

A STUDY ON THE RATIONALE USE, PRESCRIBING PATTERN AND PHARMACOECONOMICS OF BENZODIAZEPENES USED IN PSYCHIATRY DISORDERS IN A TERTIARY CARE HOSPITAL

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Article Received on 20/07/2021

Article Revised on 10/08/2021

Article Accepted on 30/08/2021

ABSTRACT

This study as stated in the title will focus on the rational use of the benzodiazepines, its prescribing patterns and their pharmacoeconomic as they are prescribed for psychiatric disorders. Benzodiazepines are a group of prescription only medicines that have a sedating / hypnotic and calming effects on the nervous system. They are used to treat a range of different nervous system disorders such as insomnia, generalized anxiety disorder, social anxiety disorder, seizure disorders such as epilepsy, anticonvulsants, muscle relaxant and panic disorder etc. The rational use in prescribing of benzodiazepines to patients with psychiatry disorders is imperative in psychiatry care not only due to the fact that these drugs have the tendency to develop dependency in the patient but the litany of side effects both mild and life threatening is reason enough to ensure that the patients are taking the medications in the right dose for the right diagnosis at the right time and at the right frequency and in rare cases in the right dosage form. Pharmacoeconomics of benzodiazepines is one of the major objectives of this study. We would like to establish a conclusion on whether the cost as a factor directly or indirectly affects the prognosis and treatment of the disorder in the patient and how that may in turn affect their quality of mental health in the long run.

KEYWORDS: Benzodiazepines, Pharmacoeconomics, Rationality, Adherence, Comorbidities, Brand, Generic.

INTRODUCTION

Benzodiazepine was first introduced in the 1960s, and since their introduction they have become progressively more popular as anxiolytic agents and sedatives, displacing the barbiturates from their previously held spot. This study as stated in the title will focus on the rational use of the benzodiazepines, its prescribing patterns and their pharmacoeconomics as they are prescribed for psychiatric disorders. Benzodiazepines are

a group of prescription only medicines that have a sedating / hypnotic and calming effects on the nervous system.

Benzodiazepines are categorized as either short acting, intermediary or long acting. Short and intermediate acting benzodiazepines are preferred for the treatment of insomnia, longer acting benzodiazepines are recommended for the treatment of anxiety.

Table 1: Classification Of Benzodiazepines.

Long acting Benzodiazepines 1-3 days	Intermediate acting Benzodiazepines 16 hours	Short acting Benzodiazepines 3-8 hours
Clorazepate Chlordiazepoxide Diazepam Flurazepam Quzepam	Alprazolam Estazolam Lorazepam Temazepam	Oxazepam Triazolam

Uses Of Benzodiazepines

They are used to treat a range of different nervous system disorders such as,

- Insomnia
- Generalized anxiety disorder

- Social anxiety disorder
- Seizure disorder such as in epilepsy
- Epilepsy
- Depression
- Schizophrenia

- Anticonvulsants
- Muscle relaxant
- Panic disorders etc

Side effects of Benzodiazepines

Side effects of benzodiazepines can include;

- Drowsiness
- Confusion
- Dizziness
- Impaired coordination
- Increased risks of falls and accidents
- Depression and increased risks of anxiety
- Memory problems
- Behavioural changes
- Delirium (especially with long term use)
- Increased risk of dementia.

In spite of extensive use worldwide, there have been only a few cases reported involving fatalities, demonstrating the wide margin of safety of benzodiazepines. But complacency must be avoided and the safety profile of these drugs should not be taken for granted as deaths have been reported in some recent cases even from unexpectedly low doses of certain benzodiazepines. There are also indications that some of the newer benzodiazepines have a slightly smaller margin of safety. This is particularly true with reference to paediatric and geriatric patients who are more susceptible to the toxicity of these drugs.

Mode of Action of Benzodiazepine

Benzodiazepine receptor agonists (BZRAs) work through GABA_A receptors to promote sleep by inhibiting brainstem monoaminergic arousal pathways, through facilitation of Ventrolateral preoptic nucleus (VLPO) inhibitory GABAergic projections to arousal centres such as the anterior hypothalamic hypocretin neurons, and the brainstem arousal regions.

The GABA receptor consists of 5 Protein subunits arranged in a ring around a central pore. Most GABA_A receptors consists of 2 alpha subunits, 2 beta subunits, and 1 Gama subunit. Upon GABA_A receptor activation, chloride ions flow into the cell, resulting in neuronal hyperpolarization.

BZRAs enhance the effect of GABA by lowering the concentration of GABA required to open the GABA channel. BZRAs bind to a modulatory site on the GABA_A receptor that is distinct from the GABA binding site and change the receptor complex allosterically to increase the affinity of the receptor to GABA thus prolonging inhibition. Although BZRAs do not directly open the chloride channel, they modulate the ability of GABA to do so thus enhancing its inhibitory effect.

The rational use in prescribing of benzodiazepines to patients with psychiatry disorders is imperative in psychiatry care not only due to the fact that these drugs have the tendency to develop dependency in the patient

but also the litany of side effects both mild and life threatening is reason enough to ensure that the patients are taking the medications in the right dose for the right diagnosis at the right time and at the right frequency and in rare cases in the right dosage form. Even in patients with no dependency issues, withdrawal symptoms can also be a problem once the medication is stopped.

One of the main objectives of this study is to analyse the prescribing pattern of physicians with respect to benzodiazepines and how the prescribing pattern of the doctors are in correlation with the guidelines. And also to find out the factors that influences such patterns in the prescriptions, and also to find out in the multitude of benzodiazepines available in the country, which ones are being regularly prescribed by the doctors and why.

Uday Venkat Mateti et al conducted a study aimed at assessing the utilization patterns of benzodiazepines in psychiatry patients.^[8] The study concluded that the most common clinical conditions treated with benzodiazepines were mental and behavioural disorders and the majority of the patients were prescribed lorezepam.

Drug utilization pattern and cost analysis among psychiatric patients treated with various benzodiazepines derivatives was the title of the study conducted by Dhivya Govindasamy et al^[9], at annamalai university in Tamil Nadu. The study found out that the majority of the patients admitted into the psychiatry department was suffering from alcohol dependency or withdrawal syndrome and that the cheapest drug was nitrazepam, and that the most commonly prescribed drug was clonazepam, whereas, in the study conducted by Christian Tjagvad et al in Denmark concluded that diazepam was the most prescribed drug in the treatment of patients with drug use disorder^[2], and there findings also point to inappropriate prescribing of benzodiazepenes in several cases.

Lorazepam was found to be the most prescribed benzodiazepine for sedation followed by anxiety^[3] in the study conducted by P Rama et al in PSG hospital in Tamil Nadu. Their study concluded that rational use of benzodiazepines and negative outcomes of benzodiazepines can be reduced by providing drug related information to the prescriber and the consumers.

In the study conducted by Ramadan W et al in Lebanon, it was found out that the use of benzodiazepines is more in the female population especially for the treatment of anxiety.

Benzodiazepine Medication Adherence

One major approach that affects the efficacy of benzodiazepines in patients which this study will explore is the presence of medication non adherence by the patient. More often than not we see a situation in which the patient will abruptly stop taking medication going against the direction of the physician and the pharmacist

just because they think they are feeling better and don't need to continue taking the medication, this can happen mainly due to ignorance on the part of the patient about the rationale behind gradually stopping the medication and speaking to the doctor before doing it.

Pharmacoeconomics of benzodiazepines is one of the major objectives of this study. We intend to find out the cost of the different benzodiazepines manufactured by different companies and match it with their already pre-established efficacy and whether or not their cost influences their frequency in prescriptions and if the cost of the medications factors into the reason why most patients discontinue the medication on their own without first consulting with the doctor knowing that he/she might ask them to continue taking them. We would like to establish a conclusion on whether the cost as a factor directly or indirectly affects the prognosis and treatment of the disorder in the patient and how that may in turn affect their quality of mental health in the long run.

Benzodiazepine, Pain, And The Geriatric population

Benzodiazepines however do cause reduction in the complaint of pain by the patient which many believe might be the cause of the dependency, but careful review of literature reveals that there is insufficient evidence to support or prove the notion that benzodiazepines can be used as analgesics^[19], although treatment with benzodiazepines may reduce pain but this seems to be an indirect effect related to their psychotropic properties such as the alleviation of anxiety and in selected cases depression.

Also, although benzodiazepines are used as antianxiety drugs in the elderly despite their usefulness and safety in the younger population, there remains a concern about the rationale for their use in the elderly or the geriatric population^[15], this is due to the fact that elderly patients experience more side effects as a result of taking multiple medications due to medical an psychiatry comorbid conditions alteration in body pharmacokinetics and pharmacodynamics which are affected by advancement in age.

Despite the recommendations to curtail or reduce benzodiazepine prescription for the elderly, benzodiazepines continue to be massively prescribed to them^[23] even when not indicated after knowing well enough that they are at more risk than any other age bracket and more susceptible to the adverse effects of these medications.

Benzodiazepines Use During Gestation And Lactation

Benzodiazepine are recommended not to be used in pregnancy and lactating mothers but even to the little extent that they are being used, very little information is available about their effect on the developing foetus and on the nursing infants.^[24] Currently available information is insufficient to determine whether the potential benefits of benzodiazepines to the mother outweigh the risks to

the foetus. The therapeutic value of a given drug must be weighed against theoretical adverse effects on the foetus before the birth, however, currently available literature suggests that it is safe to take diazepam during pregnancy but not during lactation because it can cause lethargy, sedation, and weight loss in infants as the drug can be excreted into the mammary secretion and fed to the baby.

The use of chlordiazepoxide during pregnancy and lactation seems to be safe but alprazolam must not be administered, the avoidance of alprazolam during pregnancy and lactation is prudent. To minimize the chances for the occurrence of congenital defects physicians must use the benzodiazepines that to their experience have long safety record and should prescribe benzodiazepines as monotherapy at the lowest effective dose possible and for the shortest duration, and benzodiazepines should be avoided during the first trimester as much as possible, and by so doing, the potentiality of birth defects in the infants can be reduced.

MATERIALS AND METHODS

Sources of data and materials

- Patient case sheet
- Patient prescription sheets
- Laboratory data
- Medication treatment chart
- Suitable self-designed data collection form

Sample Size

210 Patient case files were selected from Saphthagiri Institute of Medical Science and Research Centre.

Study Criteria

- Inclusion criteria
 - ❖ Inpatients
 - ❖ Outpatients
 - ❖ Adults and geriatrics
 - ❖ Male and female patients
 - ❖ Psychiatry patients
 - ❖ Psychiatry patients with any comorbidity
- Exclusion criteria
 - ❖ Pediatrics
 - ❖ Patients not diagnosed with any Psychiatry disorders
 - ❖ Pregnant women
 - ❖ Bedridden or patients in ICU
 - ❖ Cases files with insufficient data and information about the patient and his condition

Method of data collection

Patient data will be collected from medical records and interviewing patient with open ended questions. Collected data will be recorded in self-designed patient data collection form.

➤ **Patient data collection form**

A self-designed data collection form was used to record the patient's specific information. The format will provide the following information.

1. Age

2. Gender
3. Education level
4. Lifestyle
5. Economic status
6. Occupation
7. Date of admission
8. Complaints on admission
9. Past medical and medication history
10. social history
11. Comorbidities
12. Physical examination
13. Laboratory investigation
14. Diagnosis
15. Drug treatment chart
16. Assessment of medication
17. Physical examination data

their demographic details such as name, age, gender, education level, lifestyle, economic status, occupation, date of admission, reasons for admission, history of previous illness, social history were collected. The comorbid condition associated among psychiatry patients who are in treatment with the benzodiazepine drug will also be collected. Information of vitals (blood pressure, temperature, pulse rate and respiratory rate), laboratory data (haematology test, blood sugar test, liver function test, urine analysis, renal function test such as serum creatinine, blood urea etc.), final diagnosis, current treatment drug regimen and other relevant data will also be collected from case sheets of patients. All the above mentioned data will be entered into the patient data collection form. Patients or their care takers are interviewed regarding patient demographic details. The results of collected data will be analysed using statistical analysis and frequencies, percentages, mean values were calculated.

Study Procedure

This is a prospective observational study, the patient who are satisfying the inclusion criteria will be enrolled into the study with the help of patient consent form. All patients admitted in the ward will be reviewed on daily basis. Patients with known complaint will be interviewed with open ended questions regarding their past medical history and recruited if they met the study criteria. All patient who are in treatment with Benzodiazepines drug

RESULTS

1. Patient age distribution

The age of the patients from which the 210 cases was collected was divided into 3 different age brackets as expressed by the table below.

Table 2: Patient age distribution.

Age bracket	No of cases	Percentage
20-40	82	39%
41-60	106	50.5%
61-80	22	10.5%
Total	210	100%

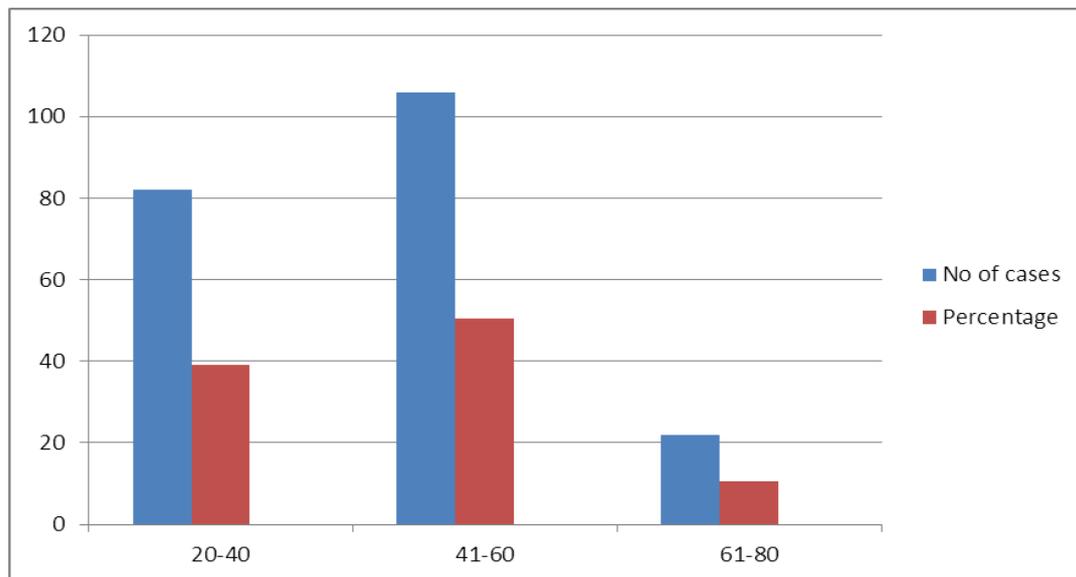


Fig 1: Patient age distribution.

2. Patient gender distribution

Out of the 210 cases that was collected for the purpose of this study, 115 of them were male and the remaining 95 were female.

Table 3: Patient gender distribution.

Gender	No of patients	Percentage
Male	115	54.67
Female	95	45.33
Total	210	100

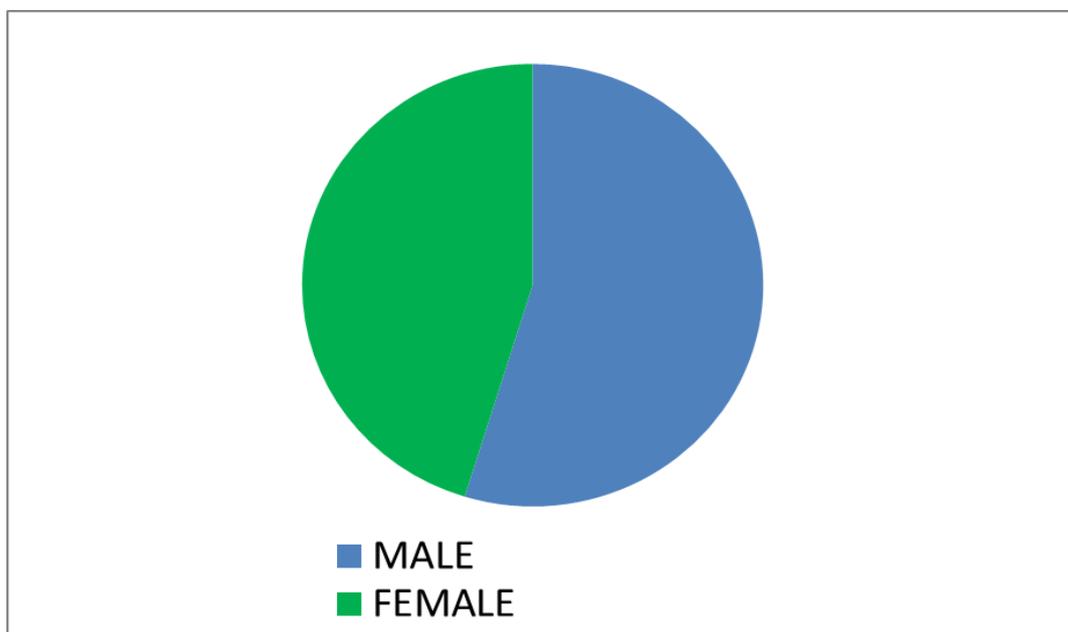


Fig 2: Patient gender distribution.

3. Number of benzodiazepines prescribed per prescription

Out of the 210 prescription which was collected for their respective cases, only 12 prescription was found to

contain more than one benzodiazepines, the remaining 198 had only one benzodiazepine prescribed.

Table 4: Number of benzodiazepines per prescription.

SN	No of Benzodiazepines per prescription	No of cases	Percentage
1	Only one benzodiazepine	198	94.3%
2	More than one benzodiazepine	12	5.7%
	Total	210	100%

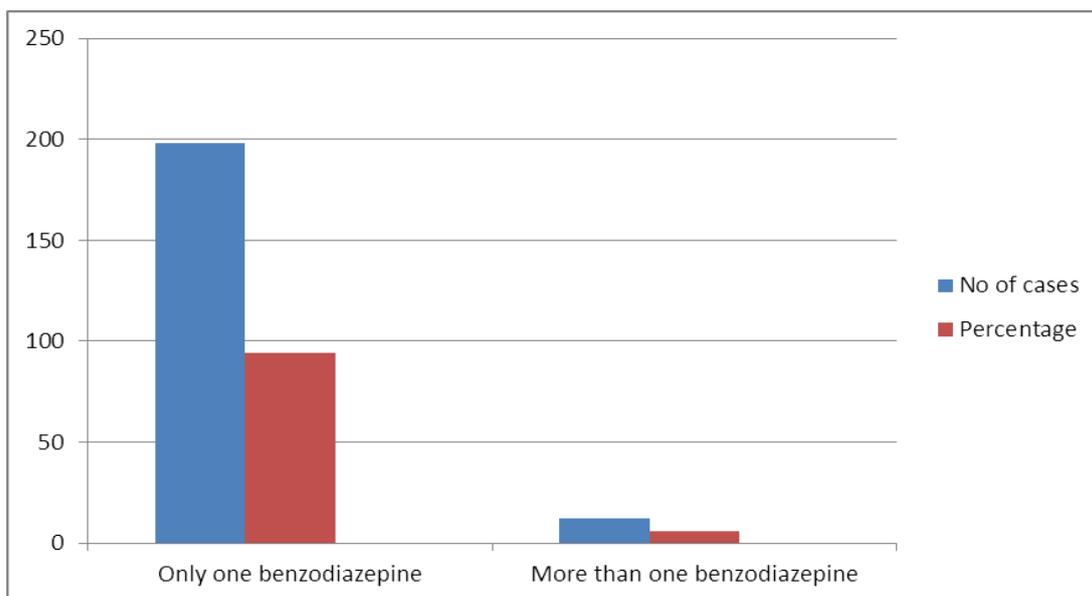


Fig 3: Number of benzodiazepines per prescription.

4. Generic and brand wise distribution among the prescriptions of the study population

Among the 210 prescriptions collected from the case files of the study population, only 25 of the prescriptions contains benzodiazepines prescribed in generic representing only 11.7% of the study population.

Whereas various benzodiazepine brands was prescribed in 189 prescriptions representing 88.3% of the entire study population.

The above information is better represented by the following table and charts.

Table 5: Brand and generic wise distribution of benzodiazepines.

Brand / Generic	No of prescriptions	Percentage
Brand	189	88.3%
Generic	25	11.7%
Total	214	100%

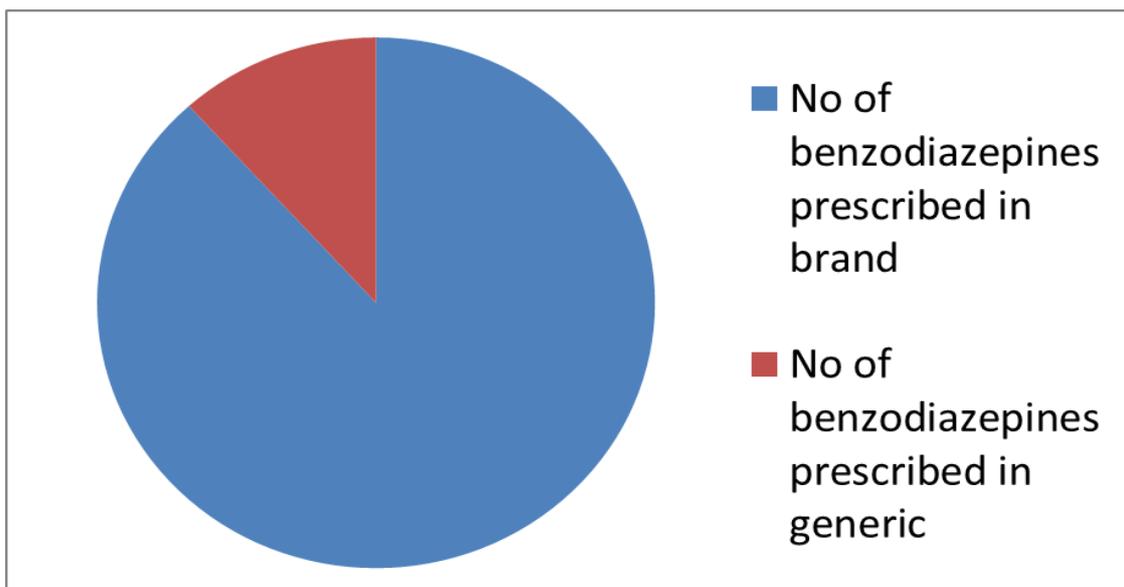


Fig 5: Brand and generic wise distribution of benzodiazepines (Pie chart).

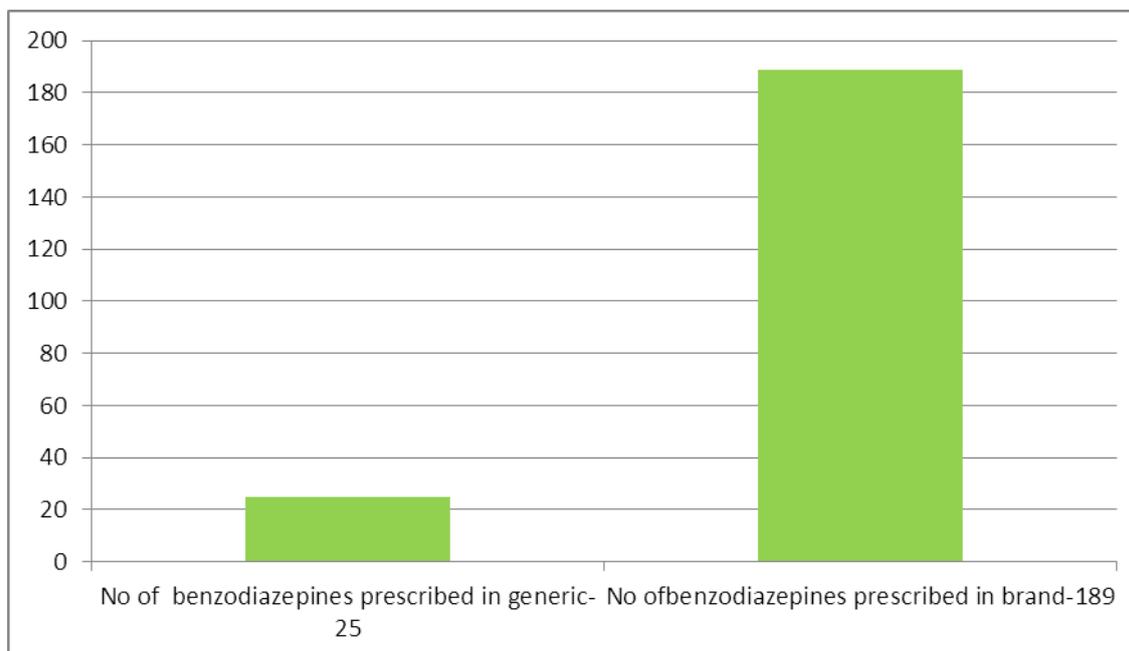


Fig 6: Brand and generic wise distribution of benzodiazepines (Bar chart).

5. Patient Diagnosis Distribution

In the 210 cases that was collected for the purpose of this study various diagnosis was seen for which

benzodiazepines were prescribed. Most common diagnosis was as follows as represented by the table and chart.

Table 7: Patient diagnosis distribution.

S/N	DIAGNOSIS	NOS OF CASES	PERCENTAGE
1	Alcohol dependence syndrome	24	11.4%
2	Depression	32	15.2%
3	Psychosis	11	5.2%
4	Schizophrenia	21	10%
5	Anxiety disorder	19	9%
6	Bipolar Affective Disorder	19	9%
7	Obsessive and compulsive disorder	10	4.8%
8	Insomnia	7	3.3%
9	Panic disorder	15	7.1%
10	Delusion disorder	4	1.9%
11	Wernicke’s Encephalopathy	2	0.9%
12	Multiple diagnosis	29	13%
13	Other less common diagnosis	17	8.1%
	Total	210	100%

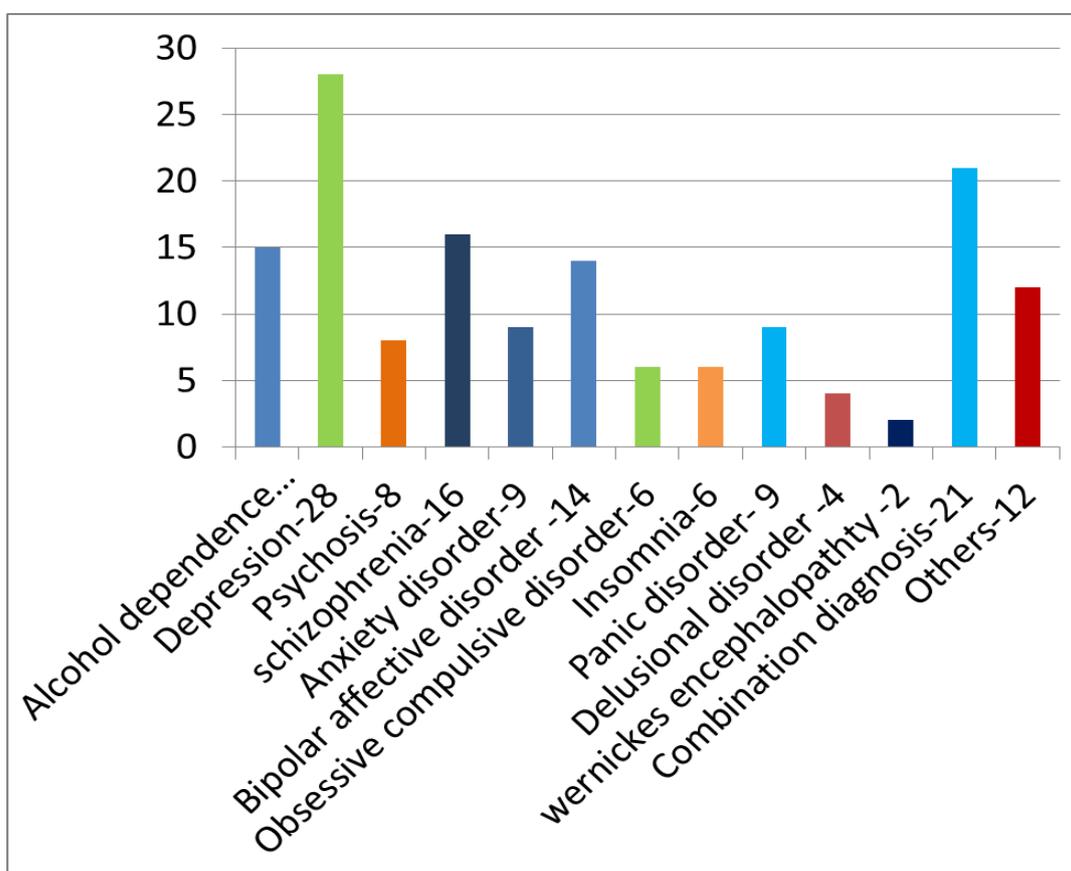


Fig 7: Patient diagnosis distribution.

List of multiple diagnosis

- Alcohol dependence syndrome with insomnia
- Bipolar affective disorder with depression and psychosis
- Anxiety disorder with depression
- Panic disorder with insomnia
- Panic disorder with depression
- OCD with depression
- Panic disorder with anxiety
- Adjustment disorder with depression
- Schizophrenia with depression

List of other less common diagnosis

- Dysthymia
- Catatonia
- Somatoform disorder with anxiety
- Acute transient psychiatry disorder
- Premenstrual dysphoric disorder
- Borderline personality disorder
- Epilepsy
- Mania
- Post traumatic stress disorder

6. Patient Comorbidity Distribution

Out of the 210 cases collected for the purpose of this study, 148 of the cases was having no present comorbidities at the time of data collection representing 70.1% of the study population. 33 cases (15.7%) was having hypertension and 10 cases (4.8%) was having diabetes mellitus as a comorbidity at the time of data

collection, while 19 cases (9.05%) had more than one comorbidities present.

List of Combination of multiple comorbidities

- Hypertension with Diabetes Mellitus
- Alcoholic liver disease with Hypertension
- Cerebral venous thrombosis with epilepsy
- Hypertension with Hypothyroidism

Table 8: Patient comorbidities distribution.

S/N	Comorbidities	No of cases	Percentage
1	No	148	70.1%
2	yes		
	Hypertension	33	15.7%
	Diabetes	10	4.8%
	Multiple comorbidities	19	9.05%
	Total	210	100%

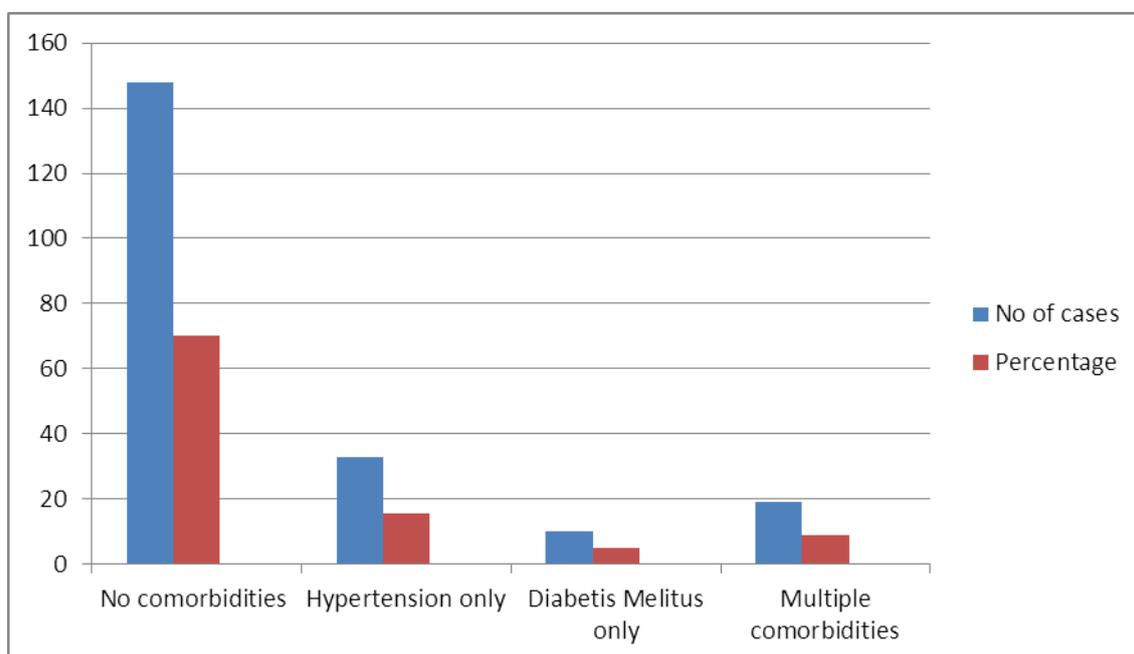


Fig 8: Patient comorbidities distribution.

7. Effects of Benzodiazepines on Comorbidities

Out of the 210 cases selected for this study 62 was with comorbidities at the time of data collection.

Out of this 62 cases only 8 (12.9%) patients reported a significant effects on their comorbidities after starting benzodiazepine therapy.

Table 9: Effects of benzodiazepines.

SN	Effects of Benzodiazepines	No of cases	Percentage
1	No	54	87.1%
2	Yes	8	12.9%
	Total	62	100%

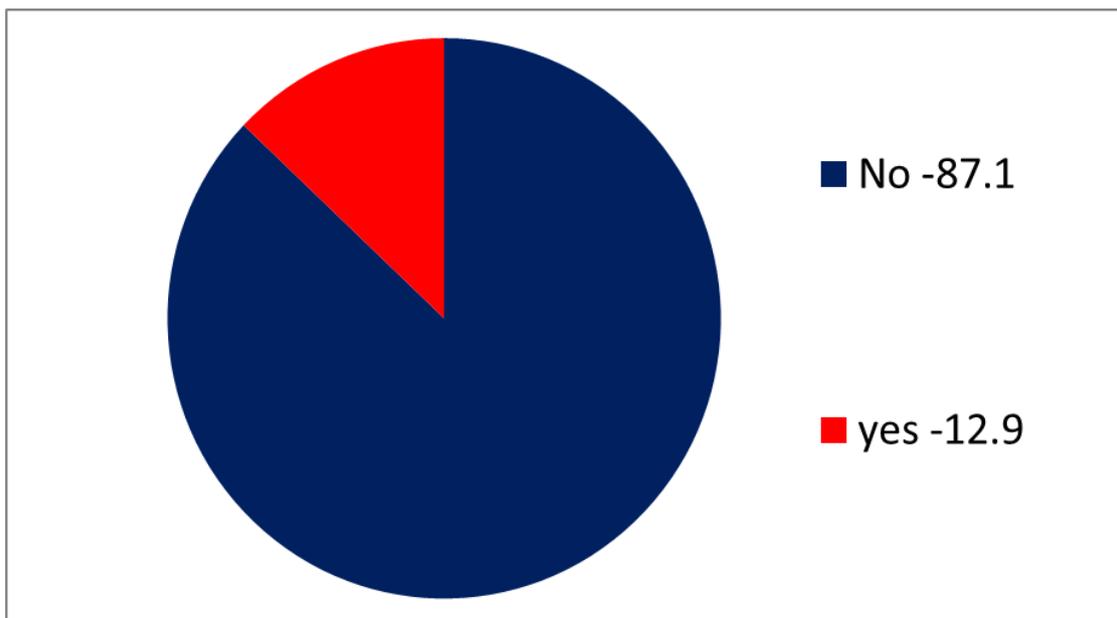


Fig 9: Effects of benzodiazepines (Pie chart).

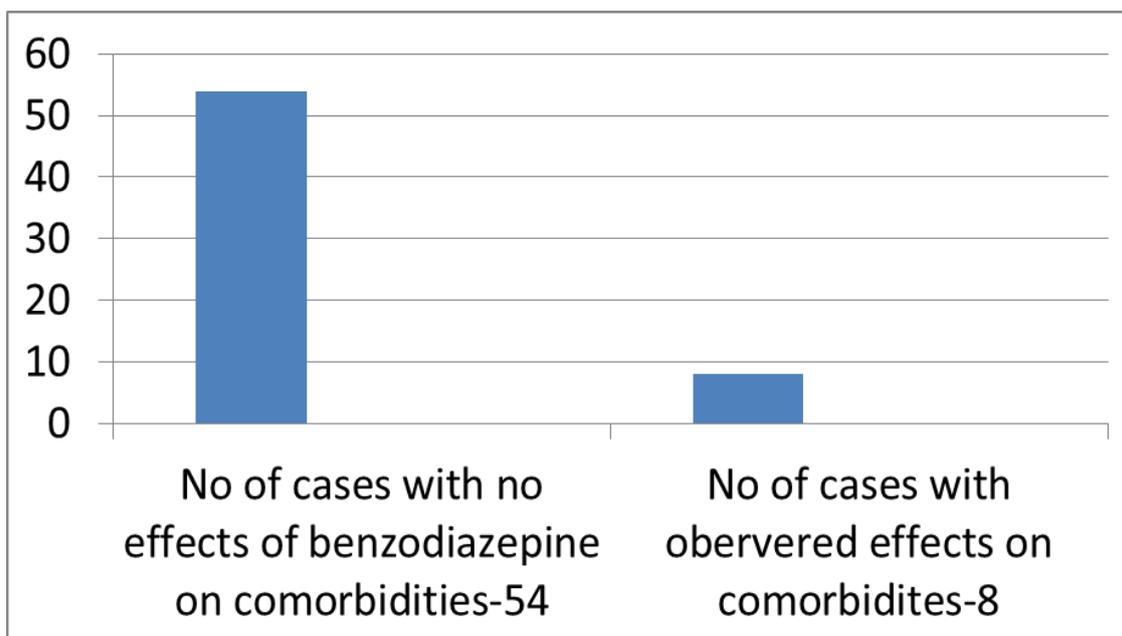


Fig 10: Effects of benzodiazepines (Bar chart).

8. Most commonly prescribed Benzodiazepine (Brands)

In the 210 cases collected for the purpose of this study, benzodiazepines of various brands was prescribed 198

times with a few prescriptions contain more than one brand, and some contain no branded drugs at all. The various brands and how common they were prescribed are represented by the following table and bar chart.

Table 10: Most commonly prescribed benzodiazepine brand names.

SN	Brand Names	Frequency	Percentage
1	Petril 0.5mg	90	45.5
2	Petril 0.25mg	25	12.6
3	Ativan 1mg	23	11.6
4	Ativan 2mg	22	11.1
5	Zapiz 0.5mg	11	5.6
6	Lopez 2mg	5	2.5
7	Valium 5mg	6	3.03
8	Valium 2mg	4	2.0

9	Valium 10mg	4	2.0
10	Librium 10mg	2	1.0
11	Zapiz 2mg	1	0.5
12	Alprax 0.25mg	1	0.5
13	Lopez 1mg	1	0.5
14	Lonazep 0.5mg	1	0.5
15	Zapiz 1mg	1	0.5
	Total	198	100

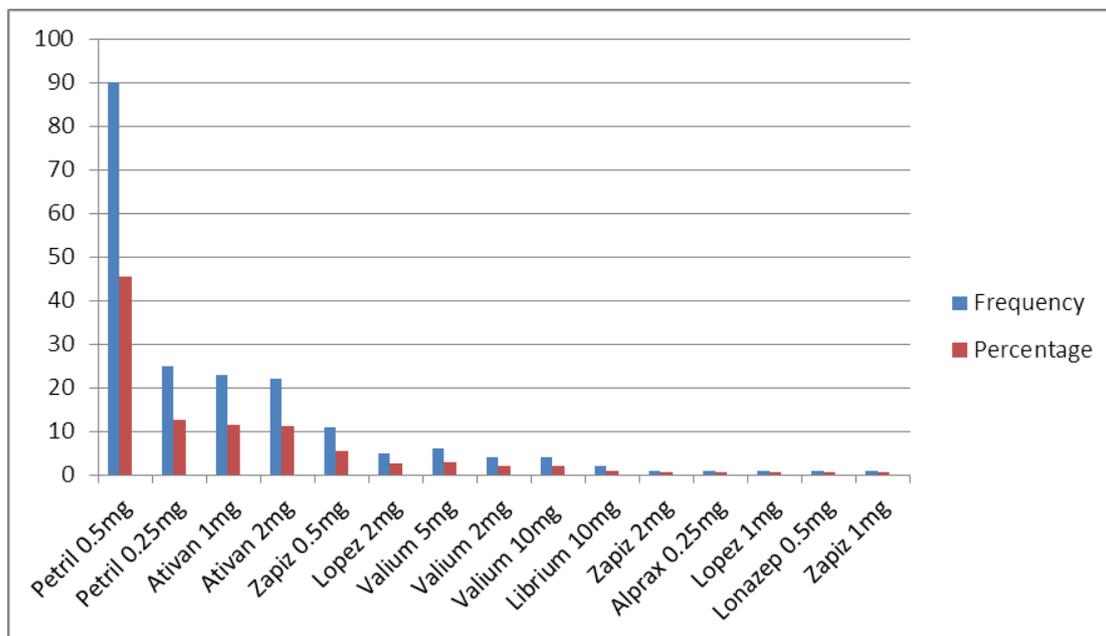


Fig 11: Most commonly prescribed benzodiazepines brand names.

9. Frequency Distribution of Benzodiazepines prescribed based on generic names

Taking into consideration both the prescription with only one benzodiazepines present and those with more than one, those having benzodiazepines prescribed only in

generic and also the brand benzodiazepine in the prescription. The following frequency distribution table of benzodiazepines based on the generic names can be drawn represented in the chart that follows later.

Table 11: Most commonly prescribed benzodiazepines generic names.

SN	Generic Names	Frequency	Percentage
1	Clonazepam	133	60.5
2	Lorazepam	51	23.2
3	Diazepam	32	14.5
4	Alprazolam	2	0.9
5	Chlordiazepoxide	1	0.45
6	Etizolam	1	0.45
	Total	220	100

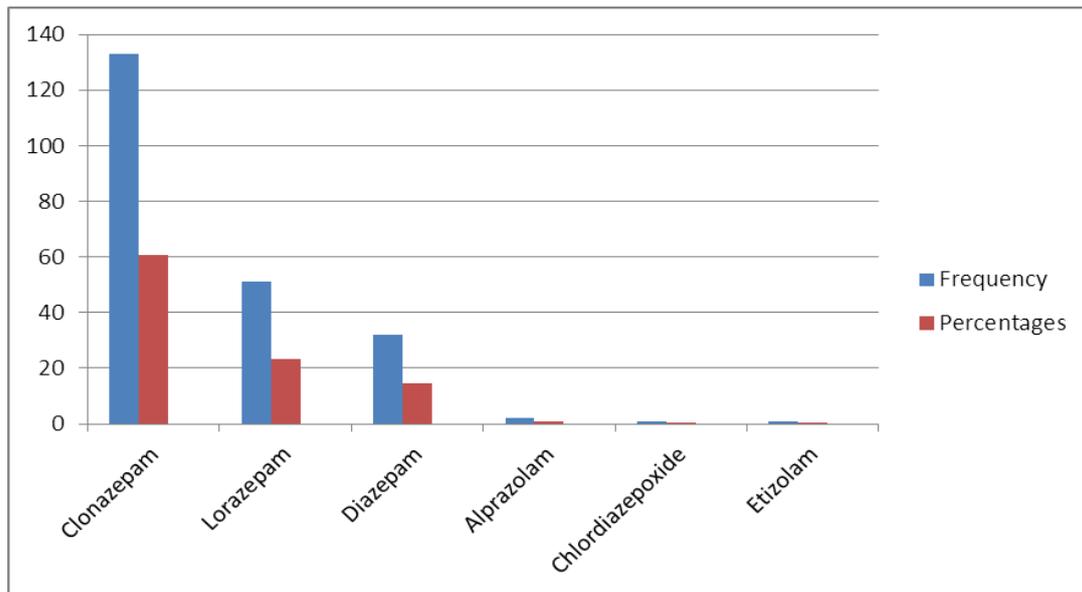


Fig 12: Most commonly prescribed benzodiazepine generic names.

10. Patient duration of treatment distribution

Out of the 210 cases collected for the purpose of this study, 4 different duration of study was observed in the

treatment regimens. The duration of treatment and the frequency at which they occur are represented in the table and chart as follows.

Table 12: Patient duration of treatment distribution.

S/N	Duration of treatment	No of cases	percentage
1	30	45	21.4%
2	20	49	23.33%
3	15	75	35.7%
4	10	41	19.5%
	Total	210	100%

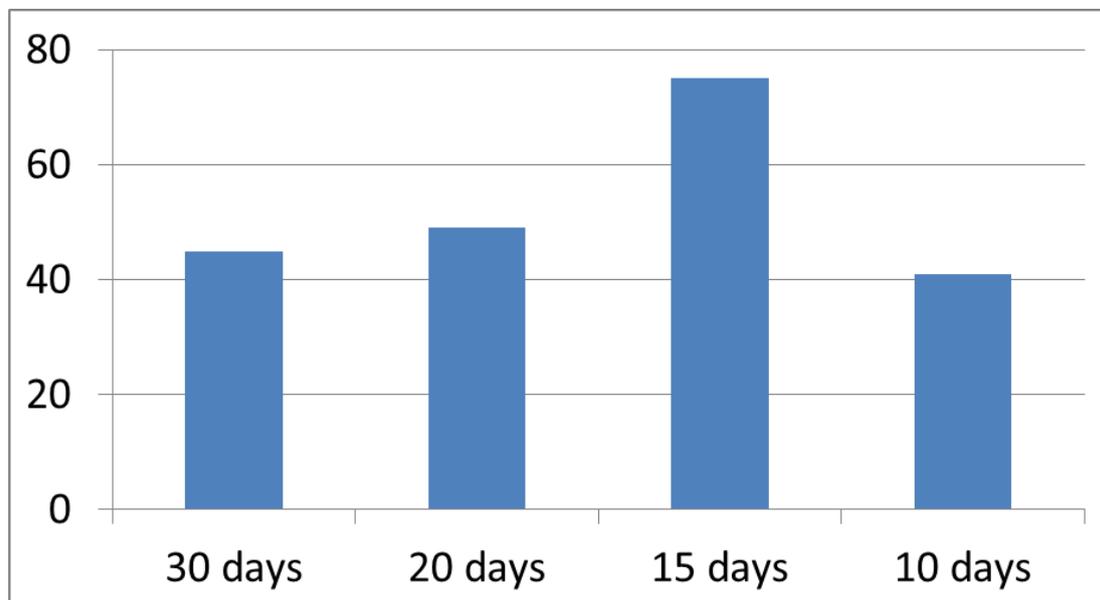


Fig 13: Patient duration of treatment distribution (Bar chart).

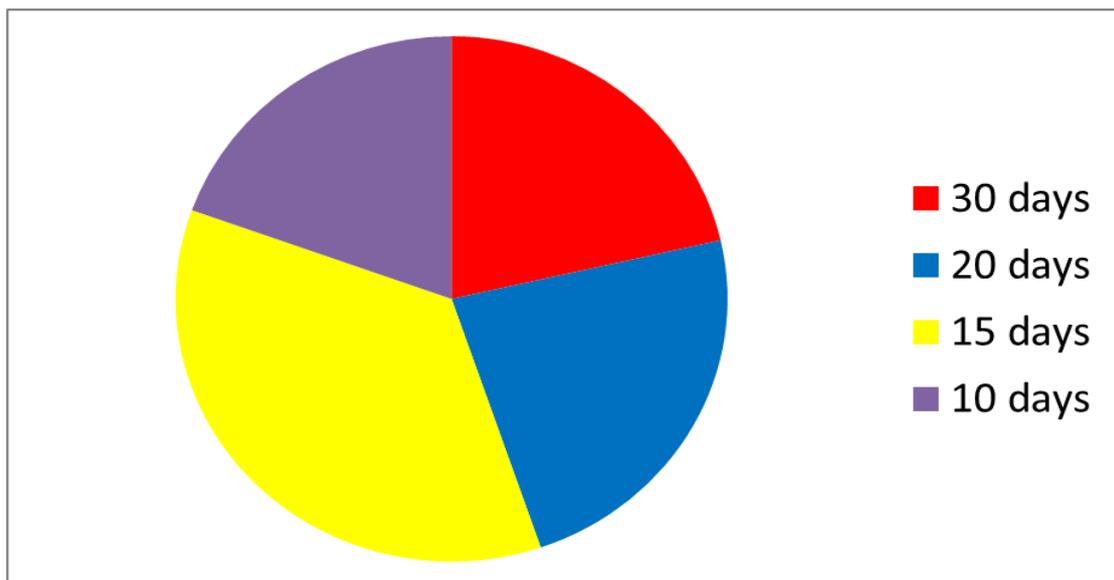


Fig 14: Patient duration of treatment distribution. (Pie chart).

11. Medication Adherence Frequency Distribution

210 patients were interviewed and 166 of them were found to adhere to their medication and the advise given by the doctor on taking the benzodiazepines. 24 of them

on the other hand didn't adhere to their medications for various reasons while the medication adherence of the remaining 20 could not be ascertained as they were visiting the hospital for the first time.

Table 13: Patient medication adherence distribution.

SN	Medication Adherence	No of cases	Percentages
1	Yes	166	79%
2	No	24	11.4%
3	First Timers	20	9.5%
	Total	210	100%

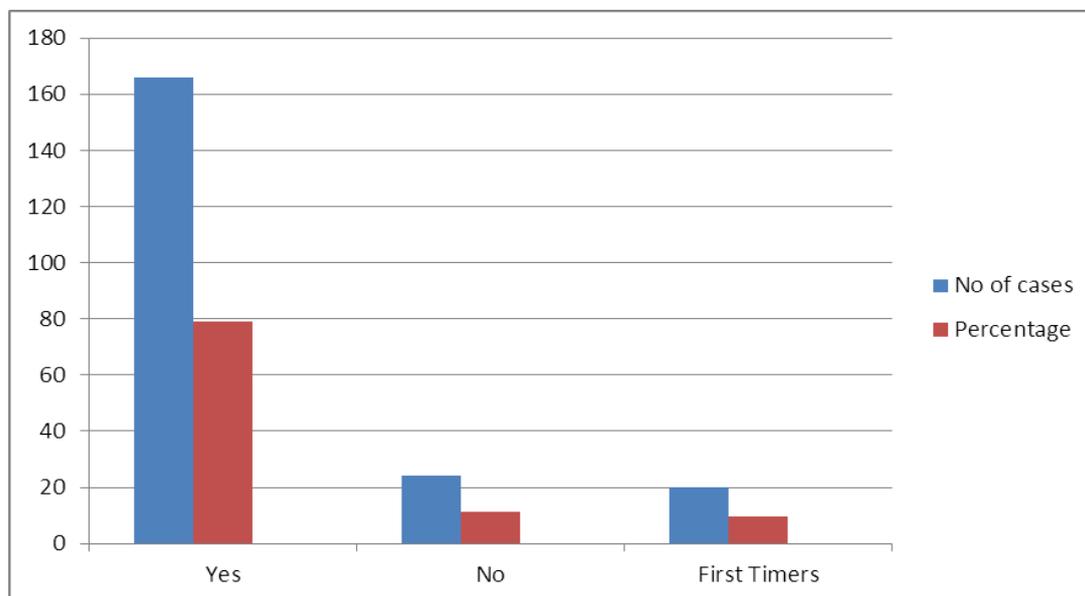


Fig 15: Patient medication adherence distribution.

12. Rationality of Benzodiazepines Prescribed

The rationality of the benzodiazepines prescribed in the 210 cases collected for the purpose of this study was analysed on the basis of efficacy, appropriateness of indication, doses, duration of treatment, mode of administration and frequency and 7 was found to be

irrational while the rest was found to be well within the limits of rationality.

Table 14: Rationality assessment.

SN	Rationality	No of cases	Percentage
1	Rational	203	96.7%
2	Irrational	7	3.3%
	Total	210	100%

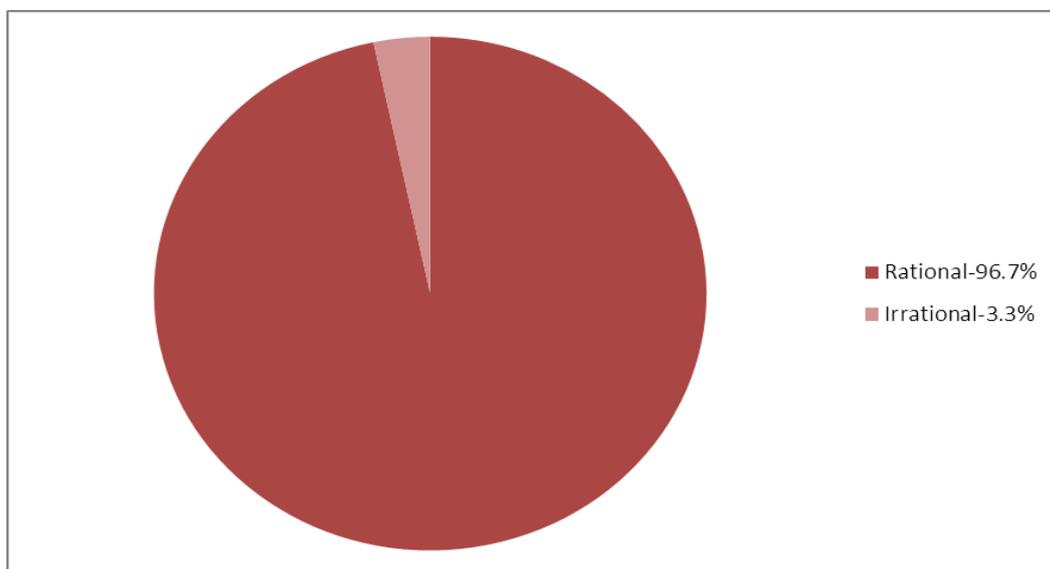


Fig 16: Rationality assessment.

13. PHARMACOECONOMICS ANALYSIS

13.1. AVERAGE COST ANALYSIS

A total of 220 benzodiazepines were prescribed for 210 cases, average number of benzodiazepines per prescription was found to be 1.04.

Average cost of branded benzodiazepines per prescription was found to be 63.61 INR, while the average cost of benzodiazepines if prescribed in generic was found to be 21.08INR.

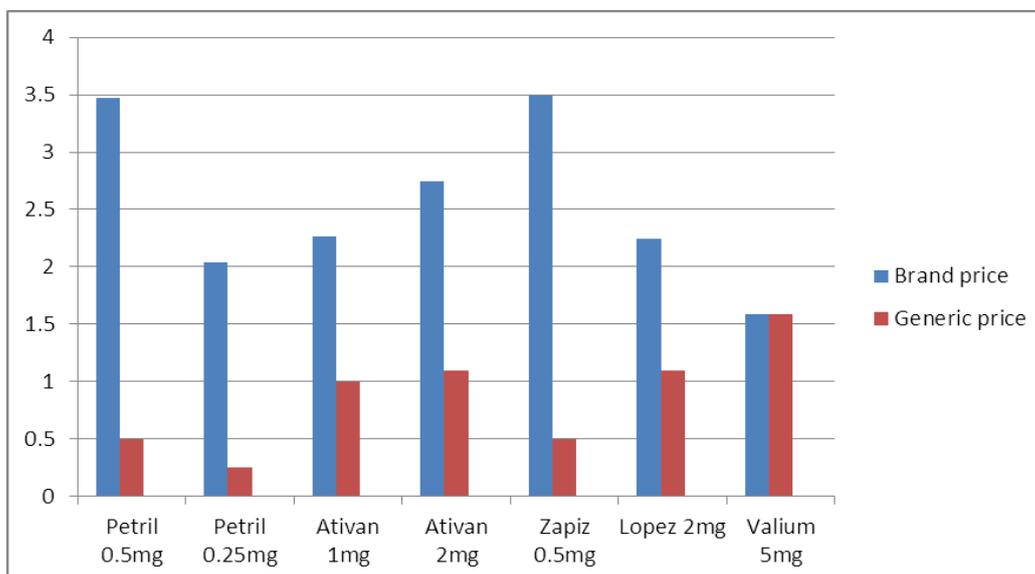
Table 15: Average cost analysis.

Average No of benzodiazepines per prescription	1.04
Avg cost of brand benzodiazepines	63.61 INR
Avg cost of generic benzodiazepines	21.08 INR

13.2 COST PER UNIT ANALYSIS

A total of 220 benzodiazepines were prescribed in the 210 cases collected for the purpose of this study, cost per

unit comparison for these antibiotics for their brand and generic cost is as follows.



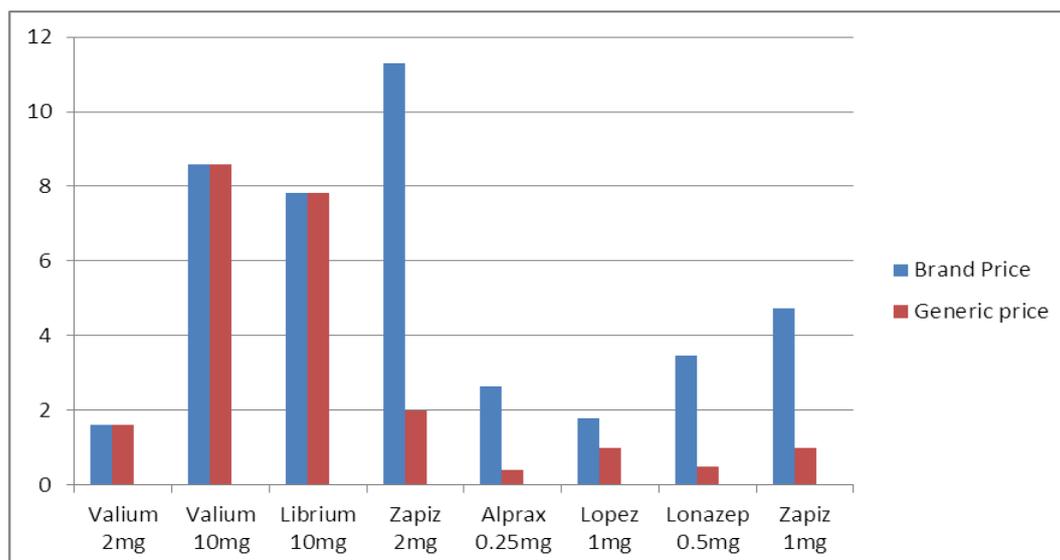


Fig 17: Cost per unit analysis of brand and generic prices of benzodiazepines.

DISCUSSION

This study offers and provides us with an overall perspective and view of the benzodiazepines used in patients of various psychiatry diagnosis in a tertiary care hospital.

The study shows that male patients was clearly predominant with 115 cases while the female patients was found to be 95 out of the 210 cases collected for the purpose of this study, the percentage occupied by both genders were 54.67% and 45.33% respectively, this pattern is similarly reflected in the findings of P Rama et al^[3], whose study saw 75.5% of the 200 subjects to be male and 25.5% to be female.

But the findings in the study carried out by Ramadan W et al^[4] in the Lebanese adult population in Lebanon would disagree as they found that out of their study population of 789 benzodiazepine users, 54.2% of them was female while males occupied the remaining 45.8%.

The age group of the patients where categorized into 3 different age brackets viz, 20-40, 41-60, 61-80, each age bracket had 82, 106, and 22 patients in it respectively and each representing 39%, 50.5%, and 10.5% of the study population respectively with the age bracket 41-60 being predominant amongst other age brackets.

Our study also finds that out of the 210 cases collected for the purpose of this study which has corresponding prescriptions containing benzodiazepine(s), 198 prescriptions contained only a single benzodiazepine, that is about 94.3% of the entire study population, while just a little over 5% of the prescriptions had more than one benzodiazepines in it.

In all the 210 prescriptions collected for this study, benzodiazepines was found to be prescribed in brand in 189 prescriptions, benzodiazepines being prescribed in

generic form was found only 25 times in the entire study population of 210 case.

Benzodiazepines are prescribed for various purposes and for different diagnosis, the most common diagnosis found in the study population of this study for which benzodiazepines was prescribed are as follows, Alcohol dependence syndrome (11.4%), various forms of depression (15.2%), Psychosis (50.2%), Schizophrenia (10%), Anxiety disorders (9%), Bipolar affective disorder (9%), Obsessive compulsive disorder (4.8%), Insomnia (3.3%), Panic disorder (7.1%) Delusion disorder (1.9%), Wernicke's encephalopathy (0.9%), Multiple or combination diagnosis like anxiety with depression, schizophrenia with depression, OCD with depression etc occupied 13% of the diagnosis in the study population, while other less common diagnosis, or diagnosis that only occurred once such as Dysthymia, PTSD, Catatonia etc all together occupied 8.1% of the diagnosis seen the study population.

It is therefore obvious that the most common treated psychiatry disorder for which benzodiazepines are being prescribed among the study population of this specific study is depression. Depression can be of different variations like Recurrent depressive disorder, organic depression, mood depressive episodes, severe depressive episodes, alcohol induced depression, persistent mild depression (dysthymia) etc. A similar analysis was done by RamadanW et al and they found out that the most common indication of benzodiazepines in the Lebanese adult population in Lebanon was for the for the treatment of Anxiety and that the population was predominantly female.

The comorbidities of the patients involved in this study was also studied and the we have found that a little over 70% of the study population had no current comorbidities at the time of collecting their data for the purpose of conducting this study.

However, 62 cases were recorded to be present with comorbidities at the time of data collection with the most common comorbidity being Hypertension which occupied 15.7% of the entire study population, followed by Diabetes mellitus at 4.8% of the entire study population.

A scenario where a patient was seen to have more than one comorbidities such as both hypertension and diabetes, or with hypothyroidism etc was also recorded, such instances occupy 9.05% of our entire study population as it was seen 19 times in the cases collected.

Out of the 62 cases in which the presence of comorbidities was seen, only 8 of them confirmed to have experienced slight or significant effects on the treatment of the comorbidities believing that the said effect started right around the time the started treatment of their psychiatry diagnosis with benzodiazepine therapy, whereas, 87.1% of the entire number of patients with comorbidities stated that they have not experienced any changes in the treatment or control of their comorbidities even after starting taking benzodiazepines for their specific psychiatry diagnosis.

So we can

As stated earlier, benzodiazepines are predominantly prescribed in brand names the physician, and seeing as one of the primary objectives of this study is to study the prescribing pattern of psychiatrist in prescribing benzodiazepines, we have analysed the various brands prescribed by psychiatrist in the prescriptions collected for the purpose of this study using the SPSS statistical software and the most commonly prescribed brand and their dose was found to be as follows, Petril 0.5mg (clonazepam) (45.5%), Petril 0.25mg (12.6%) Ativan 1mg (Lorazepam) (11.6%), Ativan 2mg (11.1%), Zapiz 0.5mg (clonazepam) (5.6%), Lopez 2mg (Lorazepam) (2.5%), Valium 5mg (Diazepam) (3.3%), Valium 2mg (2%), Valium 10mg (2%), Librium (chlordiozepoxide) (1%), Zapiz 2mg (0.5%), Alprax 0.25mg (Alprazolam) (0.5%), Lopez 1mg (0.5%), Lonazep (Lorazepam) (0.5%), Zapiz 1mg (0.5%), Etilam(etizolam) (0.5%).

Furthermore, the prescribing pattern of benzodiazepines was analysed with respect to their generic names to get a more better perspective on the overall use of each individual benzodiazepine regardless of the brand prescribed because the same active drug content for example diazepam if manufactured by two different companies will certainly be having two distinct brand names but analysing the prescribing pattern of the benzodiazepines based on their generic name will offer a more concise approach to understanding the versatility of the drug regardless of various brand names under which it is being manufactured.

The most common prescribed benzodiazepines are as follows, Clonazepam (60.5%), Lorazepam (23.2%),

Diazepam (14.5%), Alprazolam (0.9%), Chlordiazepoxide (0.45%) and Etizolam (0.45%).

The most commonly prescribed benzodiazepine in brand names is Petril (Clonazepam), followed by Ativan (Lorazepam) and the least prescribed brands are Alprax, Lonazep and Etilam.

The most commonly prescribed benzodiazepine in generic is Clonazepam, followed by Lorazepam, and diazepam. This is quite different from the results attained by P Rama et al^[3] and Ramadan W. et al^[4], the former having concluded that the most commonly used benzodiazepine is Lorazepam, used mainly for sedation followed anxiety, and the later finding reaching the conclusion that the most commonly prescribed benzodiazepine were Alprazolam and Bromazepam.

The duration of treatment is also another important factor to consider when analysing the rationality of the benzodiazepines used, in this study four most common duration of treatment for each prescription of benzodiazepine at the time of data collection was observed and they are 10, 15, 20 and 30 days and the percentage of the frequency at which they are occurring are 19.5%, 35.7%, 23.3% and 21.4% respectively with more patients seen to be prescribed benzodiazepines on a 15day treatment course than any other recorded duration of treatment.

Benzodiazepine medication adherence was also analysed and the results show that 79% of the benzodiazepine users were adhering to their medications, taking it on time and never missing a dose, 11.4% of the benzodiazepine users weren't adhering to the medication and the instruction given by the psychiatrist due to various reasons like forgetting to take the medication to not believing in the efficacy of the medication, however, 9.5% of the patients were first timers to the use of benzodiazepine so benzodiazepine medication adherence was not assessed due to the stated reason.

The rationality of each benzodiazepine was analysed and the assessment was done by collecting evidence from various published literature about individual benzodiazepines, when all the 210 prescriptions were assessed, the results were that 96.7% of the prescriptions were containing rationally prescribed benzodiazepines while the remaining 3.3% showed some discrepancies such as higher dose, wrong indication hence deemed irrational.

According to the prospective observational study on the utilization patterns of benzodiazepines in psychiatry patients in a tertiary care teaching hospital by Uday Venkat Mateti et al^[8], the prescribed daily dose and defined daily dose of benzodiazepines were 57.16 ± 30.3 and 89.69 ± 39.16 respectively. The total cost per defined daily dose of benzodiazepines was 28.9 INR.

From the current study, the average cost of benzodiazepines when prescribed in brand was 63.61 INR, which is higher when compared to the average cost of the benzodiazepines if prescribed in generic which was found to be 21.08 INR.

CONCLUSION

The use of benzodiazepines is very prevalent in the majority the therapy used to treat most of the psychiatry disorders and diagnosis Therefore it is very paramount and quintessential to monitor the prescribing pattern of benzodiazepines, their doses, frequency and duration of treatment especially in the case of geriatric patients and younger adult.

One very important fact worthy of note is that although the effects of benzodiazepines can be rarely seen of different comorbidities and their treatment, it is essential to realize that it is not entirely impossible, so care must be taken to prevent any incident that may result in a significant effect of a pre-existing comorbidity due to benzodiazepine therapy and knowing that it is a possibility is the first step.

The study can therefore conclude that males have predominantly larger quantity of benzodiazepine users than women and that the most commonly prescribed brand of benzodiazepine is Petril followed by Ativan and Zapiz, while the most commonly prescribed generic drug is clonazepam followed by lorazepam and diazepam.

The study also concludes that the rationality of benzodiazepines in the study population was good at 96.7%.

On carrying out the pharmacoeconomics analysis using cost minimization analysis method, it was found that there was significant reduction in the treatment cost if the generic alternatives of the benzodiazepines are being prescribed instead of the branded ones, the efficacy of the generic drugs are almost same as that of the branded drugs as well.

When we take into consideration the economic status of the Indian population, where the majority of the people belong to economically backward section, the cost of treatment becomes of great importance.

Therefore, generic alternatives of the benzodiazepines can be used which will tend to reduce the overall treatment cost and thus reducing the economic burden placed on the patients and users of benzodiazepines.

ACKNOWLEDGEMENTS

As he is the first and last, we thankfully bow with reverence before the almighty God who is the source of all wisdom and knowledge, the creator by whose blessings and guidance we were able to attain the completion of our project and the publication of this article.

We express our deepest gratitude to our honourable secretary Mr H R Kiran for providing the facilities need for performing this project and extending his support. We also want to thank our to our principal Dr V B Narayanaswamy for all his support. Also, we wish to extend our appreciation to our able HOD, Dr E Satheesh Kumar for all his efforts and support towards the completion of this project.

we would also love to extend our gratitude to our research guides Mr Azad Moidul Islam, Assistant professor, Department of pharmacy practice, RR College of Pharmacy, and DR Srividya B P, Assistant professor, Department of Pharmacology, Saphagiri Institute of Medical Sciences and Research Centre, for their most valuable guidance, keen interest, inspiration, unflinching encouragement and moral support throughout this project. In the same breath we would also like to thank all the doctors in psychiatry department at SIMS&RC and other hospital staff for continuously providing their support.

Lastly and certainly not the least, we would love to express our most deepest and sincerest gratitude to our parents, Igwe Emeka Kingsley, Igwe ifeoma Jacinta, Surendran P. A., Geetha N.K., Habeebur Rahiman, Nafeesa Habeeb, Bahram Mayeli, Effat Bakhtiyari for their unflagging love and unconditional support throughout our life and our studies, we are here because of you and for that we can never be grateful enough.

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