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NARROW THERAPEUTIC INDEX DRUGS - A CRITICAL STUDY ON PRESCRIPTION TRENDS IN SOUTH INDIAN TERTIARY CARE HOSPITAL

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ABSTRACT

***Background*:** Drugs with a narrow therapeutic range, which may require drug monitoring both to achieve therapeutic levels and to minimize toxicity Drugs with a narrow therapeutic index (NTI-drugs) are drugs with small differences between their therapeutic and toxic doses, implying that small changes in dosage or interactions with other drugs could cause adverse effects. The outcome of irrational use of medicines includes economic loss, development of adverse drug reactions (ADRs), development of antimicrobial resistance etc. Thus there is a need for drug evaluation which is an important component in monitoring, evaluating and making necessary modifications in the prescribing practices to achieve a rational drug use. ***Objectives*:** To evaluate prescription pattern of narrow therapeutic index drugs and to identify drug related problems associated with narrow therapeutic index drugs. ***Methodology*:** A Prospective-observational study was carried out for a periods of six months at general medicine and psychiatric department of Basaveshwara Medical College Hospital & Research Centre Chitradurga, Karnataka. Data entry was done in Microsoft excel 2007. SPSS version 16 was used to calculate the descriptive statistical parameters. **Results:** A total of 100 patients age more than 18 years were enrolled for the study among which 34 were females and 66 were males. More number of patients were from middle age group. 31% of patient were

overweight and 15% were obese. smoker patient (32%) were more prevalent than others. More number of patient was having DM-II as medical history and Asthma and epilepsy were more frequently diagnosed in the subjects. Amikacin (45.9%) was most commonly prescribed NTI antibiotic. antiepileptic drug Phenytoin was more frequently prescribed followed by valproic Acid. combination of etiofylline and theophylline was the most frequently prescribed drugs among all NTI drugs where as warfarin was more frequently used anticoagulant during the therapy. DRPs associated with the use of NTI Drugs were in the form of drug–drug interaction where significant interaction between (Theophylline- budesonides) were more prevalence (55.8%). Adverse drug reaction was more assesses in possible category(44%) and more than 22 times NTI drugs were used for no specific indication according to WHO Indicator. There were no Evidence of dose individualization in Overweight and Obese subjects. **Conclusion:** Prescribing by generic name is to be promoted to avoid confusion in understanding prescriptions; this also adheres to WHO standards of rational prescribing. The therapy associated with NTI drugs should be monitored and individualized based on the outcome. This study was carried out inorder to bring awareness in the health care professionals regarding the safe and effective use of NTI drugs.

KEYWORDS: Narrow Therapeutic Index, WHO, EDL, Drug related problems, Adverse drug reaction, drug- drug interaction, Rational drug use.

INTRODUCTION

The North Carolina Board of Pharmacy defines an Narrow therapeutic index (NTI) drugs as those pharmaceuticals having a narrowly defined range between risk and benefit. Such drugs have less than a twofold difference in the minimum toxic concentration and minimum effective concentration in the blood or are those drug product formulations that exhibit limited or erratic absorption, formulation-dependent bioavailability, and wide intra-patient pharmacokinetic variability that requires blood-level monitoring.[1]

Therapeutic window is a range of doses that produces therapeutic response without causing any significant adverse effect in patients. Generally therapeutic window is a ratio between minimum effective concentrations (MEC) to the minimum toxic concentration (MTC).[1]

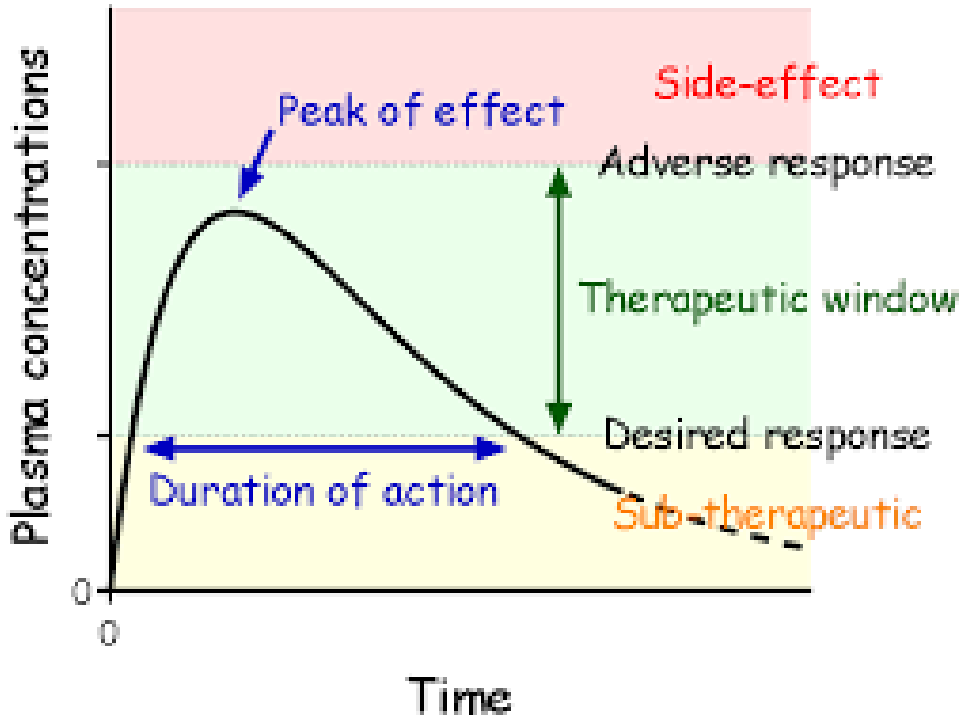

Fig. 1: Therapeutic window.

The therapeutic index (TI) is a comparison of the amount of a therapeutic agent that causes the therapeutic effect to the amount that causes toxicity. The related terms therapeutic window or safety window refer to a range of doses which optimize between efficacy and toxicity, achieving the greatest therapeutic benefit without resulting in unacceptable side-effects or toxic Drugs with a narrow therapeutic range, which may require drug monitoring both to achieve therapeutic levels and to minimize toxicity, include: phenytoin, valproic acid, dimercaprol, theophylline, warfarin and lithium carbonate. Some antibiotics require monitoring to balance efficacy with minimizing adverse effects, including: gentamicin, vancomycin, amphotericin B (nicknamed 'amphoterrible' for this very reason) and polymyxin B.[1,2]

Drug-related problems (DRPs) have been found to be associated with increased morbidity, mortality and health costs. NTI-drugs are drugs with small differences between their therapeutic and toxic doses, implying that small changes in dosage or interactions with other drugs could cause adverse effects. Many patients admitted to hospitals are severely ill and have conditions that may influence the pharmacokinetics and pharmacodynamics of drugs administered to them. Accordingly, hospitalization might increase the risk of DRPs in patients using NTI-drugs.[2]

Most physicians hesitate to treat elderly patients more aggressively. This is, in part because of a high risk of drug-drug interactions, adverse drug reactions, and lack of clinical data in this population. Monitoring the medications used in older adults and identifying drug interactions and adverse events are crucial. Drug therapy management in older adults in challenging and many factors related to normal aging, disease states and lifestyle should be considered before initiation of pharmacotherapy.[3]

Phenytoin and carbamazepize are important first – line antiepileptic drugs (AEDs) and are widely prescribed throughout the world. Control of epilepsy with phenytoin can be a difficult and lengthy process because of the drugs narrow therapeutic index and the wide inter individual range of doses required. Similarly, appropriate doses for carbamazepine take time to determine because of auto induction of metabolism and neurologic side effects generally assumed to necessitate slow dose increases. Adverse drug reactions (ADRs) are relatively common for both drugs.[4]

Most widely used anticonvulsants in psychiatric practice are carbamazepine and sodium valproate, which are indicated in the treatment of epilepsy and the treatment, prophylaxis of certain psychiatric disorders. Therapeutic drug monitoring (TDM) assists in the optimization of anticonvulsant therapy. Investigations of prescription patterns and exposure of AEDs to different patient groups are important regarding drug safety aspects. Conventional AEDs the most common enzyme-inducing medications used and they interact with a wide variety of medications. Despite many therapeutic advances, refractory epilepsy remains a risk factor for sudden unexpected death cause deleterious effects on individual health.[5]

Therapeutic Drug Monitoring

The basic assumptions underlying therapeutic drug monitoring are that drug metabolism varies from patient to patient and that the plasma level of a drug is more closely related to the drug's therapeutic effect or toxicity than is the dosage.[6]

Indications for drug monitoring

• Drugs with a narrow therapeutic index (where therapeutic drug levels do not differ greatly from levels associated with serious toxicity) should be monitored. Example: Lithium, phenytoin, digoxin.

• Patients who have impaired clearance of a drug with a narrow therapeutic index are candidates for drug monitoring. The clearance mechanism of the drug involved must be

known. Example: Patients with renal failure have decreased clearance of digoxin and therefore are at a higher risk of toxicity.

• Drugs whose toxicity is difficult to distinguish from a patient's underlying disease may require monitoring. Example: Theophylline in patients with chronic obstructive pulmonary disease.

• Drugs whose efficacy is difficult to establish clinically may require monitoring of plasma levels. Example: Phenytoin.

Situations in which drug monitoring may not be useful

• Drugs that can be given in extremely high doses before toxicity is apparent are not candidates for monitoring. Example: Penicillin.

• If there are better means of assessing drug effects, drug level monitoring may not be appropriate. Example: Warfarin is monitored by measuring INR, not by serum levels.

• Drug level monitoring to assess compliance is unreliable, since poor compliance cannot be distinguished from rapid metabolism without direct inpatient scrutiny of drug administration.

• Drug toxicity is a clinical diagnosis. Drug concentrations within the usual therapeutic range do not rule out drug toxicity in a given patient. Example: Digoxin, where other physiologic variables (eg, hypokalemia) affect drug toxicity.

In summary, therapeutic drug monitoring may be useful to guide dosage adjustment of certain drugs in certain patients. Patient compliance is essential if drug monitoring data are to be correctly interpreted.[6]

TDM has been recognized as a useful clinical tool in drug therapy with the drugs having narrow therapeutic index.[6]

Table 1: List of NTI Drugs.

Drug Category	Drugs in that Category	Treatment Use
Cardiac drugs	Digoxin, digitoxin, quinidine, procainamide, amiodarone	Congestive heart failure, angina, arrhythmias
Antibiotics	Aminoglycosides (gentamicin, tobramycin, amikacin) Vancomycin, Chloramphenicol	Infections with bacteria that are resistant to less toxic antibiotics
Antiepileptics	Phenobarbital, phenytoin, valproic acid, carbamazepine, ethosuximide, sometimes gabapentin, lamotrigine	Epilepsy, prevention of seizures, sometimes to stabilize moods
Bronchodilators	Theophylline, caffeine	Asthma, Chronic obstructive pulmonary disorder (COPD), neonatal apnea
Immunosuppressants	Cyclosporine, tacrolimus, sirolimus, mycophenolate mofetil, azathioprine	Prevent rejection of transplanted organs, autoimmune disorders
Anti-cancer drugs	All cytotoxic agents	Multiple malignancies
Psychiatric drugs	Lithium, valproic acid, some antidepressants (imipramine, amitriptyline, nortriptyline, doxepin, desipramine)	Bipolar disorder (manic depression), depression
Protease inhibitors	Indinavir, ritonavir, lopinavir, saquinavir, atazanavir, nelfinavir	HIV/AIDS

Drug Utilization Evaluation

Drug Utilization Evaluation(also called as Drug Utilization Pattern or Drug Utilization Review or Drug Utilization Research) was defined by WHO in 1977 as the marketing, distribution, prescription, and use of drugs in a society with special emphasis on the resulting medical, social and economic consequences. Since then, a number of other terms have come into use and it is important to understand the interrelationships of the different domain.[7]

Types of DUE

Based on the type of data, DUE is of two types:

1. Quantitative studies
2. Qualitative studies

Quantitative studies: These involve the collection, organisation and display of estimates or measurements of drug use. This type of data is often used for making purchasing decisions or other functional activities such as preparing drug budgets. Quantitative DUE studies may or may not be an on-going activity and are almost always a unilateral pharmacy function.

Qualitative studies: These are multidisciplinary operations, which collect, organise, analyse and report information on actual drug use. These include the concept of criteria. Drug use criteria may be based upon such items as indication of use, dose, dosing frequency and duration of therapy.

The risk to benefit equation is influenced by the stage of the epilepsy, its severity and its type; the age of the sufferer; associated medical factors; nature of the drug being proposed for treatment; the patient's individual aspirations, and what aspects of morbidity are being encompassed. Some conclusions will be firm, and some tentative, but we hope that this paper will allow the physician and the patient to understand better the basis for rational prescribing.[8]

Epilepsy is a potentially life-threatening condition, a fact which is often overlooked. The risk of death, which is obviously an important element in the risk–benefit assessment, varies with factors such as the etiology of the epilepsy and the frequency and type of seizures. Severe childhood epilepsy syndromes often have a high mortality that is usually related to the underlying cause. By contrast, in absence epilepsy or partial epilepsies, overall mortality rates in small studies did not differ from those found in the general population.[9]

Drug Utilization Review (DUR) also referred to as Drug Utilization Evaluations (DUE) or Medication Utilization Evaluations (MUE), are defined as an authorized, structured, on-going review of healthcare provider prescribing, pharmacist dispensing, and patient use of medication. DUR involve a comprehensive review of patient's prescription and medication data before, during, and after dispensing to ensure appropriate medication decision making and positive patient outcomes. DUR programs play a key role in helping managed health care systems understand, interpret, and improve the prescribing, administration, and use of medications. DUR afford the managed care pharmacist the opportunity to identify trends in prescribing within groups of patients such as those with asthma, diabetes or high blood pressure. Pharmacists can then, in collaboration with other members of the health care team, initiate action to improve drug therapy for both individual patients and covered populations. DUR serve as a means of improving the quality of patient care, enhancing therapeutic outcomes and reducing inappropriate pharmaceutical expenditures, thus reducing overall health care costs.[10]

Irrational prescribing of drugs may tend to produce an unproductive and a risky treatment to an individual; such a prescription may exacerbate or prolong the illness making higher the costs of treatment or both. On the other hand using a rational drug prescription would see to a least number of drugs being used and also to obtain the best possible therapeutic effect of the drug in short time with a reasonable cost. Clinicians often face challenges in prescribing the right medication and initiating the right therapy, especially when it comes to NTI drugs and that's where the chances of irrational prescriptions and errors usually happen. This study was designed to analyse the prescribing patterns and trends to understand the drug utilization pattern in tertiary care hospital in the city.[11]

A drug-related problem (DRP) is defined as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes. Categories of DRPs include unnecessary drug therapy, the needs for additional drug therapy, ineffective drug, dosage too low, dosage too high, adverse drug reaction(ADR) and patient noncompliance to the treatment. DRPs are frequent and may result in reduced quality of life and even morbidity and mortality. Despite excellent benefits and safety profile of most medications, DRPs pose a significant risk to patients which adversely affect quality of life, increase hospitalization and overall health care cost. DRPs may arise at all stages of the medication process from prescription to follow-up of treatment. Patients receiving anticoagulant drugs such as DVT patients must be carefully screened for DRPs. While receiving anticoagulants, patients must be monitored closely to ensure effectiveness and to prevent side effects or overdosing. Hence, it has narrow therapeutic ranges and is associated with a high rate of DRPs thus failing to monitor warfarin therapy could increase the risk of recurrent thrombosis and haemorrhagic complications. Therefore, this study was initiated to address the possible DRPs that could occur in the management of patients with DVT in the study area.[12]

A Drug-Related Problem is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes." A response to a drug that is noxious and unintended, and that occurs at doses normally used in humans for the prophylaxis, diagnosis or therapy of disease or for the modification of physiological function.[13]

Classification of Adverse Drug Reactions

Type A: reactions are common, usually expected and generally identified prior to marketing. These are mostly dose related and result from Pharmacological action of the drug and may also be due to Drug-Drug or Drug-Food interactions or subsequent illness. E.g.: Excessive

reduction of blood glucose (Hypoglycaemia) due to oral sulfonylureas, diarrhoea due to an antibiotic.

Type B: reactions are exactly opposite to Type A. These are not dose related nor bear any relation to pharmacological action of drugs. These are difficult to predict and are usually evident only after marketing.

E.g.: Mainly skin, liver and hematopoietic systems are affected by these reactions. These include hypersensitivity, malignant hyperthermia due to antipsychotics etc.

Type C- Are Uncommon, related to cumulative dose of the drug.
E.g.: Benzodiazepine dependence
Type D- Are rare, onset is late, and dose related. E.g.: Carcinogenesis, Teratogenesis
Type E- These are mainly Withdrawal symptoms.
Type F- Failure of Therapy.

Risk Factors for ADR's

-Age
-Multiple drug regimens
-Duration of therapy
-Gender
-Comorbid conditions
-Narrow therapeutic index drugs
-Ethnicity and genetics.

Assessing causality

Causality assessment is used to determine the likelihood that a drug caused a suspected ADR. There are a number of different methods used to judge causation including the Naranjo algorithm, the Venulet algorithm and the WHO causality term assessment criteria. Each have pros and cons associated with their use and most require some level of expert judgement to apply. An ADR should not be labeled as 'certain' unless the ADR abates with a challenge-dechallenge-rechallenge protocol (stopping and starting the agent in question). The chronology of the onset of the suspected ADR is important as another substance or factor may be implicated as a cause; co-prescribed medications and underlying psychiatric conditions may be factors in the ADR.[14]

Assigning causality to a specific agent often proves difficult, unless the event is found during a clinical study or large databases are used. Both methods have difficulties and can be fraught with error. Even in clinical studies some ADRs may be missed as large numbers of test individuals are required to find that adverse drug reaction. Psychiatric ADRs are often missed as they are grouped together in the questionnaires used to assess the population.[15]

Despite widespread multimorbidity, clinical guidelines are largely written as though patients have a single condition and the cumulative impact of treatment recommendations from multiple clinical guidelines is not generally considered. In people with several conditions, simply application of recommendations from multiple single disease clinical guidelines can result in complex multiple drug regimens (polypharmacy) with the potential for implicitly harmful combinations of drugs. Clinical guidelines of course are not intended to be completely comprehensive guides to practice, in that clinicians are expected to use their judgment in deciding which treatments are appropriate in individual patients. There is, however, increasing recognition that clinical guidelines should better account for patients with multimorbidity.

Adverse drug events cause an estimated 6.5% of unplanned hospital admissions in the United Kingdom, accounting for 4% of hospital bed capacity. When an admission ends in death, these are predominately the result of bleeding or renal injury. While some adverse drug events are unpredictable (such as anaphylaxis from an unrecognised allergy), many others can be predicted and prevented, including drug- disease and drug-drug interactions. A considerable proportion of adverse drug events are caused by interactions between drugs. Systematic reviews have shown that electronic alerts and prompts can improve prescribing behaviour or reduce rates of error. Nevertheless, despite the increasing availability of computerised decision support, adverse drug events as a cause for seeking ambulatory care have increased nearly doubling in the United States between 1995 and 2005, with increasing age and increasing polypharmacy being the predominant characteristics of patients associated with experiencing such an event. With an ageing population, and associated increasing multimorbidity, there is an increase in the potentially required number of drugs and so the potential for increased risk of drug interactions. The American Geriatrics Society has identified the consideration of drug-disease and drug-drug interactions as a key element of optimal care for older adults with multimorbidity.[16]

A precipitant drug may alter any portion of an object drug's pharmacokinetic\ profile. Absorption, distribution, metabolism, or elimination of the object drug may be affected and can result in either amplification or minimization not the object drug's intended pharmacological response and a potential adverse event.[17]

Keeping above facts in consideration the present study is designed to determine prescription pattern of narrow therapeutic index drug and prevalence of drug related problems associated with it.

MATERIAL AND METHOD

Study site

This study was conducted at Medicine and psychiatric department of Basaveshwara Medical College Hospital & Research centre, chitradurga.

Study approval

This study was approved by the "Institutional Human Ethical Committee" of the S.J.M College of Pharmacy, Chitradurga. (SJMCP/IEC/21/2016-2017 Date– 25/11/2016)-Annexure 1.

Study design

The study involves collection of data prospectively in medicine and psychiatric Department. This is a Prospective-Observational study.

Study period

The study was conducted for a period of six month.

Study subjects

The study includes all the patients admitted in medicine and psychiatric ward. Patient who meets the following criteria were enrolled.

Study criteria

Inclusion Criteria

- Subjects willing to participate and give consent for the study.
- Subjects of both genders.
- Subjects having age at least >18 years.

Exclusion Criteria

- Female subjects who are pregnant at time of study
- Comatose patient.

Study materials

- Ethical clearance from Institutional Ethical Committee, by SJM College of Pharmacy, Chitradurga was obtained prior to the study.
- Informed consent form**:** Patients who satisfy above study criteria were included into the study. It was signed by the patient or by their representatives was taken. [Annexure-2].
- Patient data collection form: It includes demographic details of the patients like age, sex, BMI, complaints, history, physical examination, diagnosis, treatment chart of drug prescribed among patients. [Annexure -3].
- Drug interaction evaluation form [Annexure-4].
- ADRs reporting form [Annexure-5].

Study procedure

- The patients who will satisfy the above inclusion criteria will be enrolled for the study by taking informed consent.
- The full details of the cases including patient demographics, history, diagnosis and drug therapy, drug interaction between the drug and Adverse drug reaction will be documented into the self designed data collection form.

Statistical Analysis

The data was entered in Microsoft Excel-2007 version and the results are analysed using Statistical Package for Social Services (SPSS 16). Categorical data was analyzed by using descriptiptive statistics under which Frequency and percentage was calculated.

Sources of data

- Patient's prescriptions.
- Medical records of In-patients.
- Interviews with patient and/or care givers.

RESULTS

- A Total 100 subjects were included in the study and data was collected prospectively. The data collected during the study period were analysed for various parameter like age,

genders distribution of patients, Body mass index, social history, diagnosis, and treatment given to the patients. The data was also analysed for ADRs, DDIs, and outcome. A total of 100 patients were enrolled in the study.

1: Gender wise distribution of patients (N=100)

Among 100 Subjects in the study population 34%(34) were females and 66% (66) were males. The results are shown in Table- 2 and graphically presented in Figure-2.

Table 2: Gender wise distribution of patients (N=100).

Gender	No of patients	Percentage
Male	66	66
Female	34	34
Total	100	100%

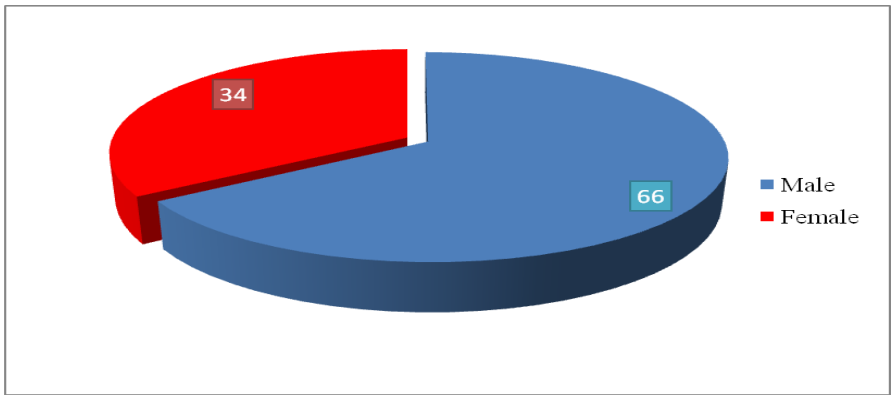

Fig. 2: Distribution of patients according to Gender.

2. Distribution of patients according to age group

Among 100 patients, 7 patients were in the age group of More than 70 years, and 14 patient belong to the age group of 60-69 years. 18 patients were in the age group of 50-59 years, and 21 were in the age group of 40-49 years. 26 patient were in the age group of 30-39 years and 14 patient were below 29 years. The age groups of the patients are given in Table- 3and presented in Graphical form in Figure -3.

Table 3: Distribution of patients according to age group (N=100).

Age groups	No of patients	Percent
Below 29 years	14	14
30-39 years	26	26
40-49 years	21	21
50- 59 years	18	18
60-69 years	14	14
More than 70 years	7	7
Total	100	100%

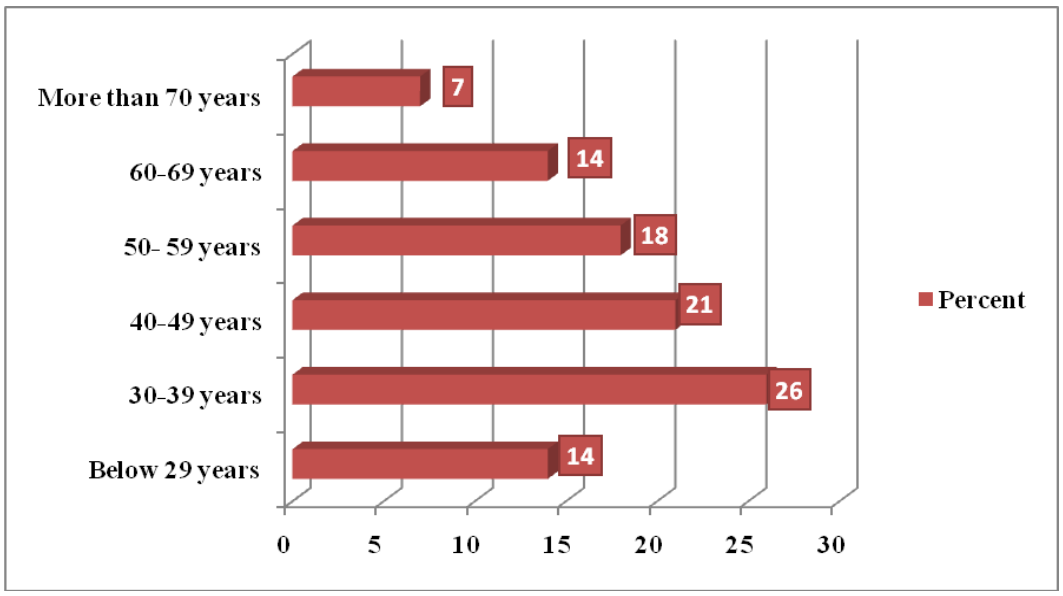

Figure 3: Distribution of patients according to Age groups.

3. Distribution of Gender in different age group of subject

Among study population (n=100), 7.5% were male and 5.9% were female in the age group of More than 70 years.18.5% patient were male and 5.9% were female belong to the age group of 60-69 years. 19.5% patients were male and 14.7 were female in the age group of 50-59 years, and 21.2% subject were male and 20.5% were female in the age group of 40-49 years. 22.7% male and 32.5% female patient were in the group of 30-39 years. 10.6% male and 20.5% female patient were in the age group below 29 years(P=0.00) Highly significant. The age groups of the patients are given in Table-4 and graphically presented in Figure -4.

Table 4: Gender Versus Age groups.

Age groups	Genders			
	Male (N=66)	%	Female(N=34)	%
Below 29	7	10.6	7	20.5
30-39	15	22.7	11	32.5
40-49	14	21.2	7	20.5
50-59	13	19.5	5	14.7
60-69	12	18.5	2	5.9
More than 70	5	7.5	2	5.9
P value= 0.000 less than 0.05 (sig)				

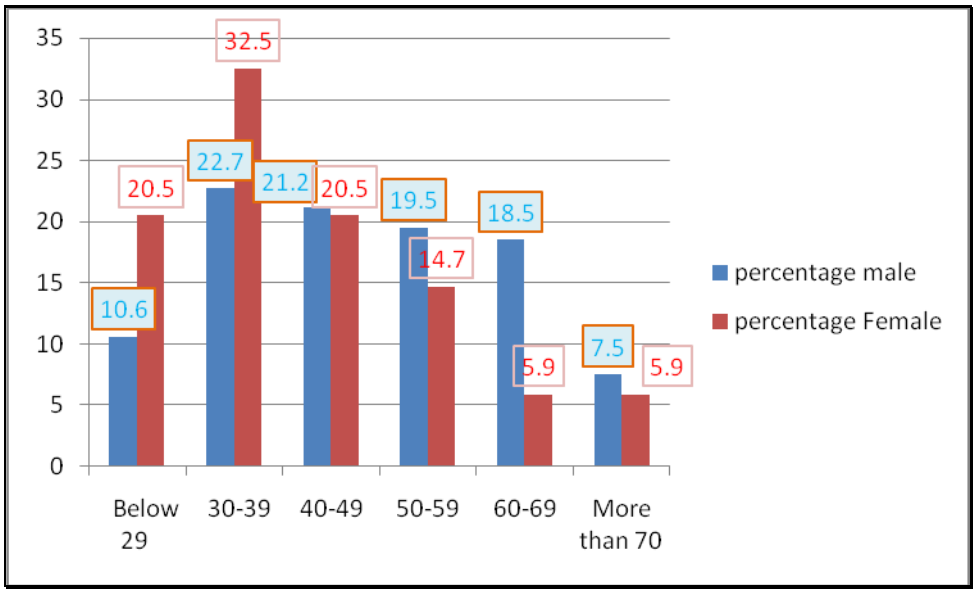

Fig. 4: Gender versus age group(n=100).

4: Distribution of patient according to BMI

Among study population (n=100), 15 Subjects were obese, 31 subject were overweight, 3 subjects were underweight and 51 subject were normal. The distribution of patients based on BMI is shown in Table-5 and graphically presented in Figure-5.

Table 5: Distribution According To BMI (N=100).

BMI (kg/m^2)	No of patients	Percentage
Underweight (below 18.5)	3	3
Normal (18.5-24.9)	51	51
Overweight (25-29.9)	31	31
Obese (more than 30)	15	15
Total	100	100%

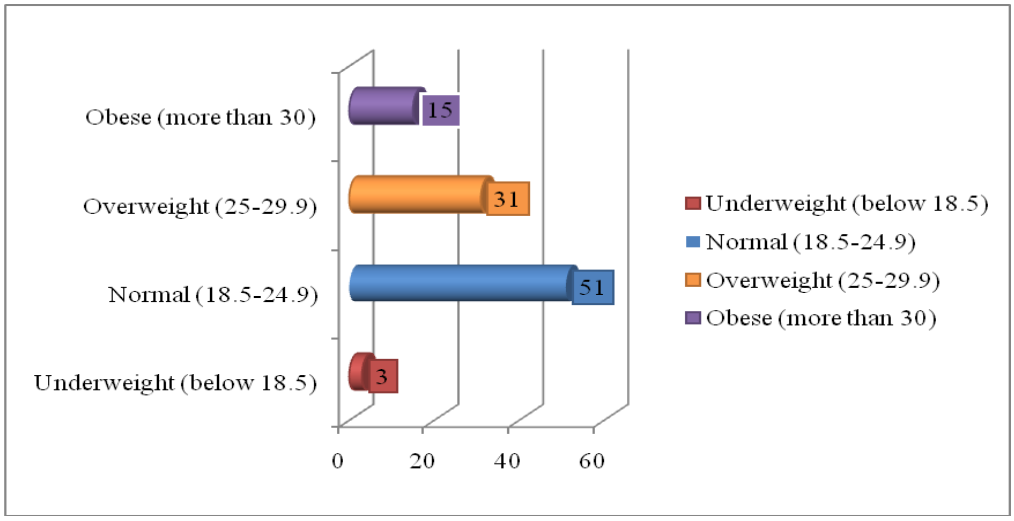

Fig. 5: Distribution of patient according to BMI (N=100).

5: Distribution of Subjects Based On Medical History

Out of 100 patients (n=100), 8 (8%) patients were with Asthma, 13 (13%) were with HTN, 12(12%) were with COPD, 17(17%) were with Diabetes. About 50% patients admitted were without Past History. The distribution of patients based on Medical history is shown in Table-6 and graphically presented in Figure-6.

Table 6: Distribution of patient based on Medical History.

History	No of patients	Percentage
Asthma	8	8
COPD	12	12
Diabetes	17	17
HTN	13	13
No history	50	50
Total	100	100

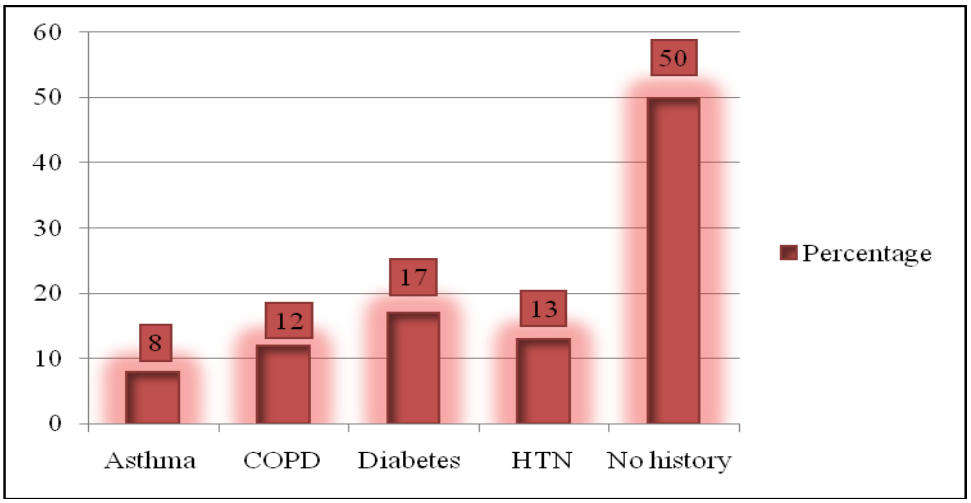

Fig. 6: Distribution of patient based on medical history.

6: Distribution of Subjects Based On Social History

Among 100 patients, (n=100), the social history like Smoking and Alcoholic was present in 36 patients was absent in 64 subjects and The distribution prevalence of social history is shown in Table-7. It is graphically represented in Figure-7.

Table 7: Distribution of patient based on social history.

Social history	No of patients	Percentage(%)
Present	36	36
Absent	64	64

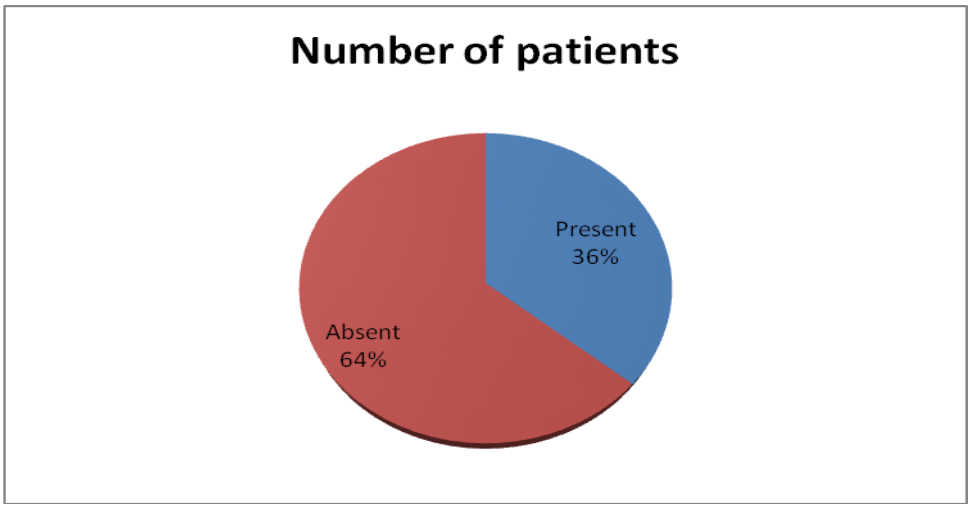

Fig. 7: Distribution of patient based on social history.

7: Distribution of Subjects Based On Diagnosis

Among 100 subject (n=100), 22(22%) patient were diagnosed with Asthma, 20(20%) patient were diagnosed with Acute exacerbation of COPD, 24(24%) patients with epilepsy, 15 (15%) patients were diagnosed with Deep vein Thrombosis and 19 (19%) patients were diagnosed with other inflammatory condition. The morbidity of the patients are illustrated in Table-8 and graphically illustrated in Figure-8.

Table 8: Distribution of patients based on diagnosis.

Medical diagnosis	No of patients	Percentage
Asthma	22	22
COPD	20	20
Epilepsy	24	24
DVT	15	15
Others	19	19
Total	100	100%

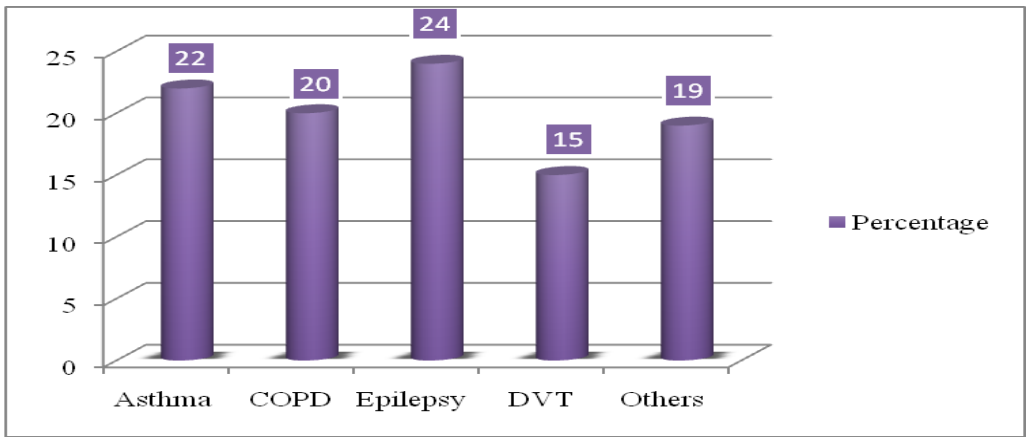

Fig. 8: Distribution of patient based on diagnosis.

8: Prescription Pattern of NTI Drugs Based on category

A total 140 drugs were prescribed to 100 subjects during the study out of which 26.2% were bronchodilator, 24.2% of anticoagulants, 22% were AEDs, 17% were antimicrobials, 3.5% were mood stabilizer and 7.1% thyroid hormones were prescribed.

Table 9: Prescription Pattern NTI Drugs.

Category of drugs	frequency	Percentage(%)
Antimicrobial	24	17
Antiepileptic	31	22
Bronchodilator	37	26.2
Anticoagulant	34	24.2
Mood stabilizer	5	3.5
Thyroid hormone	10	7.1
Total	141	100

Based on category

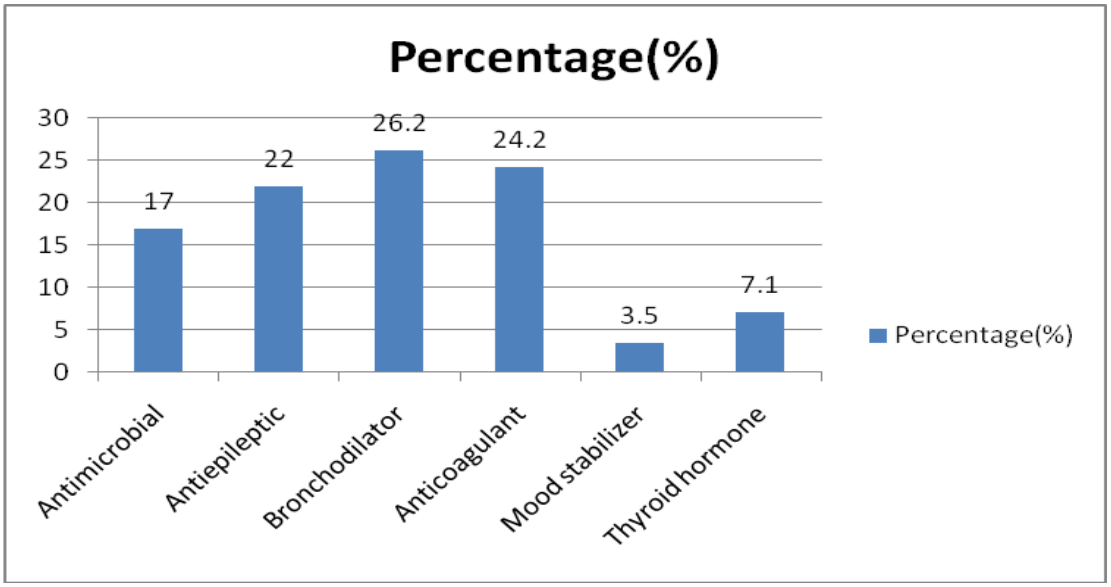

Fig. 9: Prescription Pattern based on NTI drug category.

9: Prescription Pattern of Antimicrobial drugs (n=24)

Among 100 study population (n=24), Amikacin was most frequently prescribed antibiotic in 11 (45.9%) patient followed by vancomycin in 8(33.3%) patient and Gentamycin was prescribed in 5(20.8%) patients. The Prescription pattern of Antimicrobial morbidity of the patients are illustrated in Table-10 and graphically illustrated in Figure-10.

Table 10: Prescription Pattern of NTI Antimicrobial drugs (n=24).

Antimicrobial	No of prescription	Percentage
Amikacin	11	45.9
Gentamycin	5	20.8
Vancomycin	8	33.3
Total	24	100%

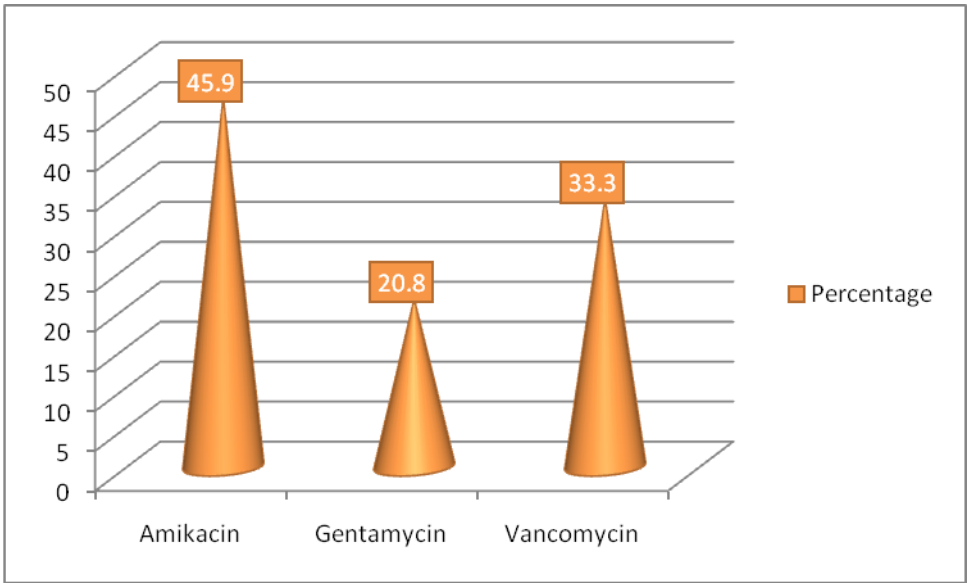

Fig. 10: Prescription Pattern of NTI Antimicrobial drugs.

10: Prescription Pattern of NTI Drugs Acting on CNS (n=36)

Among 100 study population (n=24), Antiepileptic drug phenytoin was found to be most frequently prescribed in 20(55.5%) similarly valproic acid was prescribed in 7(19.4%) and carbamazepine was found to be used in 4(11.2%) and mood stabilizer lithium was found to be used in 5(13.9%). The morbidity of the patients are illustrated in Table-11 and graphically illustrated in Figure-11.

Table 11: Prescription Pattern of NTI Drugs Acting on CNS (n=36).

Drugs	Frequency	Percentage
Phenytoin	20	55.5
Valproic acid	7	19.4
Carbamazepine	4	11.2
Lithium	5	13.9
Total	36	100%

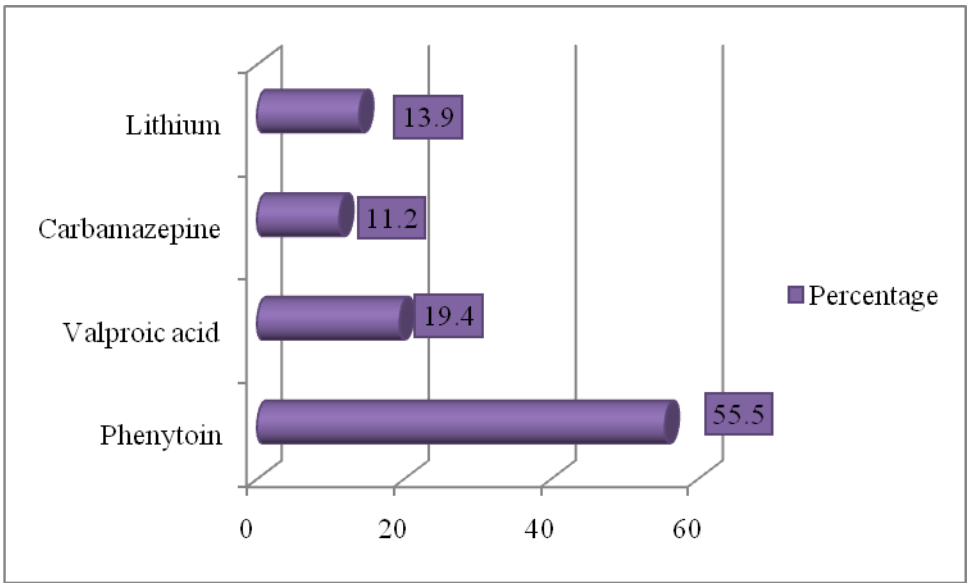

Fig. 11: Prescription Pattern of NTI Drugs acting on CNS (n=36).

11: Prescription Pattern of Other NTI drugs (n=81)

Among 100 study population, anticoagulant like warfarin was used 24.6% and Heparin was used 17.2% It was found that Methylxanthine (Etiofylline+Theophylline) was used most frequently as 45.6%. levothyroxine was found to be used 12.6% among the study population. The results are shown in Table-12and graphically illustrated in Figure-12.

Table 12: Prescription Pattern of Other NTI drugs (n=81).

Drugs	Frequency	Percentage
Warfarin	20	24.6
Heparin	14	17.2
Etiofylline+Theophylline	37	45.6
Levothyroxine	10	12.6
Total	81	100%

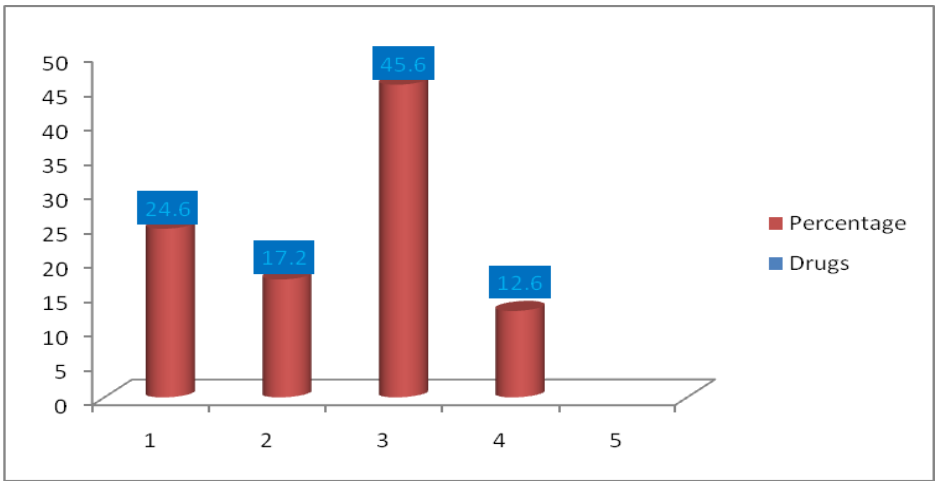

Fig. 12: Prescription Pattern of Other NTI drugs (n=81).

12. Distribution based on Therapy

In our study 62 patients were on monotherapy. Out of 100 patients 36 patients received 2 drug therapy and only 2 patients received 3 drug therapy. Results are given in Table-13 and graphically presented in Figure - 13.

Table 13: Distribution based on therapy.

Therapy	Frequency	Percent
One drug therapy	62	62
Two drug therapy	36	36
Three drug therapy	2	2

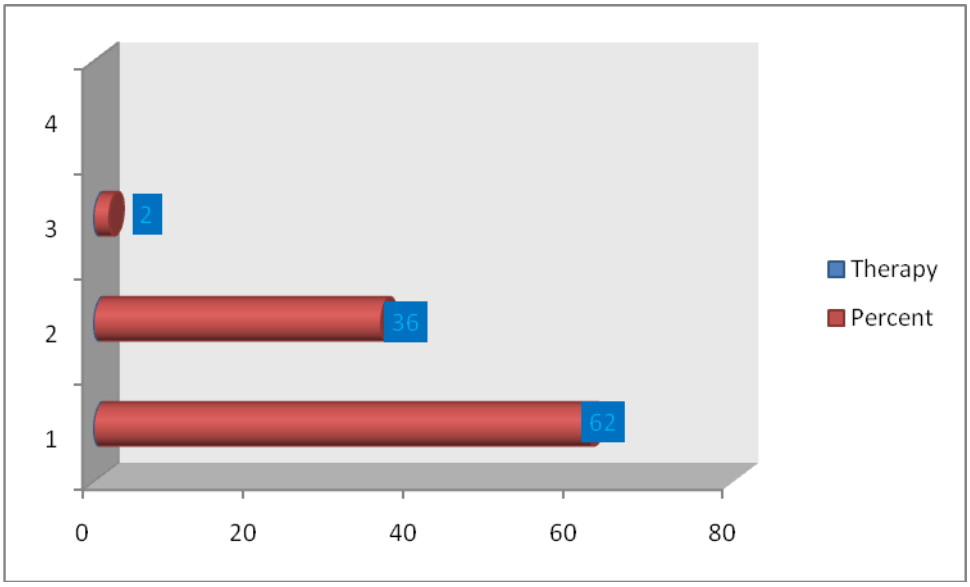

Fig. 13: Distribution based on therapy.

13. Assessment of DRPs Associated with the Use of NTI Drugs

13(A): Drug interactions identified

A total of 100 prescriptions were analyzed and was found that occurrence of DDIs were more. Total 61 Drug- drug interaction was found. Out of 61 interaction significant was found to be of 55.8%, moderate 24.9%, and minor was 19.7%. The data regarding DDIs is given in Table-14 and garphically presented in Figure-14.

Table 14: Drug interactions identified.

Drug- drug interaction	Frequency	Percentage(%)
Significant	34	55.8
Moderate	15	24.5
Minor	12	19.7
Total	61	100%

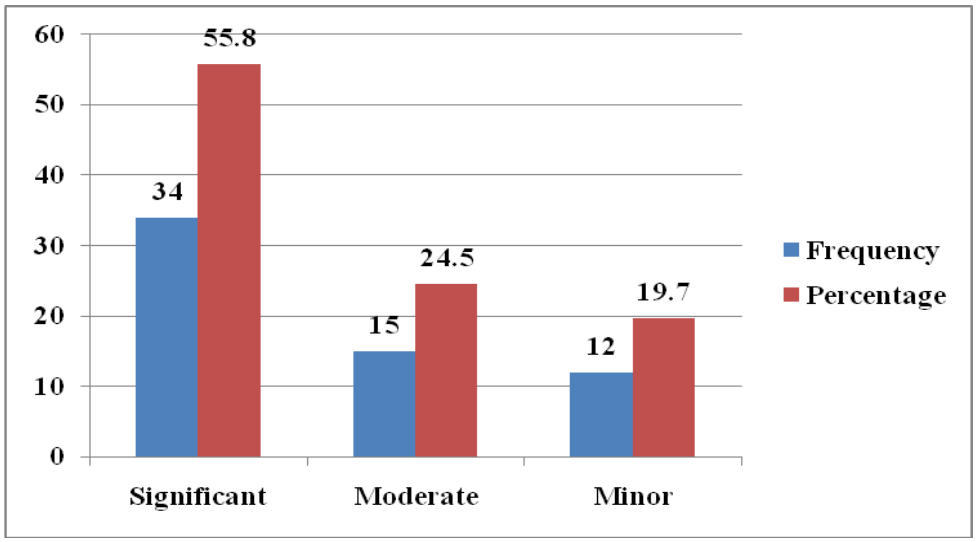

Fig. 14: Drug interactions identified.

13 (B): Assessment of ADRs

Among 100 patients, 25 patients were detected with ADRs, among which severity of definite Was present in 6 (24%) patients and possible was present in 11(44%) patients similarly the severity of probable was found in 8 (32%)patients. Severity of ADRs with frequency and percentage are shown in Table-15 and graphically represented in Figure-15.

Table 15: Adverse drug reactions observed (n=25).

Severity of ADRs	Frequency	Percentage
Definite	6	24
Possible	11	44
Probable	8	32
Total	25	100%

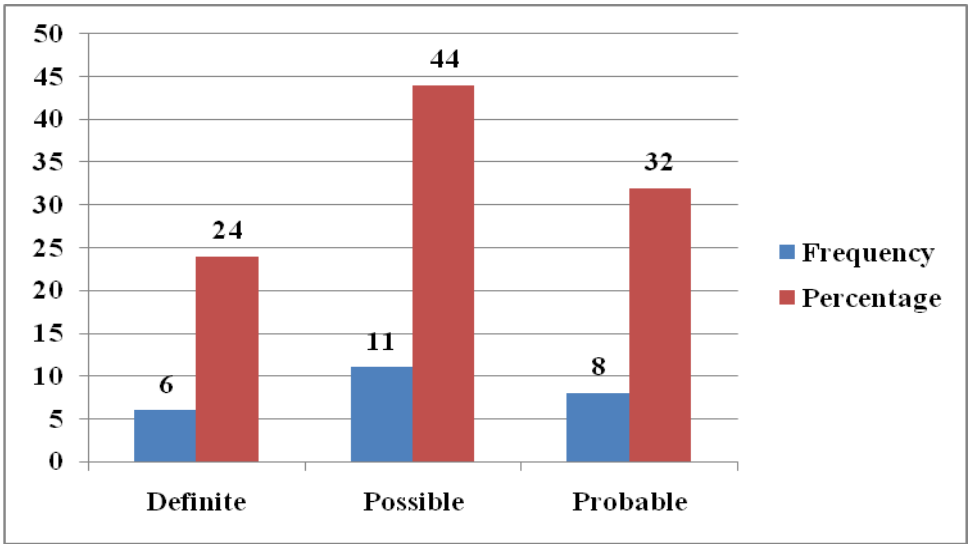

Fig. 15: Assessment of Adverse drug reactions observed (n=25).

14: Assessment of other classes of DRPs: (n=37)

In our study 27.02% patients were prescribed with under dose of NTI Drugs. Out of 100 patients 13.6% patients received over dose of drug therapy and only 22 patients received 3 drug therapy without any specific indication. Results are given in Table-16 and graphically presented in Figure- 16.

Table 16: Assessment of other classes of DRPs:(n=37).

DRPs	Frequency	Percentage
Under dose	10	27.02
Over dose	5	13.6
Without indication	22	59.4
Total	37	100%

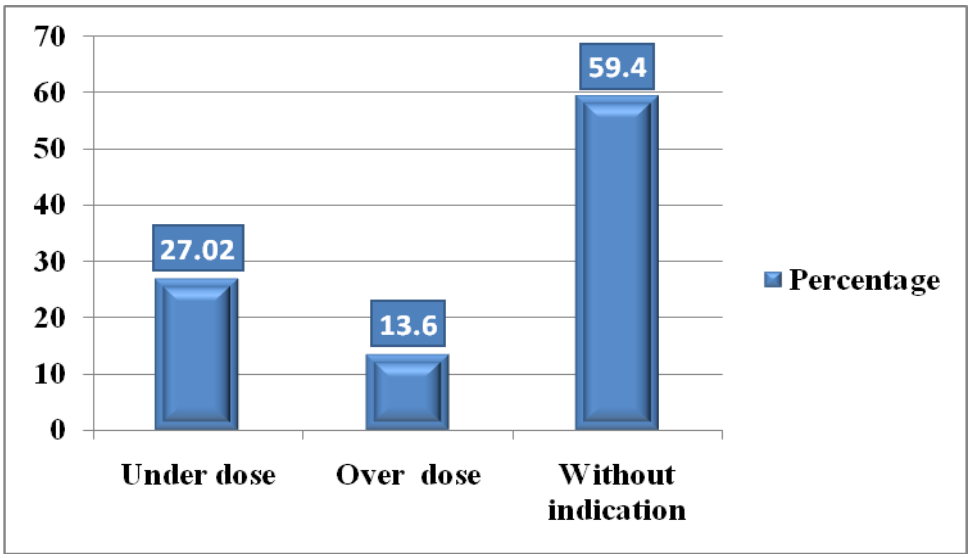

Fig. 16: Assessment of other classes of DRPs:(n=37).

DISCUSSION

The principal target of the drug utilization studies/research is to promote rational prescribing of drugs.[23] Prescription gives insights into nature of the health care delivery system in drug utilization research.[15] A prescription by a doctor may be taken as reflection of physician's attitude to disease and the role of drugs in its treatment. Analysis of prescriptions based on above criteria reveals that age group of 30-39 yrs (26%) was maximum among patients admitted followed by 40-49 years (21%), 50-59 years (18%) & 60-69years (14%) This shows that 11-40 years age group accounted for 62% of patients admitted in the hospital. It was found that females & males constituted nearly 66% and 34% respectively. An average of 2 NTI drugs were prescribed per patient. This was much more than the reported statistics of 2-3

or 3-4 drugs prescribed per person.[12,13] However the difference noted in our study was because it was carried out among in- patients.

Similar to my study, ***Jagadeesh k. et al.,*** **(2014)** conducted study of 1070 in-patient department where Prescribing of brand name (54.11%) was more common than generic name (45.89%). An average of 5.3 drugs were prescribed per person. 6.63% of prescriptions were partially legible or no treatment was recorded in treatment chart. 90.18% of total drugs prescribed were from EDL & 7.85% of prescriptions had fixed dose combinations. Amikacin were the most commonly prescribed antibiotics. 3.36% of prescriptions have nil/incomplete diagnosis. Injectables were prescribed in 74.50% admissions.[9]

This can be avoided by educating the prescribers about the importance of prescribing drugs by generic name. Example in a tertiary care hospital it is easier to procure, distribute & administer drugs when they are mentioned by their generic name except for drugs with narrow therapeutic index like lithium, phenytoin where prescribing by brand name is beneficial as it ensures proper bioavailability of drugs. 1fixed dose combinations were prescribed in our study which accounted for 9.85% of drugs prescribed, majority of which were of Theophylline and etiofylline. 90.18% of drugs that were prescribed are from EDL which is in accordance with WHO principles of good prescribing practices. Still there is some scope (more number of drugs could be prescribed from EDL) for improvements in prescribing practices based on WHO essential drugs list.

CONCLUSION

According to results obtained in our study and the following conclusions were made:

- Male patients were more prevalent than females.
- 30-39 Years Age group patients were more prevalent.
- 15% of the Subjects were 0bese Based on BMI.
- Social History was Present in 36% of the subject
- Prevalence of Infectious, Cardiovascular, and Respiratory were more.
- More numbers of drugs were prescribed by brand name
- Bronchodilator i.e deriphylline was most frequently prescribed category of drugs.
- Parenteral route of administration was frequently used.
- NTI Antimicrobial like Amikacin was more added on therapy followed by gentamycin and vancomycin.

- Antiepileptic drug phenytoin was more prescribed followed by valproic acid and cabamazepine.
- More number of patients received NTI Mono-therapy.
- Occurrence of Drug-drug Interactions, and ADRs were More frequently found.
- NTI drug use among the study subject were dominant without specific indication.
- There were no Evidence of dose individualization in Overweight and Obese subjects.
- Majority of the prescription were irrational.

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