

Study of Prescribing Patterns of Anti-Hypertensive Agents in Hypertensive Patients with Co-Morbid Conditions at a Tertiary Care Teaching Hospital

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Abstract

Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure. It can increase the risk of heart, brain, kidney and other diseases. An estimated 1.28 billion adults aged 30 to 79 years worldwide have hypertension, most (two-thirds) living in low- and middle-income countries. Overall prevalence for hypertension in India was 29.8%. Prescribing pattern describe the nature, profile of drug usage, and compliance with regional, state, or national guidelines, such as uniform prescribing patterns, the use of drugs from the list of essential medicines, and the use of generic drugs. Appropriate prescription has a beneficial effect on adherence and disease prevention. The purpose of prescribing pattern analysis is to ensure rational use of drugs, prescribed with complete knowledge on safety and tolerability of regimen and controlling not only current ailment but also the comorbid conditions. The objective of this study is drug utilization evaluation (DUE) of antihypertensive agents in hypertensive patients with cardiovascular, nephrological and neurological comorbid conditions.

Keywords: Hypertension, Prescribing pattern, Antihypertensive agents, Drug utilization evaluation

Introduction

According to WHO, Hypertension (high blood pressure) is when the pressure in your blood vessels is too high (140/90 mmHg or higher). It is common but can be serious if not treated.^[1] It is also defined as persistently elevated arterial blood pressure (BP). Isolated systolic hypertension is diastolic blood pressure (DBP) values less than 90 mm Hg and systolic blood pressure (SBP) values of 140 mm Hg or more.

Overall prevalence for hypertension in India was 29.8% (95% confidence interval: 26.7–33.0). Significant differences in hypertension prevalence were noted between rural and urban parts [27.6% (23.2–32.0) and 33.8% (29.7–37.8); $P = 0.05$]. Hypertension prevalence would increase to 44% (95% CI, 43–45%) in year 2030, a relative increase by 17%, instead of a relative decline by 25% by the year 2030 proposed by WHO.^[2]

This study was conducted with the objective of assessing the prescribing pattern of antihypertensive agents in hypertensive patients with co-morbid conditions. Further, the study also assessed the rationality and adherence of prescribing pattern with JNC-8 hypertension management guidelines. Ultimately, such a study will improve the quality of prescriptions and will provide a greater benefit to the patient.^[3]

Drug Utilization Evaluation (DUE) is an authorized and structured ongoing review of practitioner prescribing, pharmacist dispensing and patient use of medications. The purpose of DUE is to ensure drugs are used appropriately, safely and effectively to improve patient health status.

PRESCRIBING PATTERN describe the nature and profile of drug usage, and compliance with regional, state, or national guidelines, such as uniform prescribing patterns, the use of drugs from the list of essential medicines, and the use of generic drugs. Appropriate prescription has a beneficial effect on adherence and disease prevention. Patient factors like age, sex, BMI, coexisting illness, and mainly their socioeconomic status will all determine the prescription pattern.

The rational prescription of therapeutic regimen represents a physician's attitude towards selection of treatment from different classes of antihypertensive drugs. During prescription writing along with current ailment and comorbid the knowledge of safety and tolerability of regimen is also of prime importance because it leads to prevent the future hallmarks of the prescribed therapy.^[4] The antihypertensive (AHT) agents used should not only aim to control hypertension (HTN) but also at preventing and delaying the development of complications.^[5]

CLASSIFICATION:

The Eighth report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8) classifies adult BP as shown in Table:

Classification	Systolic (mm Hg)		Diastolic (mm Hg)
Normal	<120	and	<80
Prehypertension	120–139	or	80–89
Stage 1 hypertension	140–159	or	90–99
Stage 2 hypertension	≥160	or	≥100

Table 1: Classification of Blood Pressure in Adults

Hypertensive crisis (BP >180/120 mm Hg) may be categorized as hypertensive emergency with extreme BP elevation with acute or progressing target-organ damage) or hypertensive urgency (high BP elevation without acute or progressing target-organ injury).^[6]

Hypertension has been identified as a major risk factor not only for the development of diabetes but also for the development of micro and macro vascular complications, that is, neuropathy, nephropathy, retinopathy, coronary artery disease, stroke, peripheral vascular disease in diabetic patients.^[7]

CARDIOVASCULAR CO-MORBID CONDITIONS:

High blood pressure can cause many heart conditions, including:

- Coronary artery disease - High blood pressure can narrow and damage the arteries that supply blood to the heart. This damage is known as coronary artery disease. Too little blood flow to the heart can lead to chest pain, called angina. It can lead to irregular heart rhythms, called arrhythmias. Or it can lead to a heart attack.
- Heart failure - High blood pressure strains the heart. Over time, this can cause the heart muscle to weaken or become stiff and not work as well as it should. The overwhelmed heart slowly starts to fail.
- Enlarged left heart - High blood pressure forces the heart to work harder to pump blood to the rest of the body. This causes the lower left heart chamber, called the left ventricle, to thicken and to enlarge. A thickened and enlarged left ventricle raises the risk of heart attack and heart failure. It also increases the risk of death when the heart suddenly stops beating, called sudden cardiac death.
- Metabolic syndrome - High blood pressure raises the risk of metabolic syndrome. This syndrome is a cluster of health conditions that can lead to can lead to heart disease, stroke and diabetes. The health conditions that make up metabolic syndrome are high blood pressure, high blood sugar, high levels of blood fats called triglycerides, low levels of HDL cholesterol, which is the "good" cholesterol, and too much body fat around the waist.

NEUROLOGICAL COMORBID CONDITIONS:

The brain depends on a nourishing blood supply to work right. High blood pressure may affect the brain in the following ways:

- Transient ischemic attack (TIA) - Sometimes this is called a ministroke. A TIA happens when the blood supply to part of the brain is blocked for a short time. Hardened arteries or blood clots caused by high blood pressure can cause TIAs. A TIA is often a warning sign of a full-blown stroke.
- Stroke - A stroke happens when part of the brain doesn't get enough oxygen and nutrients. Or it

can happen when there is bleeding inside or around the brain. These problems cause brain cells to die. Blood vessels damaged by high blood pressure can narrow, break or leak. High blood pressure also can cause blood clots to form in the arteries leading to the brain. The clots can block blood flow, raising the risk of a stroke.

➤ Dementia - Narrowed or blocked arteries can limit blood flow to the brain. This could lead to a certain type of dementia, called vascular dementia. A single stroke or multiple tiny strokes that interrupt blood flow to the brain also can cause vascular dementia.

➤ Mild cognitive impairment - This condition involves having slightly more troubles with memory, language or thinking than other adults your age have. But the changes aren't major enough to impact your daily life, as with dementia. High blood pressure may lead to mild cognitive impairment.

NEPHROLOGICAL COMORBID CONDITIONS:

➤ Kidneys filter extra fluid and waste from the blood — a process that requires healthy blood vessels. High blood pressure can damage the blood vessels in and leading to the kidneys. Having diabetes along with high blood pressure can worsen the damage.

➤ Damaged blood vessels prevent the kidneys from being effective at filtering waste from the blood. This allows dangerous levels of fluid and waste to collect. When the kidneys don't work well enough on their own, it's a serious condition called kidney failure. Treatment may include dialysis or a kidney transplant. High blood pressure is one of the most common causes of kidney failure.^[8]

TREATMENT:

Management of hypertension - Many guidelines exist for the management of hypertension. Most groups, including the JNC, the American Diabetes Associate (ADA), and the American Heart Association/American Stroke Association (AHA/ASA) recommend lifestyle modification as the first step in managing hypertension. Initial drug selection depends on the degree of BP elevation and presence of compelling indications for selected drugs.

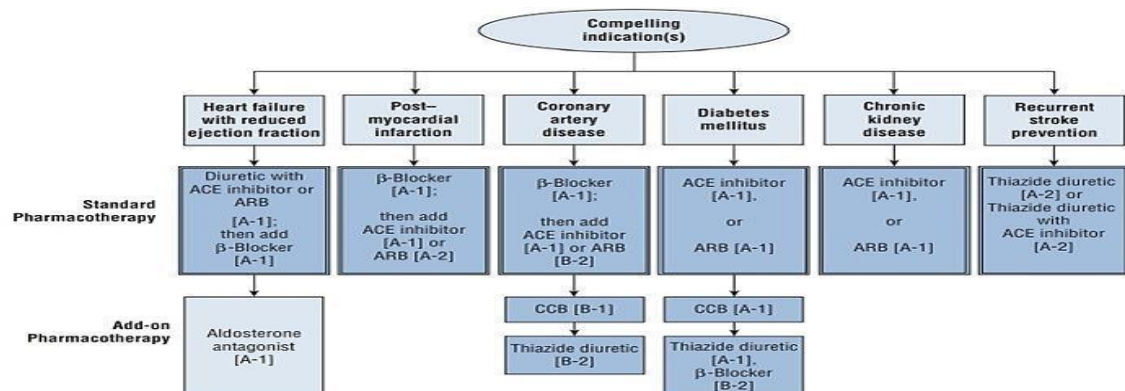
➤ Angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), and thiazide diuretics are acceptable first-line options.

➤ β -Blockers are used to either treat a specific compelling indication or as combination therapy with a first-line antihypertensive agent for patients without a compelling indication.

➤ Most patients with stage 1 hypertension should be treated initially with a first-line antihypertensive drug or a two-drug combination. Combination therapy is recommended for patients with stage 2 hypertension, preferably with two first-line agents.

➤ There are six compelling indications where specific antihypertensive drug classes provide unique benefits.

➤ Other antihypertensive drug classes (α 1-blockers, direct renin inhibitors, central α 2-agonists, peripheral adrenergic antagonists, and direct arterial vasodilators) are alternatives that may be used for select



Compelling indications for individual drug classes. Compelling indications for specific drugs are evidence-based recommendations from outcome studies or existing clinical guidelines. (ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; CCB, calcium channel blocker.)

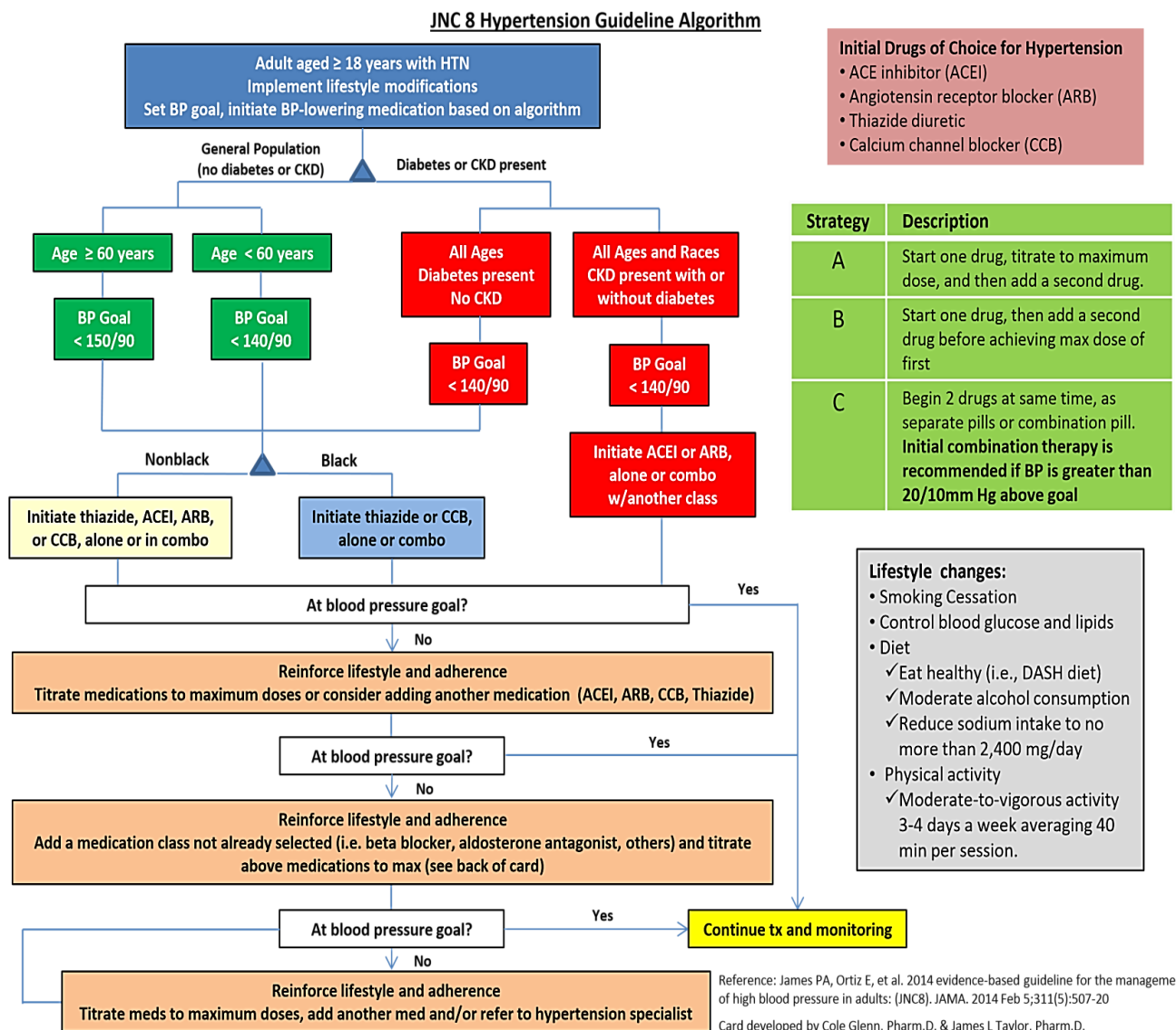
patients after first-line agents.^[10]

Algorithm 1: Compelling indications for individual drug class of antihypertensives

Compelling Indications	
Indication	Treatment Choice
Heart Failure	ACEI/ARB + BB + diuretic + spironolactone
Post –MI/Clinical CAD	ACEI/ARB & BB
CAD	ACEI, BB, diuretic, CCB
Left ventricular dysfunction	Diuretic, ACEI/ARB & BB
CKD	ACEI/ARB
Recurrent stroke prevention	ACEI, diuretic
Diabetes	ACEI/ARB, CCB, diuretic

Table 2: Compelling indications of comorbidities for antihypertensive treatment

Algorithm 2: Standard algorithm for treatment of hypertension [11]



Materials And Methods

MATERIALS:

Patient Informed Consent Form (ICF) Patient data collection form Questionnaire form

Patient information Sheet

Study design: Prospective Observational Cohort study

Study population: 250 cases with complete data were screened and used for evaluation.

Study site: The study has been conducted in Gayatri Vidya Parishad Institute of Health Care & Medical Technology, KIMS Hospital and other clinics in and around Visakhapatnam.

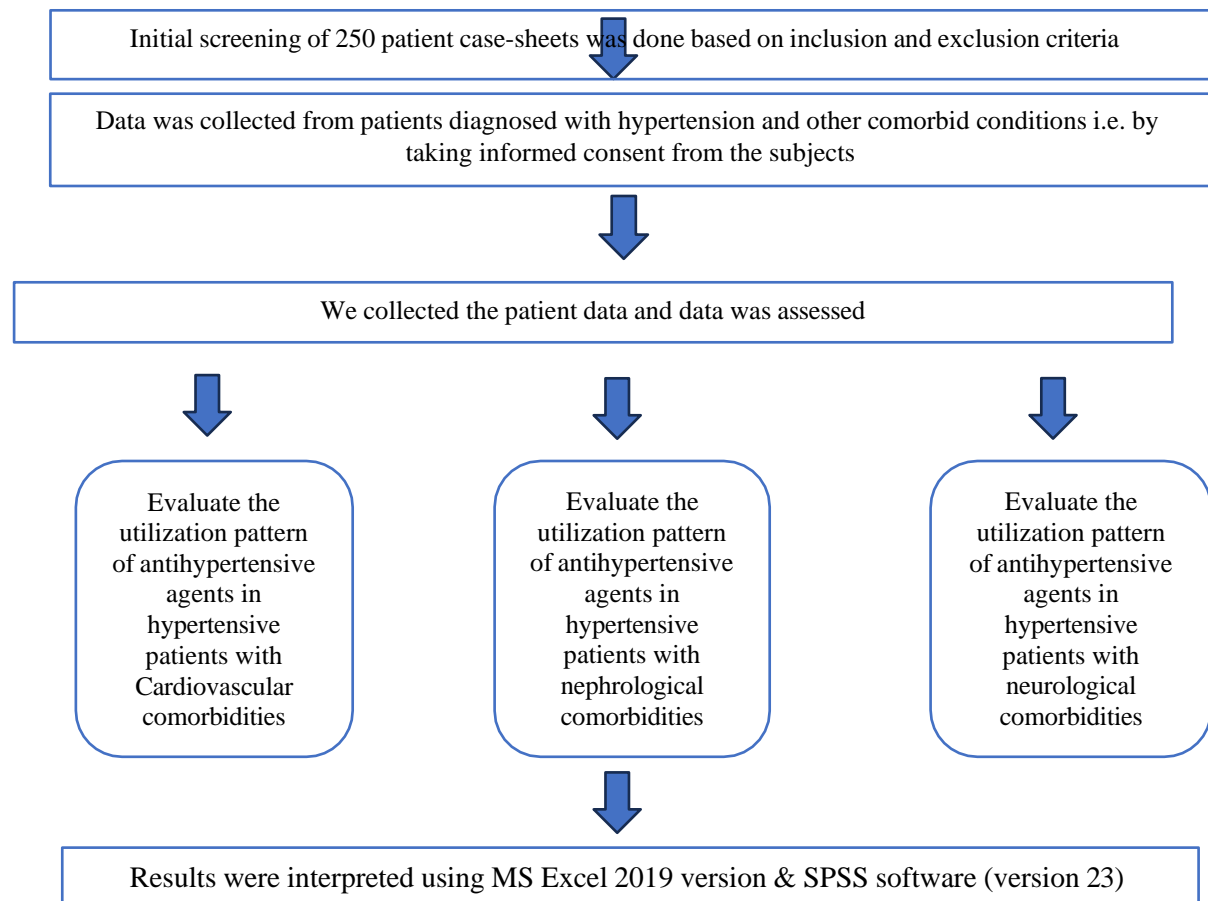
Study period: The study was conducted for a period of 6 months.

INCLUSION CRITERIA

- Patients who are willing to participate in the study with age >18 years of either gender were included.
- Only those patients who are diagnosed with Hypertension and other comorbidities are recruited.

EXCLUSION CRITERIA

- Patients who are not willing to participate in the study
 - Pregnancy and lactating women are excluded
 - Cancer patients are excluded
 - <18 years old patients are excluded
- METHODOLOGY FLOWCHART:



Algorithm 3: Methodolgy flow chart

RESULTS & DISCUSSION

***Data organized using MS Excel 2019 version and represented through bar charts and pie charts*

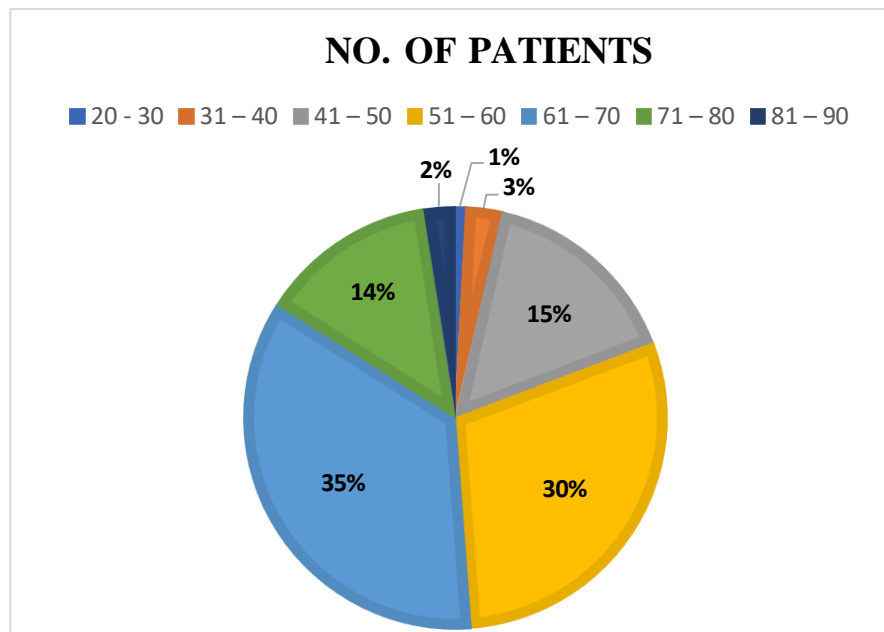
1) AGE:

In the present observed study, a total of 250 patient cases were screened, in which patients were divided into 7 groups depending on the ages, i.e., 20 - 30, 31 - 40, 41-50, 51- 60, 61- 70, 71-80, 81-90 & ≥ 90 years. The age group of the patients varies from 20 to 90 years. The majority of patients lie in the age range of 61-70 years (35%) followed by 51-60 years (30%) (Graph 1).

Age (years)	No. of patients
20 - 30	2
31 - 40	7
41 - 50	39
51 - 60	74
61 - 70	88
71 - 80	34
81 - 90	6
Total	250

Table 3: Demographic representation of Age of the patients

Graph 1: Percentage distribution of patients as per their age group

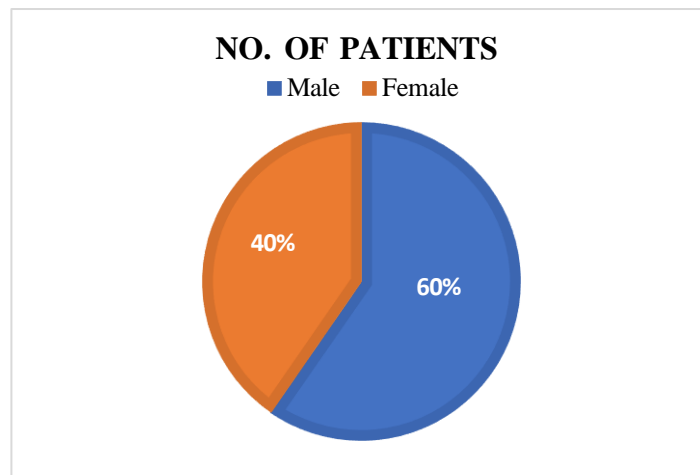


2) GENDER:

In the present observed study, a total of 250 patient cases were screened, of which 149 were male and 101 were female. Male patients were slightly higher than female patients with a difference of 20% (Graph 2)

Gender	No. of patients
Male	149
Female	101
Total	250

Table 4: Demographic representation of Gender of the patients

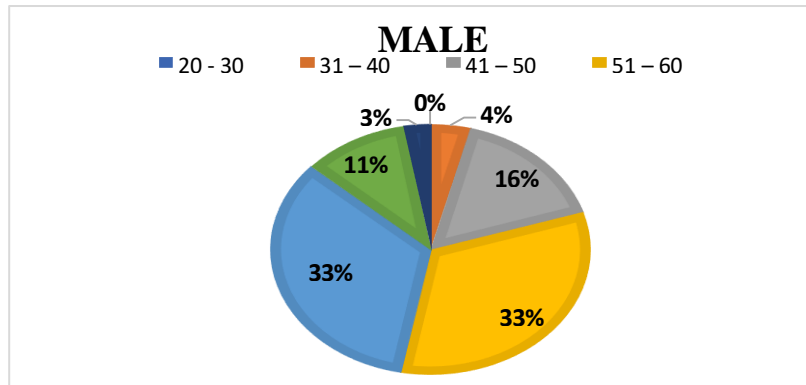


Graph 2: Percentage distribution of patients as per their gender

a) **Male patients:** As stated above we categorized the patients in 7 different age groups and considered both genders. Among 250 patients, 149 were male patients where we observe greater incidence of 33% involving 50 patients & 49 patients in both age groups of 51-60 years, 61-70 years followed by incidence of 16% & 11% in age groups of 41-50 years & 71-80 years respectively.

Age (years)	Male
20 - 30	0
31 - 40	6
41 - 50	24
51 - 60	49
61 - 70	50
71 - 80	16
81 - 90	4
Total	149

Table 5: Demographic representation of Male patients

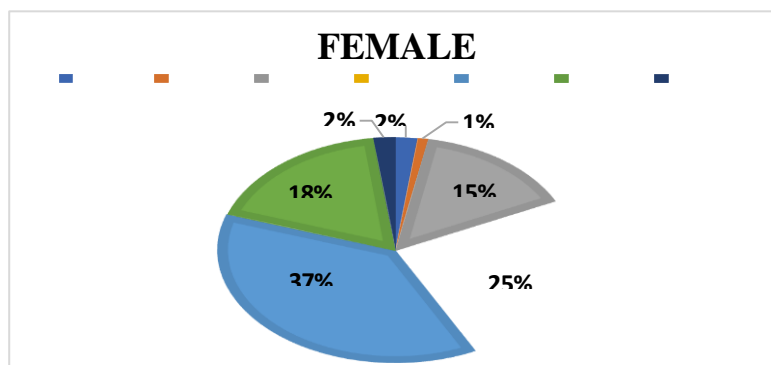


Graph 4: Percentage distribution of Male patients

b) **Female patients:** As stated above we categorized the patients in 7 different age groups and considered both genders. Among 250 patients, 101 were female patients where we observe greater incidence of 37% & 25% involving 38 patients & 25 patients in both age groups of 61-70 years, 51-60 years followed by incidence of 18% & 15% in age groups of 71-80 years & 41-50 years respectively.

Age (years)	Female
20 - 30	2
31 - 40	1
41 - 50	15
51 - 60	25
61 - 70	38
71 - 80	18
81 - 90	2
Total	101

Table 6: Demographic representation of Female patients



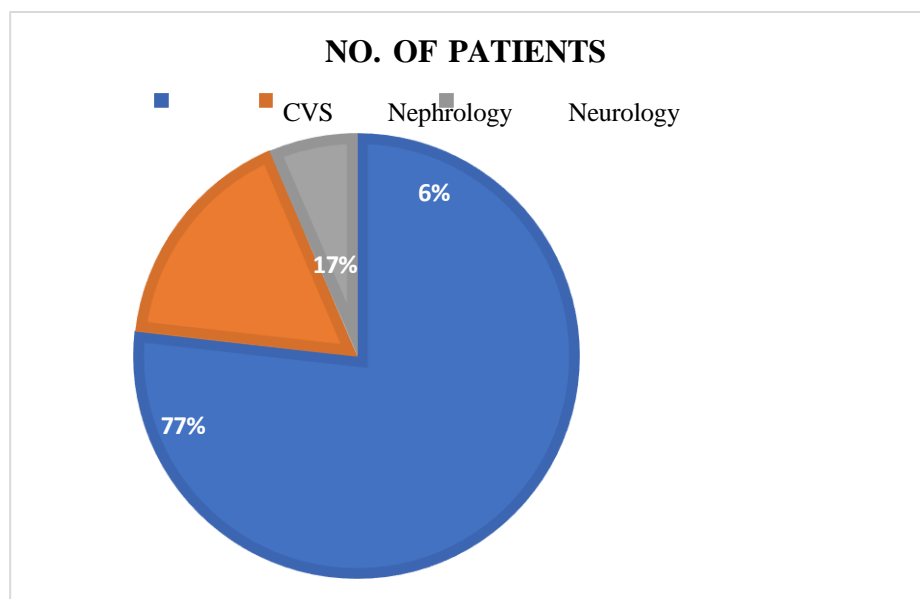
Graph 5: Percentage distribution of Female patients

3) OVERALL PATIENT COMORBIDITY DATA:

This study reveals that there were 250 patients with comorbidities. Out of 250, 192 patients were having CVS comorbidities (77%), 42 with Nephrology comorbidities (17%), 16 with Neurology comorbidities (6%).

Comorbidities	No. of patients
CVS	192
Nephrology	42
Neurology	16
TOTAL	250

Table 7: Distribution of number of patients with various comorbidities



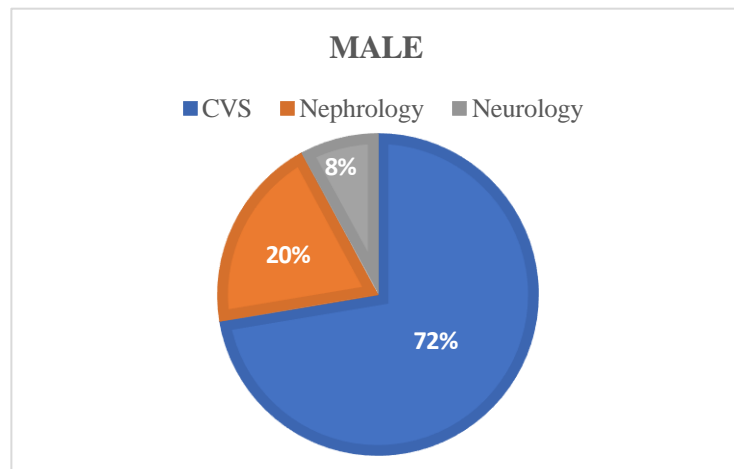
Graph 6: Graphical representation of number of patients with various comorbidities

A) Comorbidities – Gender:

Out of 250 patients, 110 male patients & 82 female were having Cardiovascular comorbidities, 30 male patients & 12 female patients were having Nephrological comorbidity, 12 male patients & 7 female patients were having Neurological comorbidity.

Comorbidities	Male	Female
CVS	110	82
Nephrology	30	12
Neurology	12	7

Table 8: Distribution of number of patients with various comorbidities based on gender



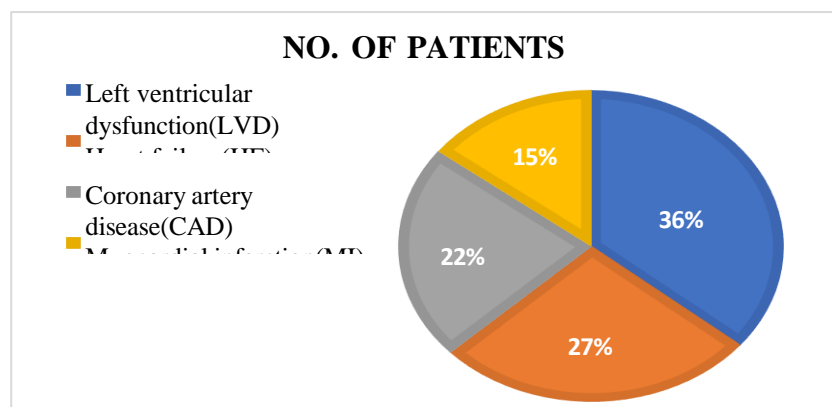
Graph 7: Graphical representation of number of patients with various comorbidities based on gender

B) Patients with various cardiovascular comorbidities:

As we have already stated that there were 192 patients with cardiovascular comorbid conditions. Out of 192, 69 patients were having Left ventricular dysfunction (36%), 52 patients were having heart failure(27%) followed by 43 patients with coronary artery disease(22%) and 28 patients with myocardial infarction(15%).

CVS condition	No. of patients
Left ventricular dysfunction(LVD)	69
Heart failure(HF)	52
Coronary artery disease(CAD)	43
Myocardial infarction(MI)	28
Total	192

Table 9: Distribution of number of patients with various cardiovascular comorbidities



Graph 8: Graphical representation of number of patients with various cardiovascular comorbidities

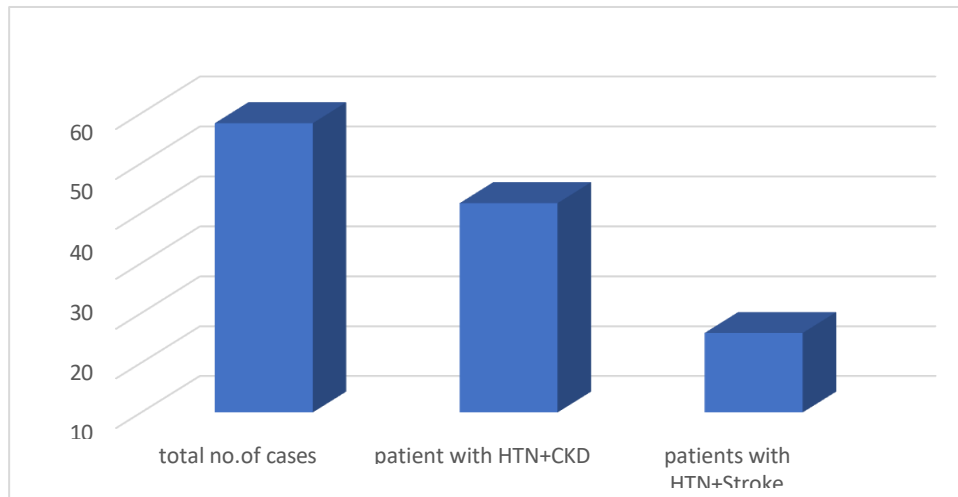
C) Patients with various nephrological and neurological comorbidities:

As we have already stated that there were 42 patients with nephrological comorbidities and 16 patients with neurological comorbidities. Out of 42 nephrology patients, all of them were diagnosed with chronic kidney

disease (100%) while in neurology patients, 16 patients were diagnosed with stroke.

Comorbid condition	No. of patients
CKD	42
Stroke	16
Total	58

Table 10: Distribution of number of patients with nephrological & neurological comorbidities



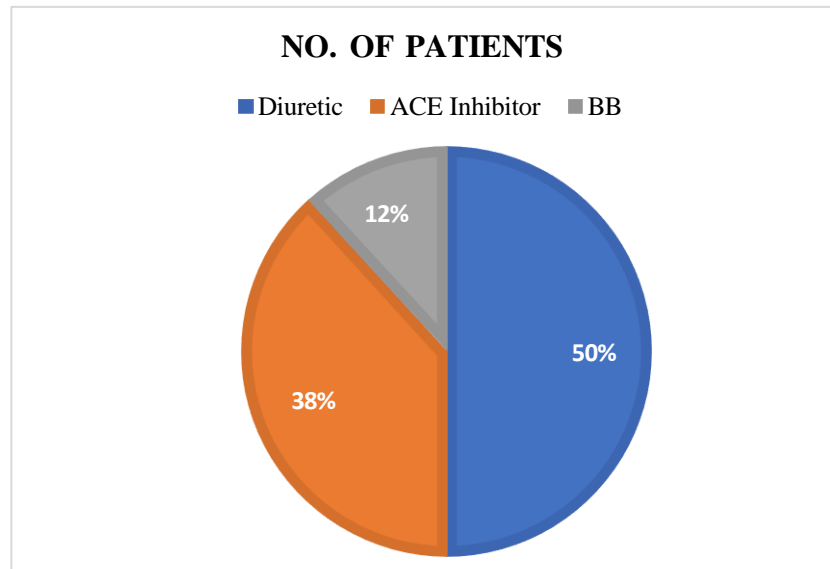
Graph 9: Graphical representation of number of patients with nephrological & neurological comorbidities

D) Antihypertensive therapy for patients with hypertension (HTN) & left ventricular dysfunction (LVD):

In our observed study of 250 patients, 69 patients were diagnosed with left ventricular dysfunction. Out of 69 patients, 19 were prescribed with Diuretics (50%), 26 with ACE inhibitors (38%) followed by 8 with Beta blockers (12%).

Antihypertensive therapy for patients with HTN + LVD	No. of patients
Diuretic	34
ACE Inhibitor	26
BB	8

Table 12: Distribution of number of patients based on type of antihypertensive therapy prescribed in patients with HTN & LVD



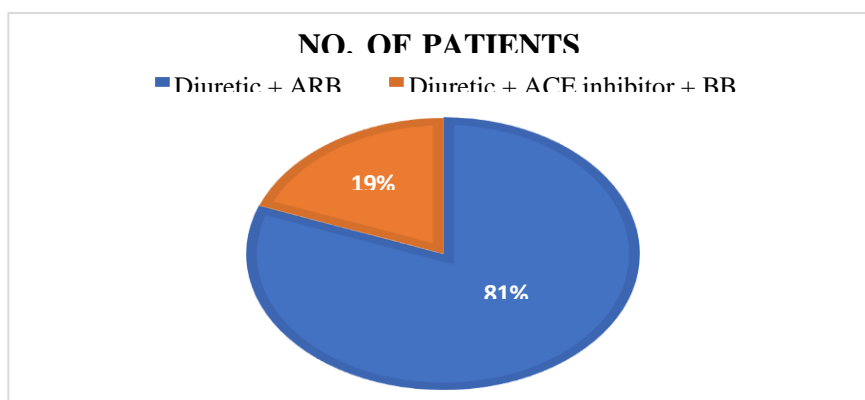
Graph 11: Percentage representation of drug class prescribed in number of patients having HTN + LVD

D) Antihypertensive therapy for patients with hypertension (HTN) & heart failure (HF):

In our observed study of 250 patients, 52 patients were diagnosed with heart failure. Out of 52 patients, 42 were prescribed with Diuretic + Angiotensin-II receptor blocker (81%), 10 with Diuretic + ACE inhibitor + Beta blocker (19%).

Antihypertensive therapy for patients with HTN + HF	No. of patients
Diuretic + ARB	42
Diuretic + ACE inhibitor + BB	10

Table 13: Distribution of number of patients based on type of antihypertensive therapy prescribed in patients with HTN & HF



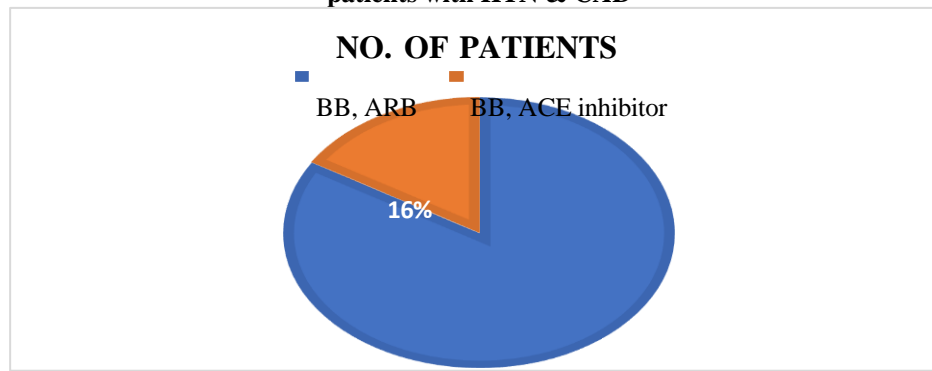
Graph 12: Percentage representation of drug class prescribed in number of patients having HTN + HF

E) Antihypertensive therapy for patients with hypertension (HTN) & coronary artery disease (CAD):

In our observed study of 250 patients, 43 patients were diagnosed with coronary artery disease. Out of 43 patients, 36 were prescribed with Beta blocker & Angiotensin-II receptor blocker (84%), 7 with Betablocker & ACE inhibitor (16%)

Antihypertensive therapy for patients with HTN + CAD No. of patients	
BB, ARB	36
BB, ACE inhibitor	7

Table 14: Distribution of number of patients based on type of antihypertensive therapy prescribed in patients with HTN & CAD



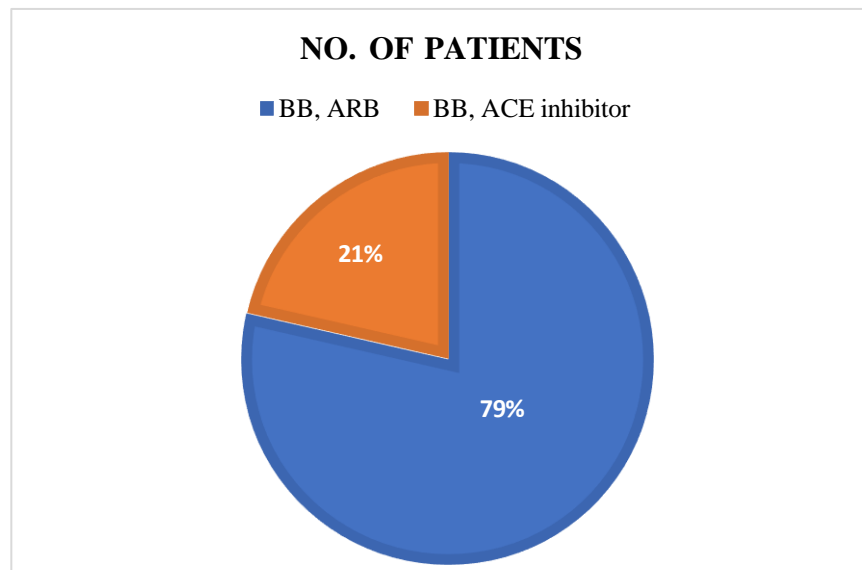
Graph 13: Percentage representation of drug class prescribed in number of patients having HTN + CAD

F) Antihypertensive therapy for patients with hypertension (HTN) & myocardial infarction (MI):

In our observed study of 250 patients, 28 patients were diagnosed with myocardial infarction. Out of 28 patients, 22 were prescribed with Beta blocker & Angiotensin-II receptor blocker (79%), 6 with Beta blocker & ACE inhibitor (21%)

Antihypertensive therapy for patients with HTN + MI	No. of patients
BB, ARB	22
BB, ACE inhibitor	6

Table 15: Distribution of number of patients based on type of antihypertensive therapy prescribed in patients with HTN & MI



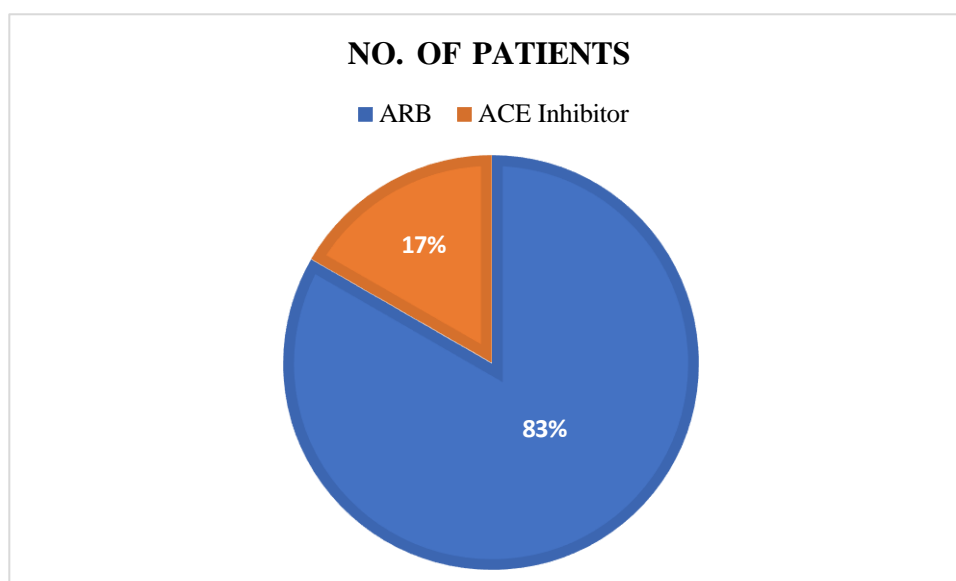
Graph 14: Percentage representation of drug class prescribed in number of patients having HTN + MI

G) Antihypertensive therapy for patients with hypertension (HTN) & chronic kidney disease (CKD):

In our observed study of 250 patients, 42 patients were diagnosed with chronic kidney disease. Out of 42 patients, 35 were prescribed with Angiotensin-II receptor blocker (79%), 7 with ACE inhibitor (21%)

Antihypertensive therapy for patients with HTN + CKD	No. of patients
ARB	35
ACE Inhibitor	7

Table 16: Distribution of number of patients based on type of antihypertensive therapy prescribed in patients with HTN & CKD



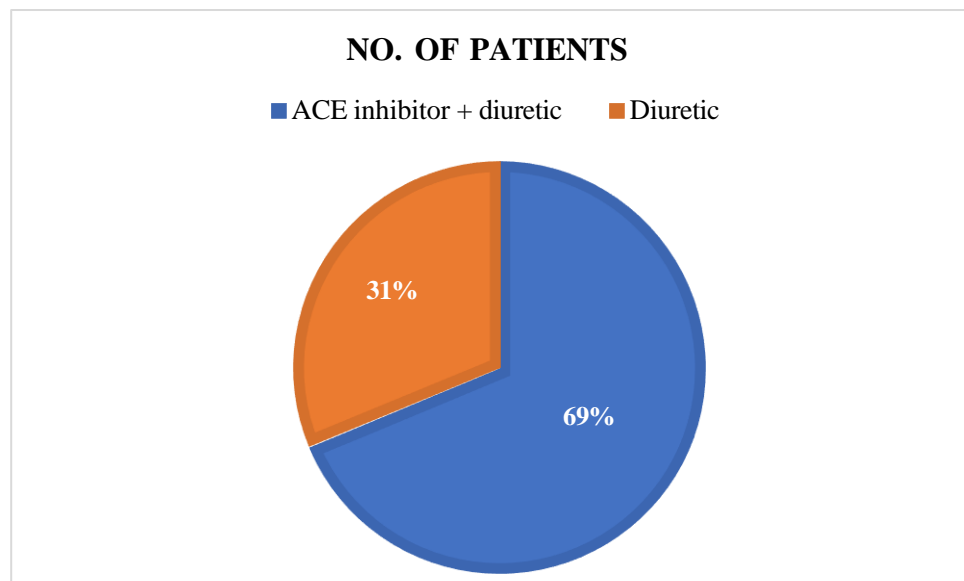
Graph 15: Percentage representation of drug class prescribed in number of patients having HTN + MI

H) Antihypertensive therapy for patients with hypertension & stroke:

In our observed study of 250 patients, 16 patients were diagnosed with stroke. Out of 16 patients, 11 were prescribed with ACE inhibitor + Diuretic (69%), 5 with Diuretic (31%)

Antihypertensive therapy for patients with HTN + Stroke	No. of patients
ACE inhibitor + diuretic	11
Diuretic	5

Table 17: Distribution of number of patients based on type of antihypertensive therapy prescribed in patients with HTN & CKD



Graph 16: Percentage representation of drug class prescribed in number of patients having HTN + Stroke
STATISTICAL ANALYSIS (SPSS SOFTWARE – Version 23)

• DESCRIPTIVE ANALYSIS

. Using SPSS software, we had conducted the descriptive Statistical Analysis for gender and comorbidities.

1. Gender

Male had shown greater percent (59.6%) when compared to female (40.4%) among the total population involved in the study.

Male population had shown mean of 126.05 with standard error (SE) of 5.862 followed by standard deviation 71.549 while female population had shown mean of 124.69 with standard error (SE) of 7.341 followed by standard deviation 73.777 respectively.

Gender					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	149	59.6	59.6	59.6

	Female	101	40.4	40.4	100.0
	Total	250	100.0	100.0	

Table 12: Gender frequencies

Descriptive					
	Gender	N	Mean	Std. Deviation	Std. Error Mean
No. of patients	male	149	126.05	71.549	5.862
	female	101	124.69	73.777	7.341

Table 13: Descriptive analysis of gender

T-TEST

1. Comorbidities – gender:

Hypothesis:

H₀: There is no significant difference in comorbidities between male and female patients

H₁: There is a significance difference in comorbidities between male and female patients

T-Test: Two-Sample Assuming Unequal Variances		
	<i>MALE</i>	<i>FEMALE</i>
Mean	50.66666667	33.66666667
Variance	2721.333333	1758.333333
Observations	3	3
Hypothesized Mean Difference	51	
df	4	
t Stat	-0.879866322	
P(T<=t) one-tail	0.214309137	
t Critical one-tail	2.131846786	
P(T<=t) two-tail	0.428618273	
t Critical two-tail	2.776445105	

Interpretation: At α 0.05 and table t-value 0.4, the calculated t value is more than table t- value (0.4), hence we accept alternative hypothesis and reject null hypothesis.

As observed in the above table, there is a significant difference in the mean between male and female patients and that coincides with our interpretation.

Therefore our data is significant

CONCLUSION:

The current study aimed at studying current prescribing trends for antihypertensives among hypertensive patients with various comorbidities. The observed study found that majority of patients having hypertension with comorbidities were of 61 to 70 age group followed by 51-60 age group and male patients were found to be 2/3rd than females. Out of 250 patients involved in our study, 192 patients were having Cardiovascular comorbidities, 42 with Nephrological comorbidities, 16 with Neurological comorbidities.

Among CVS comorbidities, 69 patients were diagnosed with Left ventricular dysfunction, followed by 52 with Heart failure, 43 with Coronary artery disease, and 28 with Myocardial infarction. The drug utilization pattern of antihypertensive agents in Hypertensive patients with Left ventricular dysfunction (LVD) was diuretics followed by ACE inhibitor, While in Heart failure (HF), it was Angiotensin-II receptor blockers + Diuretics (81%), in Coronary artery disease(CAD) was Beta blocker & Angiotensin-II receptor blockers, in Myocardial infarction(MI) was Angiotensin-II receptor blockers + Betablockers.

Among 42 patients with Nephrological comorbidities, 42 patients were diagnosed with chronic kidney disease (CKD). The drug utilization pattern of antihypertensive agents in Hypertensive patients with CKD was Angiotensin-II receptor blockers.

Among 16 patients with Neurological comorbidities, 16 patients were diagnosed with Stroke. The drug utilization pattern of antihypertensive agents in Hypertensive patients with Stroke was Angiotensin converting enzyme inhibitors + Diuretics, followed by Diuretics.

After complete analysis of the study, we found that the prescription pattern of antihypertensive classes of drugs for hypertensive patients with various comorbid conditions was found to be considerably in adherence to JNC 8 guidelines for the management of hypertension. Hence, this complete observed study brings a complete knowledge on current prescribing patterns of antihypertensive drug therapy in Hypertensive patients with comorbidities which further helps in improvising the patterns of drug therapy, determine better choice of drug, and a knowledge to continue further clinical researches. This study also suggests the role of clinical pharmacist in better understanding of the effectiveness of a drug therapy based on DUE program in order to promote rational use of drugs and provide better clinical care.

Acknowledgments

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Conflict of interest

Nil

Ethics committee

The institutional Ethics committee GVPIHCMT had approved for project title —Study of prescribing patterns of anti- hypertensive agents in hypertensive patients with Co-morbid conditions at a tertiary care teaching hospital Approval Number: GVIHCMT/ICE/20221003/01

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