs of appetite loss.***

## DETAILED DESCRIPTION ABOUT ANTIBIOTICS

- AMOXICILLIN + CLAVULANIC ACID

### Mechanism of action (MOA)

It is used to treat Infections caused by certain Bacteria. A single dosage form containing Amoxicillin and Clavulanic acid belongs to the group of Antibiotic medications. Amoxicillin works by killing the bacteria that cause infection. Clavulanic acid helps the Amoxicillin to act more effectively.

### Dosage schedule

Recommended adult doses are 500mg every 8-12 hours, 250mg every 8 hours, 875mg every 12 hours or 2000 mg every 12 hours.

- Dosing is based on the amoxicillin component.
- Pediatric patients weighing more than 40 kg should receive adult doses.
- Pediatric patients weighing less than 40kg should receive 20 to 45 mg/kg every 8 or 12 hours.[14]

### Pharmacokinetic parameters

***Absorption:*** Peak plasma time: 2hour (Amoxicillin); 1.1 hour (Clavulanic Acid).
Peak Concentration: 8-22 mcg/mL (Amoxicillin); 0.8-2.6 mcg/mL (Clavulanic Acid).
Area Under Curve: 40-80 mcg.hr/mL (Amoxicillin); 2-6 mcg.hr/mL (Clavulanic Acid).
***Distribution:*** Protien Bound: 18% (Amoxicillin); 25% (Clavulanic Acid). Widely distributed (Except Central Nervous System).
***Metabolism*:** Partially metabolized by Liver.

### Elimination

EXCRETION: Urine, Unchanged; 50-70% (Amoxicillin), 25-40% (Clavulanic Acid).
HALF-LIFE: Amoxicillin: 3.7(full-term neonates); 1-2 hour (Infants and children); 0.7-1.4hr (Adults).
Clavulanic Acid: 0.8-1.4 hour.

### Therapeutic uses

Amoxicillin+clavulanic acid is widely used to treat or prevent many infections caused by susceptible bacteria, such as:

- urinary tract infections
- respiratory tract infections
- skin and soft tissue infections
- sinus infections
- cat scratches

Infections caused by the bacterial flora of the mouth, such as:

- dental infections
- infected animal bites
- infected human bites (including uncomplicated "clenched-fist" or "reverse-bite" injuries)

### Contraindications

Augmentin is contraindicated in patients who develop hypersensitivity to Amoxicillin & Potassium Clavulanate. Augmentin is contraindicated in patients with a history of allergic reactions to beta-lactams such as penicillin's and cephalosporins. It is also contraindicated in patients associated with Augmentin induced hepatic dysfunction. [15]

## CEFTRIAXONE

Ceftriaxone, sold under the trade names Rocephin, is an antibiotic useful for the treatment of a number of bacterial infections.

| Brand Name | Contains | Dosage Form |
|---|---|---|
| **DICEPHIN IV** | Ceftriaxone **250mg**, **500mg** & **1gm** vial (with water) | Injection (IV) |
| ENOCEF IM | Ceftriaxone **250mg**, **500mg** & **1gm** vial (with **lidocaine**) | Injection (IM) |
| **ENOCEF IV** | Ceftriaxone **250mg**, **500mg** & **1gm** vial (with water) | Injection (IV) |

### Mechanism of action

Ceftriaxone is a third-generation antibiotic from the cephalosporin family of antibiotics. It is within the β – lactam family. Ceftriaxone selectively and irreversibly inhibits bacterial cell wall synthesis by binding to transpeptidases, also called transamidases, which are protein-binding protiens (PBPs) that catalyze the cross-linking of the peptidoglycan polymers forming the bacterial cell wall. The peptidoglycan cell wall is made up of pentapeptide units attached to a polysaccharide backbone with alternating units of N-acetylglucosamine and N-acetylmuramic acid. PBPs act on a terminal D-alanyl-D-alanine moiety on a pentapeptide unit and catalyze the formation of a peptide bond between the penultimate D-alanine and a glycine unit on an adjacent peptidoglycan strand, releasing the terminal D-alanine unit in the process. The structure of ceftriaxone mimics the D-alanyl-D-alanine moiety, and the PBP attacks the beta-lactam ring in ceftriaxone as if it were its normal D-alanyl-D-alanine substrate. The peptidoglycan cross-linking activity of PBPs is a construction and repair mechanism that normally helps to maintain bacterial cell wall integrity, so the inhibition of PBPs leads to damage and destruction of the cell wall and eventually to cell lysis. [16]

### Pharmacokinetics

### Absorption

Ceftriaxone can be administered intravenously and intramuscularly, and the drug is completely absorbed. It is not available orally.

### Distribution

Ceftriaxone penetrates tissues and body fluids well, including cerebrospinal fluid to treat central nervous system infections. The average volume of distribution in adults is 5.8–13.5 liters.

### Metabolism

33–67% of ceftriaxone is renally excreted as unchanged drug, but no dose adjustments are required in renal impairment with dosages up to 2 grams per day. The rest is excreted in the bile as inactive compounds from hepatic and gut flora metabolism.

### Elimination

The average elimination half-life in healthy adults is 5.8–8.7 hours. In people with renal impairment, the average elimination half-life increases to 11.4–15.7 hours.

### Therapeutic uses

- Ceftriaxone is used to treat a wide variety of bacterial infections
- This medication belongs to a class of drugs known as cephalosporin antibiotic. It works by stopping the growth of bacteria.
- This drug is not recommended for use in newborns with high blood bilirubin levels and premature infants due to increased risk of side effects.

### Adverse effects

Although generally well tolerated, the most common adverse reactions associated with ceftriaxone are changes in white blood cell counts, local reactions at site of administration, rash, and diarrhea.

Incidence of adverse effects greater than 1%:

- Eosinophilia (6%)
- Thrombocytosis (5.1%)
- Elevations in liver enzymes (3.1–3.3%)
- Diarrhea (2.7%)
- Leukopenia (2.1%)
- Elevation in BUN (1.2%)
- Local reactions—pain, tenderness, irritation (1%)
- Rash (1.7%)

Some less frequently reported adverse events (incidence < 1%) include phlebetis, itchiness, fever, chills, nausea, vomiting, elevations of bilirubin, elevations in creatinine, headache and dizziness.

### Usual Adult Dose

1 to 2 g IV or IM once a day (or in equally divided doses twice a day)

### Usual Pediatric Dose

1 month or older: 50 to 75 mg/kg/day IV or IM in divided doses every 12 hours. Maximum dose: 2 g/day. [17]

## CIPROFLOXACIN

**Pharmacologic classification:** Fluoroquinolone antibiotic

**Therapeutic classification**: Antibiotic pregnancy risk category C

### Mechanism of action

Fluoroquinolones enter bacteria through porin channels, inhibits DNA gyrase and exhibit antimicrobial effects on bacterial topoisomerase II and bacterial topoisomerase IV.

- Inhibition of DNA gyrase results in relaxation of supercoiled DNA, promoting DNA strand breakage.
- Inhibition of topoisomerase IV impacts chromosomal stabilization during cell division, thus interfering with the separation of newly replicated DNA

### Dosage schedules

### Available forms

Ciprofloxacin for systemic administration is available as immediate-release tablets, extended-release tablets, oral suspension, and a solution for intravenous infusion. It is also available for local administration as eye drops and ear drops.

- Tablet-100 mg, 250 mg, 500 mg, 750 mg.
- Injection for infusion-200 mg/20 ml
- Vial-400 mg/40 ml
- Oral suspension-250 mg/5 ml, 500 mg/ml. [18]

### Pharmacokinetic parameters

### Absorption

About 70% of the drug is absorbed after oral administration. Administration of the drug after food, delays the rate of absorption.

### Distribution

Serum levels peak within 1 to 2 hrs after oral tablet dosing. 20% to 40% of the drug binds to plasma proteins. 10% of drug crosses blood brain barrier.

### Metabolism

Metabolism is probably hepatic. Four metabolites have been identified. Each has less antimicrobial activity than the parent compound.

### Excretion

Excretion is primarily renal. Serum half-life is about 4 hrs in adults with normal renal function

### Therapeutic uses

### Ciprofloxacin can be used for following purpose

- ***Urinary tract infections****:* High cure rates in complicated cases such as indwelling catheters & prostatitis. Chronic Pseudomonas infections respond slowly to ciprofloxacin.
- ***Gonorrhea****:* Initially a single 500 mg dose was nearly 100% curative in non-PPNG as well as PPNG infections, but cure rate has declined in the recent years due to emergence of resistance.
- ***Chancroid*****:** 500 mg BD for 3 days is an excellent alternative to ceftriaxone/ erythromycin.
- ***Bacterial gastroenteritis***: Severe cases due to EPEC, Shigella, Salmonella and Campy. Jejuni respond quickly. It has also been used to reduce stool volume in cholera.
- ***Typhoid*****:** Ciprofloxacin is the first choice drug in typhoid fever since chloramphenicol, ampicillin and cotrimoxazole have become unreliable due to development of resistance. In India, 95% S. typhi isolates are sensitive to ciprofloxacin. A dose of 500-750 mg BD for 10 days is recommended. Patients unable to take the

drug orally may be treated with 200 mg. i.v. 12 hourly in the beginning. It can also be used to treat typhoid carriers (750 mg B D for 4-8 weeks).

- ***Bone, soft tissue, gynaecological and wound infections*:** caused by resistant Staph and gram negative bacteria: high cure rates have been obtained but prolonged treatment with high doses is required in osteomyelitis and joint infection.

## CONTRAINDICATIONS

- Ciprofloxacin and other FQs are contraindicated during pregnancy.
- FQs should be used cautiously in children (under 18 years).
- Ciprofloxacin is contraindicated in persons with a history of hypersensitivity to ciprofloxacin.
- Concomitant administration with tizanidine is contraindicated.

## DRUG-DRUG INTERACTIIONS

- Amino glycosides, beta-lactums show synergistic effects have occurred with concurrent use.
- Antacids supplements containing aluminum, calcium and magnesium may interfere with ciprofloxacin absorption. [19]

## PIPERACILLIN AND TAZOBACTAM

### Mechanism of action

**Antibiotic action:** piperacillin is an extended spectrum pencillin that inhibits cell wall synthesis during microorganism multiplication. Tazobactam increases pipercillin effectiveness by inactivating beta-lactamases, which destroys penicillins.

### Dosage schedules

| Disease | Dose | ROA | Frequency |
|---|---|---|---|
| Haemophilus influenza | 3.375 gms | IV | q 6hrs |
| Nosocomial pneumonia | 4.5gms | IV | Q 6hrs for7-14 days |
| Peritonitis | 3.375 gms | IV | q 6hrs for 7-14 days |

### Pharmacokinetics parameters

***Absorption***: Unknown

***Distribution***: Both piperacillin and tazobactam binds to plasma protein bound at the rate of 30%.

***Metabolism***: Piperacillin is metabolized to a minor microbiologically active desethyl metabolite. Tazobactam is metabolized to a single metabolite that lacks pharmacologic and anti-bacterial activity.

***Excretion***: Both piperacillin and tazobactam are eliminated via kidneys by glomerular filtration and tubular secretion. Piperacillin is excreted rapidly as unchanged drug (68% of the dose) and tazobactam is excreted as unchanged drug (80%) in the urine. Piperacillin, tazobactam and desethyl piperacillin also secreted into the bile. [20]

### Therapeutic uses

- Combination of piperacillin and tazobactam is used to treat many different infections caused by bacteria, such as
- Urinary tract infections
- Bone and joint infections
- Severe vaginal infections
- Stomach infections
- Skin infections
- Pneumonia
- This medication is combined with other antibiotics to treat severe bacterial infections.

### Contra Indications

Piperacillin and tazobactam are contraindicated in patients with

- Drug allergies (especially to cephalosporins)
- Bleeding tendencies
- Uremia
- Hypokalemia
- Kidney disease with reduction in kidney function. [21]

# ERYTHROMYCIN

## Mechanism of Action (MOA)

Erythromycin and other macrolide antibiotics inhibit protein synthesis by binding to the 23S rRNA molecule (in the 50S subunit) of the bacterial ribosome blocking the exit of the growing peptide chain of sensitive microorganisms. (Humans do not have 50 S ribosomal subunits, but have ribosomes composed of 40 S and 60 S subunits). Certain resistant microorganisms with mutational changes in components of this subunit of the ribosome fail to bind the drug. The association between erythromycin and the ribosome is reversible and takes place only when the 50S subunit is free from tRNA molecules bearing nascent peptide chains. Gram-positive bacteria accumulate about 100 times more erythromycin than do gram-negative microorganisms. The non-ionized from of the drug is considerably more permeable to cells, and this probably explains the increased antimicrobial activity that is observed in alkaline pH.

## Dosage schedules

400 mg erythromycin (as erythromycin ethylsuccinate) every 6 hours is the usual dose. Dosage may be increased up to 4 g per day according to the severity of the infection. If twice-a-day dosage is desired, one-half of the total daily dose may be given every 12 hours. Doses may also be given three times daily by administering one-third of the total daily dose every 8 hours. In the treatment of streptococcal infections, a therapeutic dosage of erythromycin (as erythromycin ethylsuccinate) should be administered for at least 10 days. In continuous prophylaxis against recurrences of streptococcal infections in persons with a history of rheumatic heart disease, the usual dosage is 400 mg twice a day. For prophylaxis against bacterial endocarditis in patients with congenital heart disease, or rheumatic or other acquired valvular heart disease when undergoing dental procedures or surgical procedures of the upper respiratory tract, give 1.6 g (20 mg/kg for children) orally 1.5 to 2 hours before the procedure, and then 800 mg (10 mg/kg for children) orally every 6 hours for 8 doses. For treatment of urethritis due to C. trachomatis or U. urealyticum 800 mg every 6 to 8 hours for 7 days or 400 mg every 6 to 8 hours for 14 days. For treatment of primary syphilis: Adults 48 to 64 g given in divided doses over a period of 10 to 15 days. For intestinal amoebiasis: Adults 400 mg four times daily for 10 to 14 days. Children 30 to 50 mg/kg/day in divided doses for 10 to 14 days. For use in pertussis: Although optimal dosage and duration have not been established, doses of erythromycin utilized in reported clinical studies were 40 to 50 mg/kg/day, given in divided doses for 5 to 14 days. For treatment of Legionnaire's Disease: Although optimal doses have not been established, doses utilized in reported clinical data were 1.6 to 4 g daily in divided doses.[22]

## Paediatric Populations

Age, weight, and severity of the infection are important factors in determining the proper dosage. In mild to moderate infections the usual dosage of erythromycin (as erythromycin ethylsuccinate) for children is 30 to 50 mg/kg/day in equally divided doses every six hours. For more severe infections this dosage may be doubled. If twice-a-day dosage is desired one-half of the total daily dose may be given every 12 hours. Doses may also be given three times daily if desired by administering one-third of the total daily dose every 8 hours.

## Pharmacokinetic parameters

Pharmacokinetic properties following oral administration, erythromycin ethyl succinate is absorbed intact and undergoes hydrolysis to yield the active erythromycin base. Individual peak serum levels show considerable variability; the peak after each dose occurs in 1-2 hours. The extent of plasma protein binding has been variably reported but is probably of the order of 75%. Erythromycin diffuses readily into most body fluids with the exception of cerebrospinal fluid, synovial fluid and vitreous humor. In the presence of normal renal function, the plasma half-life is approximately 1.4 hours; this may increase to 6 hours in anuric patients but does not usually require dosage adjustment. Erythromycin is not removed by dialysis. In the presence of normal hepatic function, erythromycin is concentrated in the liver and high concentrations appear in the bile. However, approximately 1.5% of the absorbed erythromycin can be recovered unchanged in bile over a period of 8 hours. Substantial quantities appear in the faeces and probably represent the unabsorbed drug plus the drug excreted into the

bile. Approximately 5% of an orally administered dose appears in the urine. A large proportion of the absorbed drug remains unaccounted for and is presumably metabolised, probably in the liver. Erythromycin appears in breast milk at levels which are approximately 50% of the plasma concentration. It crosses the placenta and fetal plasma levels are usually 5%-20% of the maternal plasma concentration.

### Therapeutic use

Upper and lower respiratory tract, skin and soft tissue infections of mild to moderate severity. When oral medication is preferred for treatment of streptococcal pharyngitis and in long term prophylaxis of rheumatic fever, erythromycin is an alternate drug of choice.

### Side effects

Uncommon (may affect up to 1 in 100 people): – Fungal infections (candidiasis) of the mouth with white coating – Vaginal inflammation – Itching of the vulva in women – Allergic reactions – Widespread skin rash (urticarial exanthema) – Skin itchiness – Redness of the skin with increase of blood flow (hyperaemia) – Abnormal liver and gallbladder function detected by blood tests – Pain or irritation at the site of injection – Swelling and redness along a vein which is extremely tender when touched Rare (may affect up to 1 in 1,000 people): – Swelling of certain part of your body including face and neck (allergic oedema/angioedema, anaphylaxis) – Symptom of poor appetite (anorexia) – Epigastric pain radiating to the back with nausea, vomiting, diarrhoea and loss of appetite (pancreatitis) – Itchiness with jaundice, pale stool and dark urine (cholestasis and cholestatic jaundice) – Swollen joints – Fever – Hives – Skin eruptions – Inflammation of the colon with severe diarrhoea Very rare (may affect up to 1 in 10,000 people): – Unmasking or worsening of a rare disease associated with muscle weakness (myasthenia gravis) – Ringing in the ears (tinnitus) and mainly transient loss of hearing – Inability of the liver to perform normal function – Inability of the kidney to perform normal function – Severe skin reactions (Stevens-Johnson syndrome and erythema multiform) – Skin peeling (toxic epidermal necrolysis)

### Contraindications

Erythromycin is contraindicated in patients with known hypersensitivity to erythromycin or any of the excipients in the formulation, or to other antibiotics from the macrolide family. Severely impaired hepatic function. Concurrent treatment with cisapride, pimozide, and ergotamine or dihydroergotamine is contraindicated. [23]

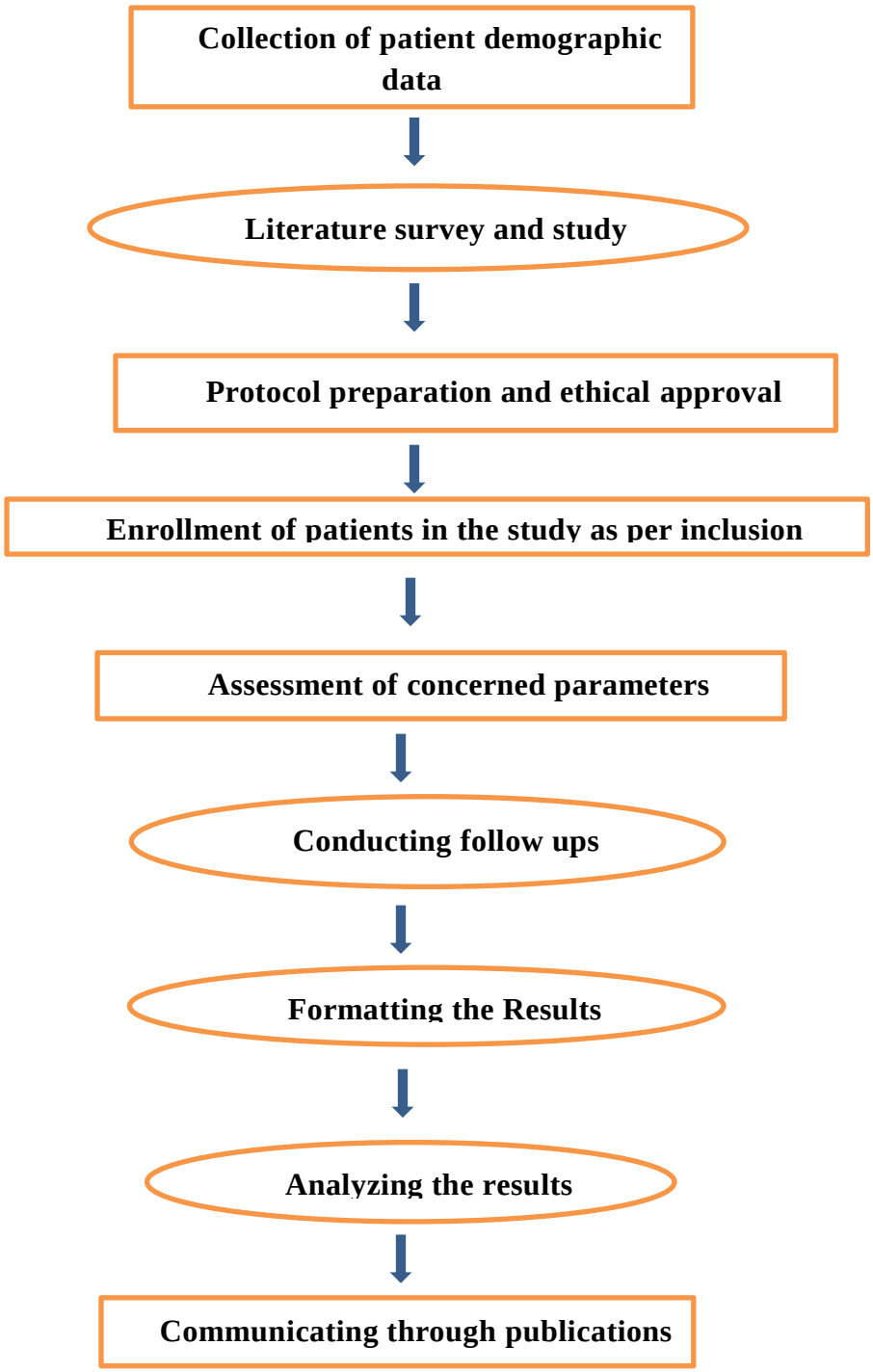
## OBJECTIVES OF STUDY

1) To determine the number and percentages of Male & Female patients containing atleast one Antibiotic in their prescription.
2) To determine the number and percentages of Literate & Illiterate patients containing atleast one Antibiotic in their prescription.
3) To determine the number and percentages of Socio-Economic status of patients containing atleast one Antibiotic in their prescription. To determine the number and percentages of patients with rational & irrational prescribed use of antibiotics.
4) To determine the number and percentage of prescriptions containing one antibiotic, two antibiotics and three antibiotics.
5) To compare the most frequently used antibiotic category drugs with other antibiotic categories.
6) To intervene the strategies from pharmacist's perspective to promote rational use of antibiotics that improve therapeutic outcomes and quality of life (QOL) of patients.

## STUDY DESIGN

A hospital based prospective, observational study was carried with the inclusion of 3685 patients and 4700 prescribed antibiotics in general medicine ward. Demographical data of patient was documented and includes Age, Sex, Occupation, Date of admission, Date of discharge, History of present illness, past medical history, Diagnosis and prescription drugs.

## PLAN OF WORK




## STUDY SITE

DEPARTMENT OF GENERAL MEDICINE, SHADAN INSTITUTE OF MEDICAL SCIENCES (SIMS), HYDERABAD.

The study was conducted in General medicine department in a tertiary care teaching hospital. SIMS Hospital is one of the private runned hospitals, managed by senior professionals, highly experienced specialist of departments like general medicine, gastroenterology, psychiatry etc. SIMS hospital also operates all surgical cases especially

cardiology, neurology, nephrology, orthopedic and gynecology.

## STUDY APPROVAL

Permission for collecting patient's data was approved from Superintendent of SIMS hospital and Clinical guide of General medicine department. In addition, I also request Hospital management to permit to utilize the facilities for regular follow ups of prescriptions for undergoing a smooth and sophisticated research work.

## STATISTICAL ANALYSIS

Results were represented as frequencies, percentages, mean and medians as appropriate. Percentage method was used for analyzing the data. Appropriate statistical parameters are used to evaluate comparative study effects of three drug regimens. Graph pad prism software will be applied to analyze the data. In some cases, inferential statistics like Analysis of variance (ANOVA) followed by student t-test, (at 95% confidence interval and $P<0.05$ considered as significant) using SPSS 21.0 software also be utilized.

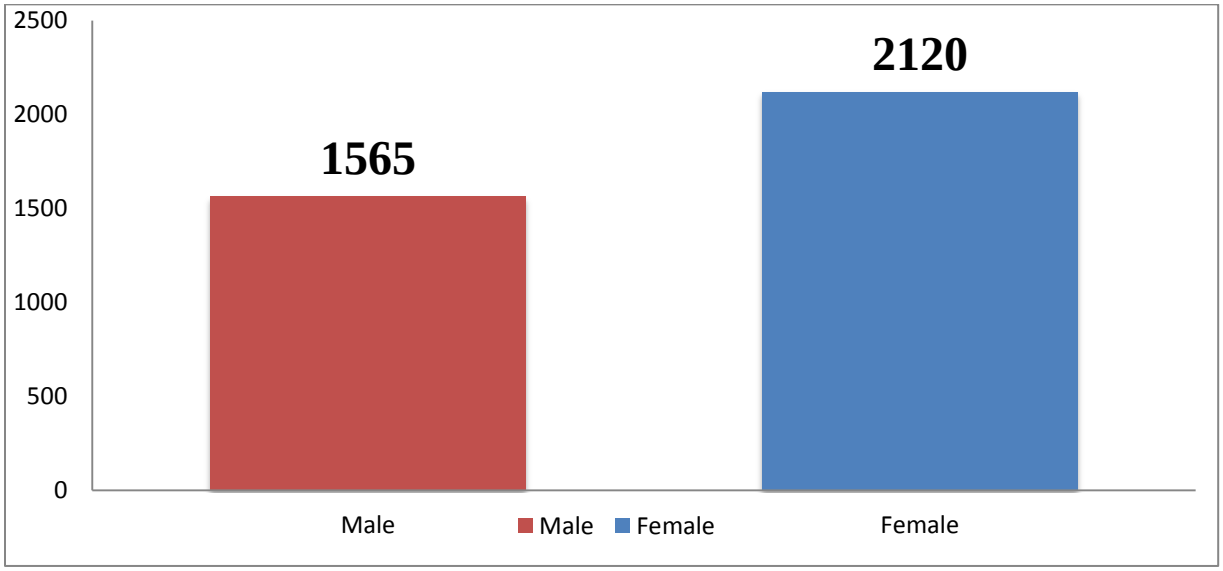
### Rationality assessment criteria as per World Health Organisation (WHO) [24]

| Rational | Irrational |
|---|---|
| Definitive therapy based on symptoms & laboratory investigations | Poly pharmacy |
| Appropriate dose | Inappropriate use of higher class of antibiotics |
| Appropriate time | Inappropriate dosing, over dosing and under dosing |

## RESULTS

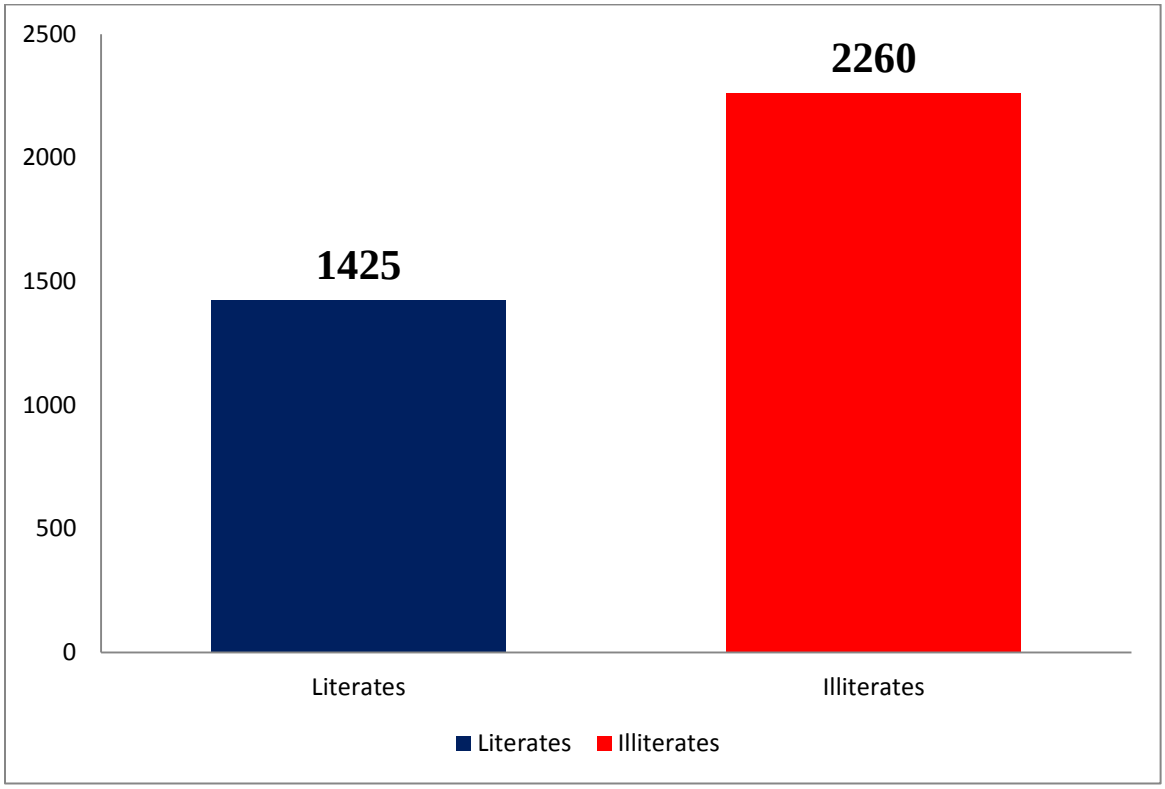
### Patient distrubution based on gender

3685 cases were collected and 4700 antibiotics were prescribed which accounted for 100%. On assessment, it was found that male (1565 cases) patients constituted for 42% whereas female (2120 cases) patients constituted for 58%.



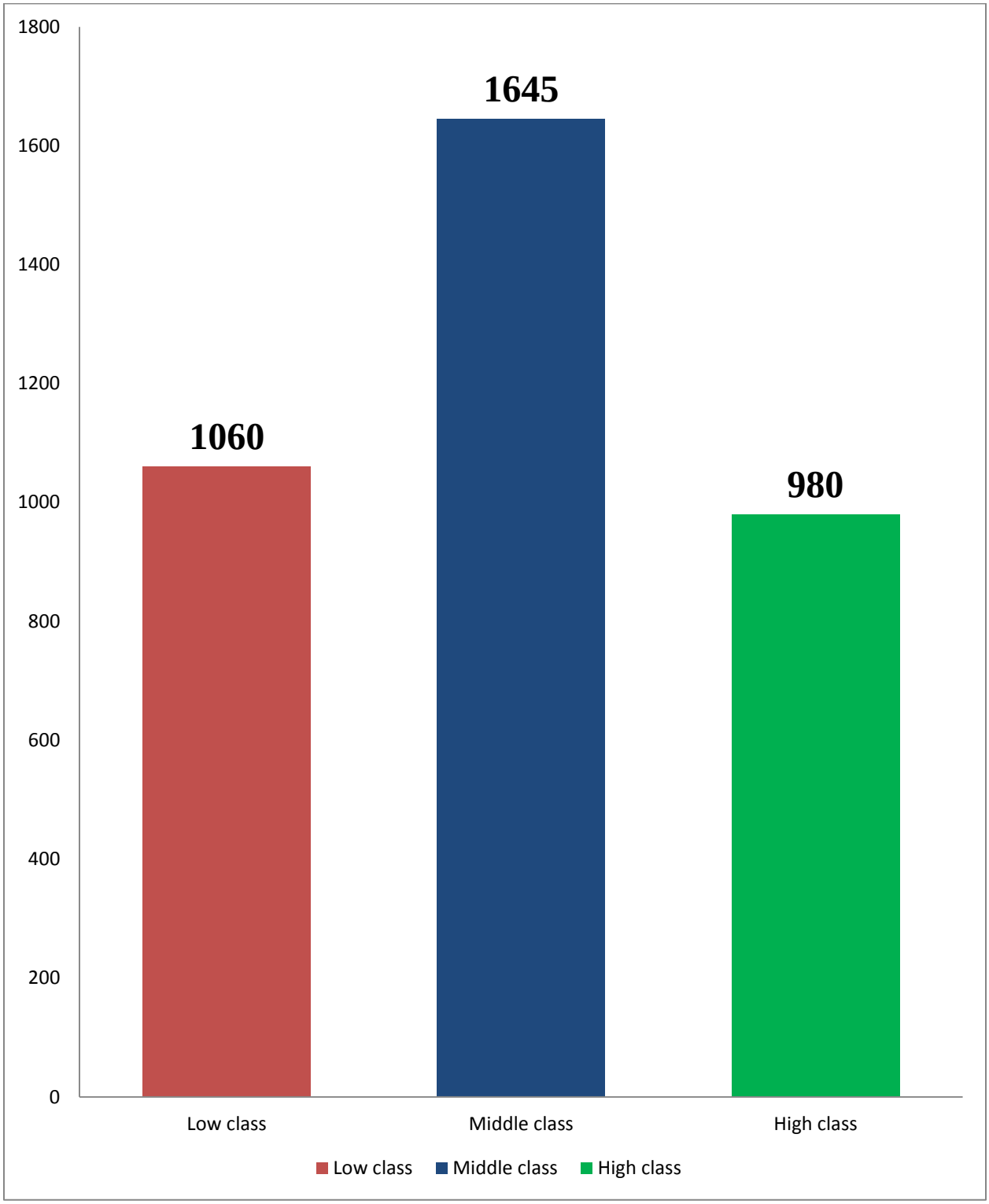

### Patient distrubution based on literacy rates

3685 cases were collected and 4700 antibiotics were prescribed which accounted for 100%. On assessment, it was found that Literates were 1425 patients constituted for 39% whereas Illiterates were 2260 patients constituted for 61%.



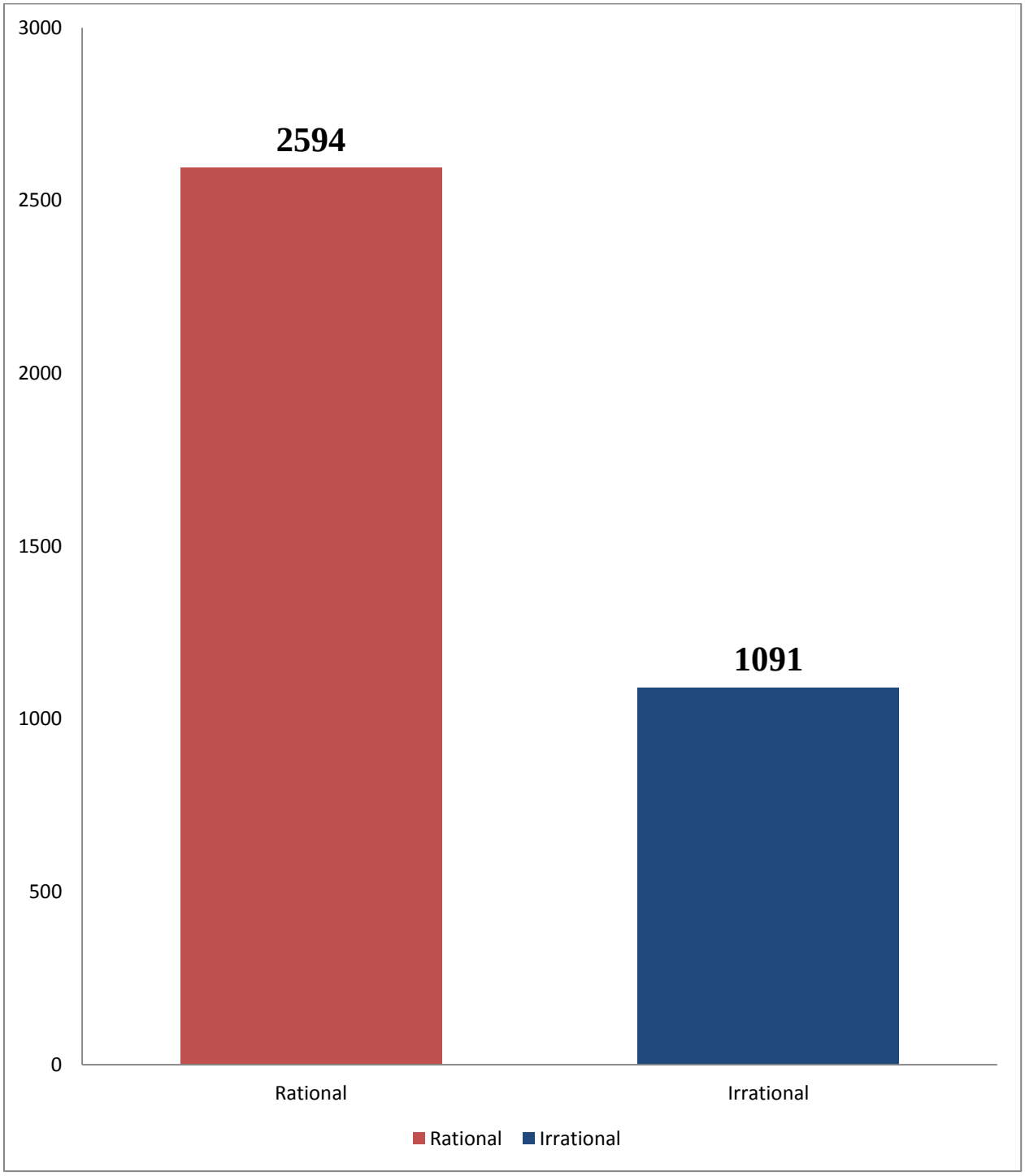

## Patient distrubution based on economic status

3685 cases were collected and 4700 antibiotics were prescribed which accounted for 100%. On assessment, it was found that Low class patients were 1060, constituted for 29%, Middle class patients were 1645, constituted for 44% and High class patients were 980, constituted for 27%.



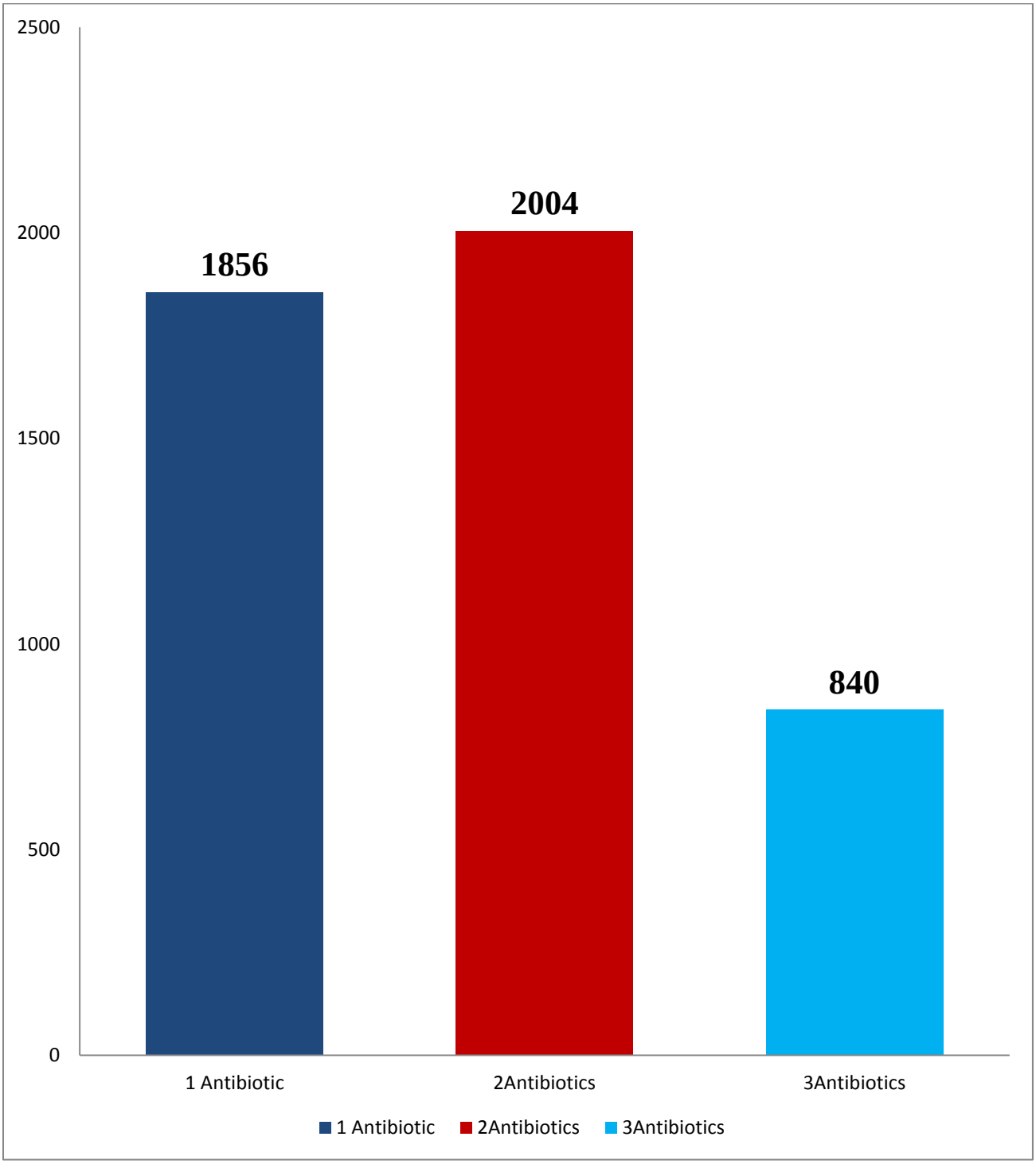

## Patient distribution based on rationality assessment

Rationality assessment for all prescriptions was carried using WHO assessment criteria as mentioned in the methodology. 3685 cases were collected and 4700 antibiotics were prescribed which accounted for 100%. On assessment, it was found that 71% (2594 out of 3685 cases) were rationally prescribed to treat infections, while remaining 29% (1091 out of 3685 cases) have fewer drugs prescribed irrationally.



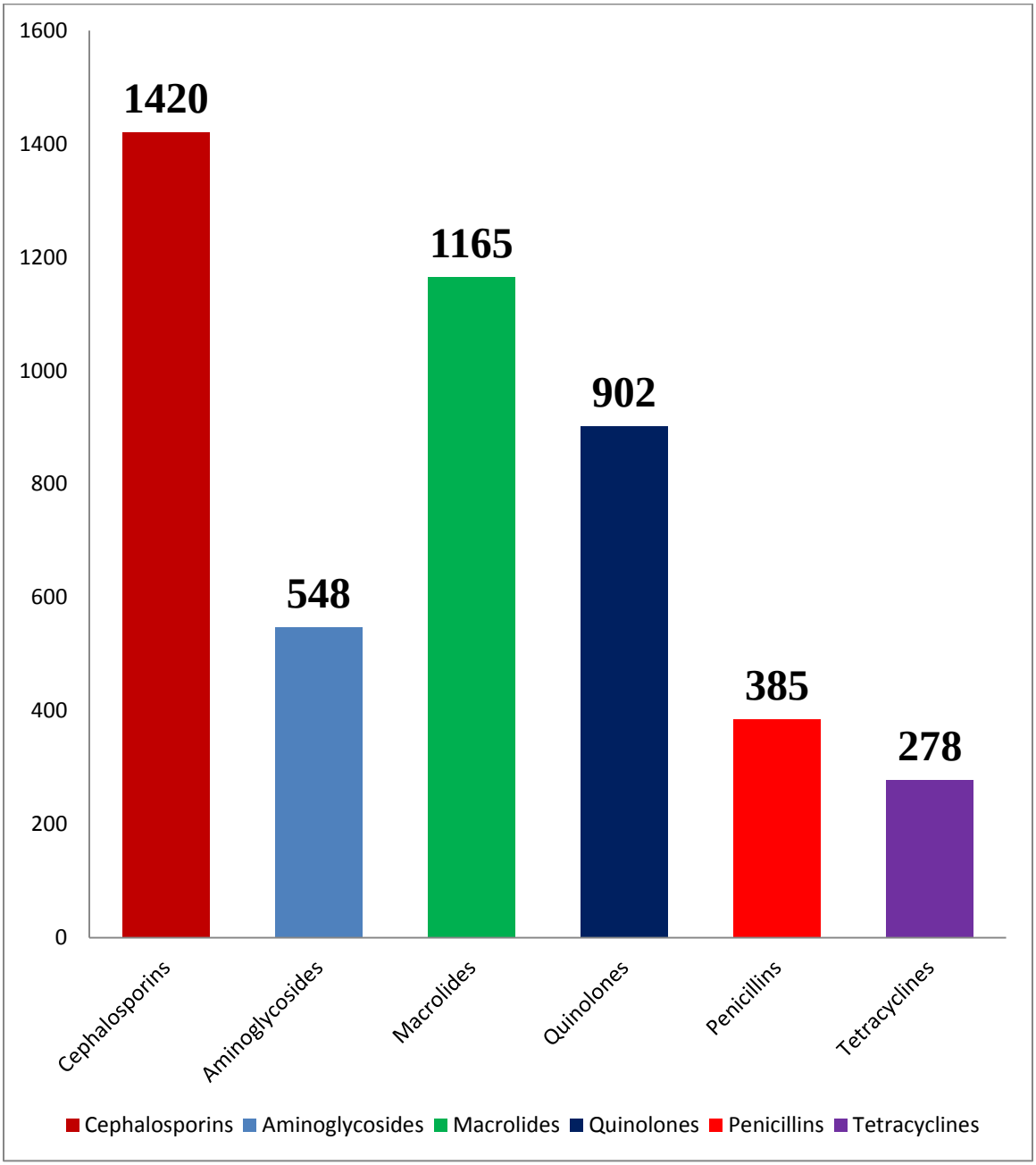

## Comparitive analysis of monotherapy & polytherapy prescriptions (Monotherapy v/s Polytherapy)

In general medicine department, 3685 cases i.e., 3685 prescriptions were collected and 4700 antibiotics were prescribed which accounted for 100%. Prescriptions (1856 out of 4700 prescriptions) with single antibiotic accounted for 39%. Prescriptions (2004 out of 4700 prescriptions) with 2 antibiotics accounted for 44% and Prescriptions (840 out of 4700 prescriptions) with 3 antibiotics accounted for 17%.




## Comparitive analysis of penicillins, cephalosporins, macrolides, aminoglycosides, tetracyclins & quinolones

In General medicine department, 3685 cases were collected and 4700 antibiotics were prescribed which accounted for 100%. On assessment, Cephalosporins (1420 out of 4700 antibiotics) was found to be highly prescribed antibiotic category accounted for 30.21%. Aminoglycosides (548 out 0f 4700 antibiotics) accounted for 11.65%, Macrolides (1165 out 0f 4700 antibiotics) accounted for 24.78%. Quinolones (902 out 0f 4700 antibiotics) accounted for 19.19%. Penicillins (385 out of 4700 antibiotics) accounted for 8.19% and Tetracyclines (278 out of 4700 antibiotics) accounted for 5.91%.




## DISCUSSION

Rational use of drugs have attained more significance in present days in terms of medical, socio economical and legal aspects which is defined as "prescribing right drug, in adequate dose for the sufficient duration & appropriate to the clinical needs of the patient at lowest cost. Information about rationality assessment of antibiotic use is lacking in primary health care centers, non-government organization (Anganwadis) and also in multi-specialty hospitals. 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. This study deals with the rationality assessment and comparative analysis of antibiotics in a general medicine department over a period of 24-36 months. Essential drug lists play a significant role in acute primary health care settings and their utility in our study is limited. 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. Rational prescribing of antibiotics can be achieved by adjusting baseline prescribing; duration of the intervention and prescribing narrow-spectrum antibiotics. Awareness programs should be launched and seminars should be conducted so as to minimize problems which are common at ward level. News Letters and Drug bulletins about the rational use of antibiotics should be released periodically. Cost effective prescription should be encouraged. Academic detailing practice of western countries can also be initiated in India, refers to one-on-one educational communications to alter physician's prescription if needed. Specific principles of academic detailing includes emphasizing effective techniques of patient-physician communication, using graphic materials, involving opinion leaders and encouraging 2-sided communication. All these factors have to be taken into consideration during antibiotic prescribing and to improve rational use of antibiotics.

## CONCLUSION

This study clearly highlights the Rational use and Comparative study analysis of different antibiotics used in General medicine department of a Tertiary care hospital. On assessment, in a total of 3685 patients, it was concluded that, 1565 cases (42%) were male, 2120 cases (52%) were female, 1425 patients (39%) were Literates, 2260 patients (61%) were Illiterates, 1060 patients (29%) belongs to Low class, 1645 patients (44%) belongs to Middle class and 980 patients (27%) belongs to High class. In a total of 3685 prescriptions, it was concluded that, 2594 prescriptions (71%) were rationally prescribed and 1091 prescriptions (29%) were prescribed irrationally. In a total of 4700 antibiotics, it was concluded that, Prescriptions with single antibiotic are 1856, accounted for 39%, Prescriptions with 2 antibiotics are 2004, accounted for 44% and Prescriptions with 3 antibiotics are 840, accounted for 17%. In a total of 4700 antibiotics, it was concluded that, Cephalosporins (1420 out of 4700) was found to be highly prescribed antibiotic category accounted for 30.21%. Aminoglycosides (548 out 0f 4700) accounted for 11.65%, Macrolides (1165 out 0f 4700) accounted for 24.78%. Quinolones (902 out 0f 4700) accounted for 19.19%. Penicillins (385 out of 4700) accounted for 8.19% and Tetracyclines (278 out of 4700) accounted for 5.91%. Rational use of the antibiotics is the foremost goal in writing a prescription. Rational use of antibiotics improves quality of life (QOL) of patients. There is a need of educational programs to promote rational use of antibiotics. Such programs should be initiated within a multidisciplinary framework including doctors, pharmacists, social scientists, government agencies and non-profit organizations. Medical education in clinical pharmacology and pharmacotherapy should include the principles of rational therapeutics. In collaboration with other health care professionals, Pharmacists play a significant role in educating patients about hazards of self-medication, over use of drugs and poly-pharmacy. Hence, teamwork involvement of Health care professionals in safe use of antibiotics and overall health care of the patient is very crucial.

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**How to cite this article:** Shaik Kareemulla, Dr. Pankaj Kumar Sharma, Dr. Birendra Shrivastava, Dr. Khaja Pasha. Comparative study analysis and rationality assessment of antibiotics in general medicine department of a tertiary level teaching hospital in south India. Int J of Allied Med Sci and Clin Res 2018; 6(3): 574-592.