

# CLINICAL PHARMACY ACTIVITIES IMPACTING CONTEMPORARY PRESCRIPTION PATTERN OF ANTIHYPERTENSIVE DRUGS AND ITS COMPELLING INDICATIONS IN A TERTIARY CARE TEACHING HOSPITAL

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## ABSTRACT:

Hypertension has been recognized as a common cardiovascular disease & a major risk factor for congestive heart failure, ischemic heart disease, chronic renal failure & stroke. The aim of the study is to observe the impact of clinical pharmacy activities on contemporary prescription pattern of antihypertensive drugs and its compelling indications in a tertiary care teaching hospital. This prospective, study was conducted by reviewing and collecting the data of patients who were diagnosed with Hypertension and admitted in the hospital. Patient demographic details such as name, age, sex was collected. In present study we found 387 drug drug interactions in prescriptions of 450 hypertension patients. However there is a need for improve patient education on adherence to therapy and greater attention by clinicians to issues of life style modifications, so as to improve BP control rate in this hospital.

**Keywords:** *Clinical pharmacy, Prescription pattern, Antihypertensive drugs, Tertiary care teaching hospital*

## INTRODUCTION

Hypertension is a elevated BP and perfuse to tissues & organs. Elevated blood pressure means systolic BP greater or equal to 140 mmHg & diastolic blood pressure greater or equal to 90 mmHg ( $\geq 140/90$  mmHg) Hypertension has been recognized as a common cardiovascular disease & a major risk factor for congestive heart failure, ischemic heart disease, chronic renal failure & stroke<sup>1</sup>.

The general objective is to study prescription pattern of antihypertensive drugs in a tertiary care hospital. A specific objective is to assess the rationality of antihypertensive drugs in hypertensive patients, to provide the clinical pharmacy activities for anti-hypertensive patients such as drug interaction, ADR's, medication errors, patient counselling, medication history interview, other specific objectives are to study the efficacy of antihypertensive drugs and to study the comparison of efficacy between mono and combinational therapy.

### **MATERIAL AND METHODOLOGY**

**Study site:** This study conducted in general medicine department at a tertiary care hospital

**Study design:** Prospective Observational study,

**Study period:** The study carried out for a period of 2 years from June 2016 to April 2018.

#### **Study criteria**

**Inclusion criteria:** Inpatients of either gender aged  $\geq 18$  years who have been diagnosed with primary and secondary hypertension, and Patients who were receiving anti-hypertensive drugs.

**Exclusion criteria:** Patients attending outpatient department, Pregnant women, children below 18 years

**Source of data:** The data for this study was obtained by interviewing patients for their demographic details, past medical history, past medication history, patient case notes, treatment chart, laboratory reports and discharge cards.

**Study method:** This is a prospective, longitudinal study was conducted in the general medicine department at a tertiary care hospital on assessment of prescribing patterns on antihypertensive drugs. The data was obtained by reviewing and collecting the case sheets of patients who were diagnosed with Hypertension and admitted in the hospital. Common and uncommon signs and symptoms observed in patients were noted. Past medical history of patients as well as family was noted. Past medication history of patients was documented. Smoking, drinking and other social habits of the patients were noted in patient profile form. Therapeutic data such as name of drug, dose, frequency and duration of therapy was collected from treatment chart of patients. Drug interactions in treatment regimen of patients were assessed using drug data base Micromedex 2.0 and the interactions found were documented in the drug-drug interaction form, any interventions made during the study time were documented using intervention reporting forms, follow up of all patients were done until discharge from the hospital. The assessment of the patient data was analyzed as per the guidelines of JNC 7 and IGH-II. The inpatient data was collected and created separately in computer-based formats, stored and retrieved whenever required in MS office assess format.

**Statistical analysis:** Data analysis was done using the statistical software Graphpad Prism Version 5. Continuous data are presented as mean  $\pm$  SEM, while categorical data was presented as percentages. Differences between means of two groups were compared using unpaired student's *t* test. A *p*-value less than 0.05 were considered as statistically significant.

### **RESULTS:**

#### **Age group and gender wise categorization of hypertensive patients**

In the present gender wise categorization was estimated. A total of 450 patients were included in the study. Among 450 patients, 265 (58.88%) were male and 185 (41.11%) were female. Majority 123 (27.33%) were 70 years & above age group, followed by 119 (26.44%) were 60-

69years, followed by 102 (22.66%) 50-59years, followed by 80 (17.77%) were 40-49years, followed by 24 (5.33%) 30-39years, followed by 2 (0.44%) were 20-29years of age group patients. (fig 1 & 2).

### **Percentage of Co-morbidities in Antihypertensive patients.**

Among the study population 450 in-patients presented . 213 (53.77%) were found with one co-morbidity, 155(34.44%) were two co-morbidity, 60(13.33%) were three co-morbidity, 29 (6.44%) of presented with > four co-morbidity and 03 (0.66%) mortality was found. The average co-morbidity observed in the study patient population.(fig 3)

### **Class of anti-hypertensive drugs prescribed for hypertensive patients**

Eight different class of antihypertensive drugs were prescribed in the present study. The most prescribed drugs were 187(29.21%) for hypertensive patients followed by,  $\beta$  blockers 129 (20.15%), followed by calcium channel blockers 128 (20%) angiotensin receptor blockers 97 (15.15%), ACE inhibitors 67(10.46%),  $\alpha$  blockers 12 (1.87), centrally acting drugs 13 (2.88) and  $\alpha+\beta$  blockers 10 (1.56) were prescribed.(fig 4).

### **Pattern of drug regimen prescribed for hypertensive patients:**

Out of 450 patients mono drug regimen were prescribed in more than 193 (42.88%) hypertensive patients followed by two drug regimen in 173 (38.44%) patients. three drug regimens in 68 (15.11%) patient, and  $\geq 4$  drug combination 16(3.55%) prescriptions.( fig 5). out of 193 mono drug regimen Amlodipine were prescribed more 80 (17.77%) followed by furosemide 47 (10%) followed by ramipril 12 (2.66%) followed by metoprolol 10(2.22%), followed by nebivolol 07(1.55%) followed by telmisartan, propranolol,atenolol each 5 (1.11%) prescriptions followed by hydrochlorthiazide 4 (0.88%) followed by olmesartan ,enalapril 02 (0.44%) and clinidipine ,carvedilol each 01 (0.22%) prescriptions.(fig 6). 173 two drug regimen were prescribed .majority are amlodipine+atenolol 65(14.44%) were found amlodipine+hydrochlorthiazide 40(8.88%) torsemide+sporanolactone 10(2.22%) furosemide+spiranolactone 07(1.55%) amlodipine+furosemide, furosemide + losartan 05(1.11%) losartan+hydrochlorthiazide, losartan+ramipril 04(0.88%) followed by amlodipine+losartan 03(0.66%) and very less ramipril+torsemide, furosemide+telmisartan, amlodipine+metoprolol, telmisartan+amlodipine 02(0.44%) prescriptions were found.(fig 7).68 prescriptions were found as three drug regimen of antihypertensive drugs majority are amlodipine+atenolol+furosemide 20(4.44%)and very less prescriptions were found amlodipine+metoprolol+hydrochlorthiazide 02(0.44%)16 prescriptions were found as  $\geq 4$  drug regimen of antihypertensive drugs majority are furosemide+amlodipine+losartan+hydrochlorthiazide 06(1.33%) followed by bisoprolol+amlodipine+torsemide+spiranolactone 04(0.88%) followed by furosemide+clonidine+amlodipine+atenolol 03(0.66%) followed by amlodipine+atenolol+furosemide+losartan+hydrochlorthiazide 02(0.44%) and amlodipine+atenolol+furosemide+prazosin 01(0.22%) were found. The results were shown in fig 8

### Assessment of Drug-Drug Interactions in anti-hypertensive prescriptions

During the study total 395 DDI's were found. Out of these 137 (30.44%) were major, 255 (56.66%) were moderate drug interactions, and 7 (1.55%) were minor drug interactions. major DDI's 85 were of Aspirin + clopidogrel and 13 DDI's were insulin + moxifloxacin, 9 DDI's were amlodipine + clopidogrel. In 255 moderate interactions majority interactions 12 DDI's were of Aspirin + ramipril and followed by 6 DDI's between diclofenac + losartan. (fig 9 & 10).

### Assessment of rationality of antihypertensive drug prescribed for patients

Rationality of prescriptions were assessed by using JNC 7 guidelines out of 450 patients 427 (94.88%) patients were prescribed antihypertensive drugs rationally and remaining 23 (5.11%) patients were prescribed antihypertensive drugs irrationally. (fig 11).

### Efficacy of antihypertensive agents on hypertension patients

In the present study various types of antihypertensive drugs were prescribed to patients to reduce SBP & DBP. Out of which Amlodipine significantly reduced DBP ( $p=0.216$ ), Furosemide reduced SBP significantly ( $p=0.0034$ ) and there was significant reduction were found in SBP ( $P=0.0034$ ) on discharge when compared with respective BP on admission.

In combination therapy Amlodipine + metoprolol showed significant reduction in SBP ( $p=0.034$ ) and DBP ( $p=0.144$ ) on discharge day when compared with BP on admission respectively and other combinations like Amlodipine + ramipril show reduced SBP ( $p=0.6253$ ) significantly as compared with SBP on admission. The results are shown in table 1, 2 & 3.

### Comparison of efficacy between mono and combination therapy

In the present study we had chosen 4 drug and their combinations to compare the efficacy of drugs. mean reduction in SBP increased significantly ( $p=0.018$ ) in patients prescribed. Amlodipine and Atenolol combination when compared with mean reduction in SBP of only Amlodipine treated patients. Likewise, Table 7b reveals mean reduction in SBP increased significantly ( $p=0.451$ ) in Furosemide and Losartan received patients as compared with Furosemide alone treated and there is significant increase in mean reduction in DBP in patients treated with combination of Furosemide and Losartan as compared with Furosemide alone remaining combinations doesn't show any significant difference. The results are shown in table 4, 5, 6 & 7.

### Clinical Pharmacy Services in Hypertensive Patients at A Tertiary Care Hospital:

clinical pharmacy services were provided in hypertension patients admitted in a tertiary care hospital. out of 450 patients 387 (27.77%) drug drug interactions (major+moderate), 300 (66.66%) patient counseling were provided, 02 (0.44%) adverse drug reactions were found, and 24 (5.33%) medication errors were found in patients admitted in a tertiary care hospital. (fig 12).

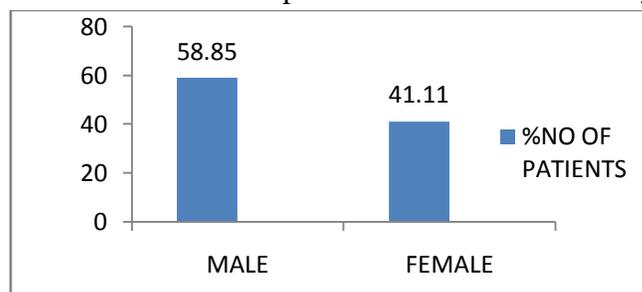


Figure 1: According to Gender Wise Distribution:

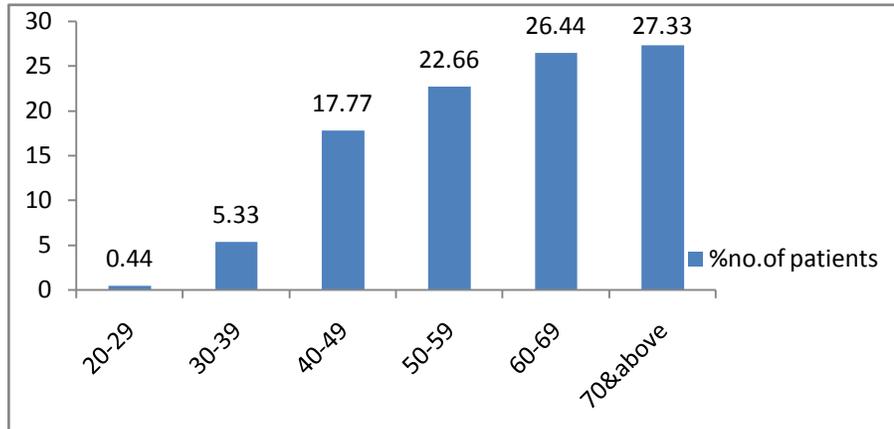


Figure 2: Age Wise Distribution

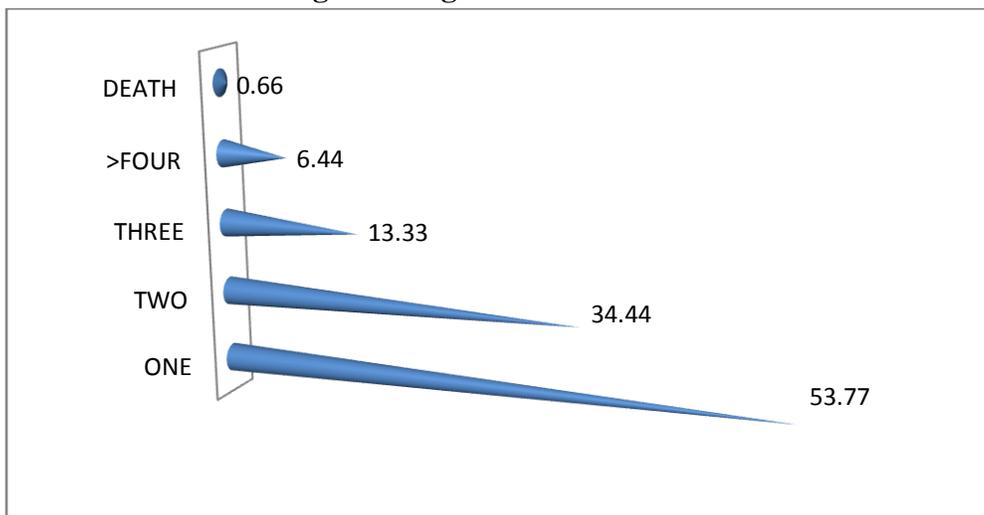


Figure 3:Percentage of Co-morbidities in Antihypertensive in-patients at tertiary care hospital

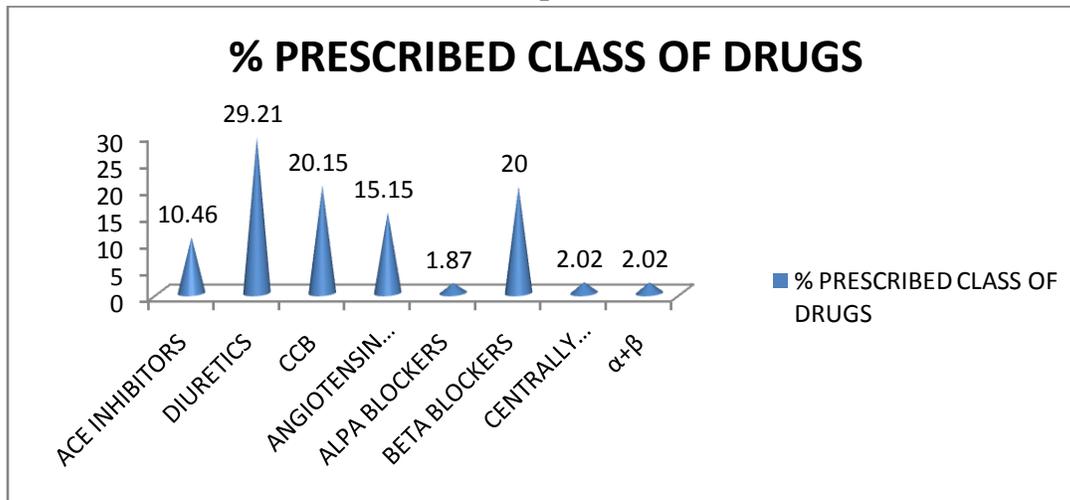


Figure 4:Percentage Classof Antihypertensive Drugs Prescribed for Hypertension Patients

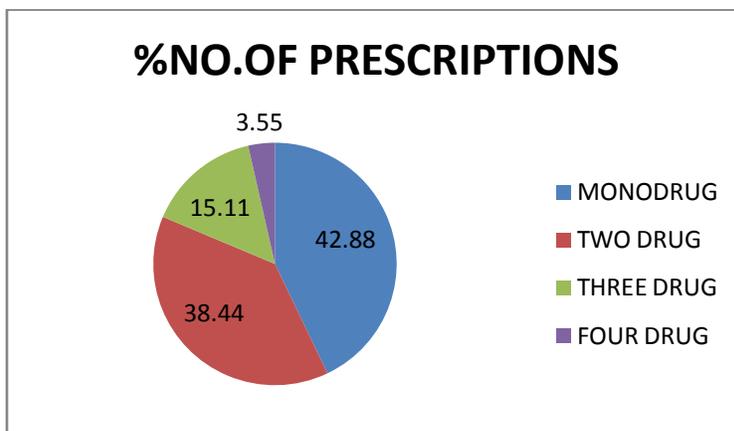


Figure 5: Percentage Pattern of drug regimen prescribed for hypertensive patients

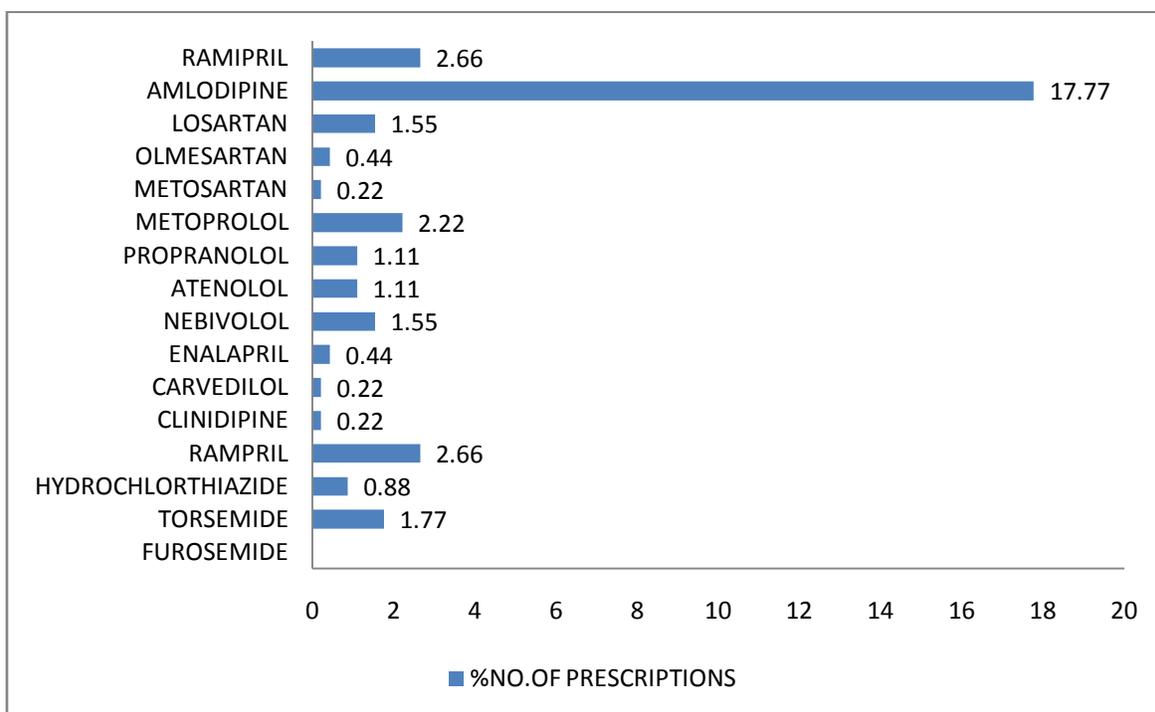
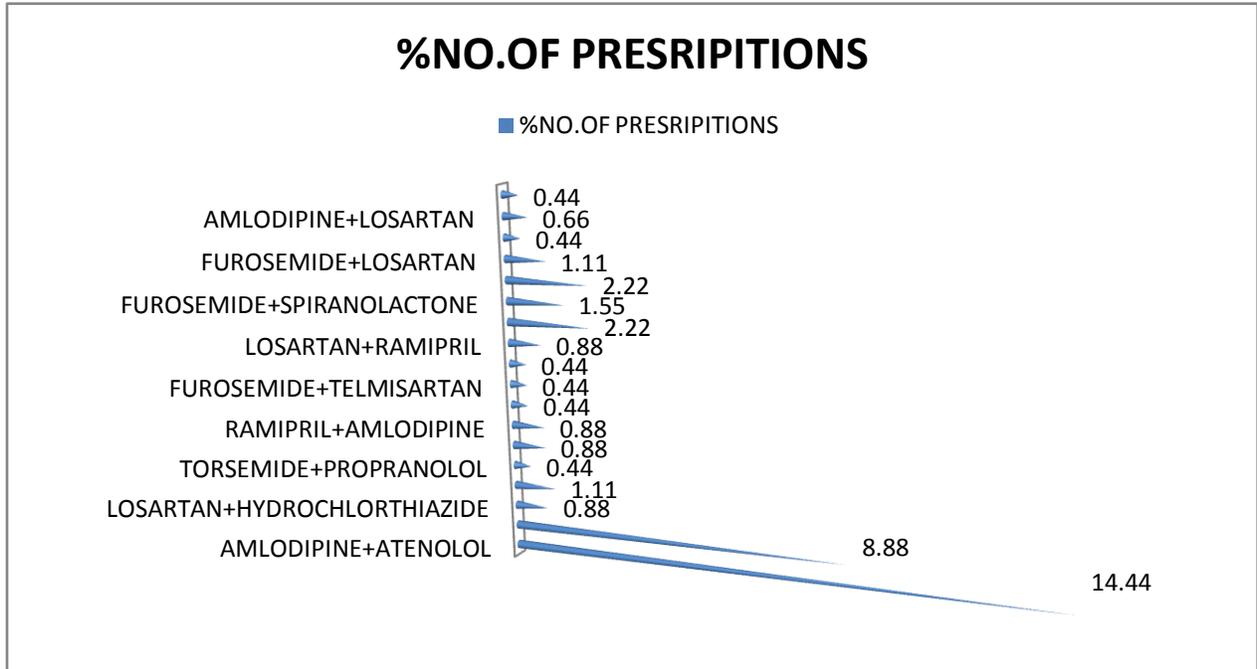
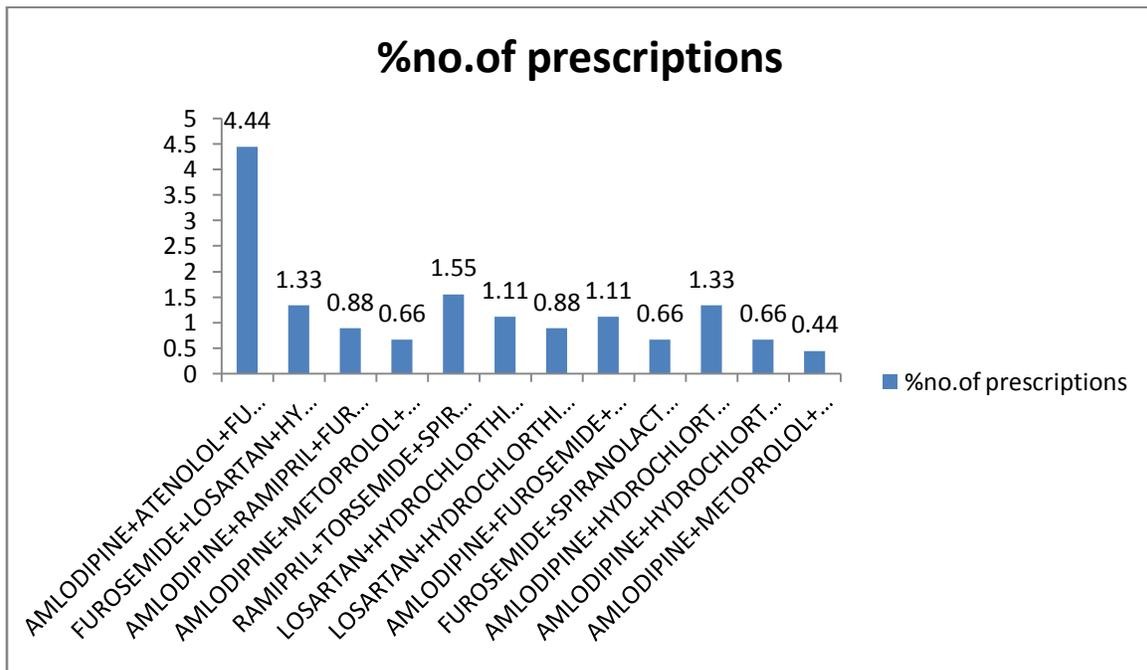


Figure 6: percentage of mono drug regimen prescribed for hypertensive patients



**Figure 7: Two Drug Regimen Prescribed for Hypertensive Patients**



**Figure 8: Three Drug Regimen Prescribed for Hypertensive Patients**

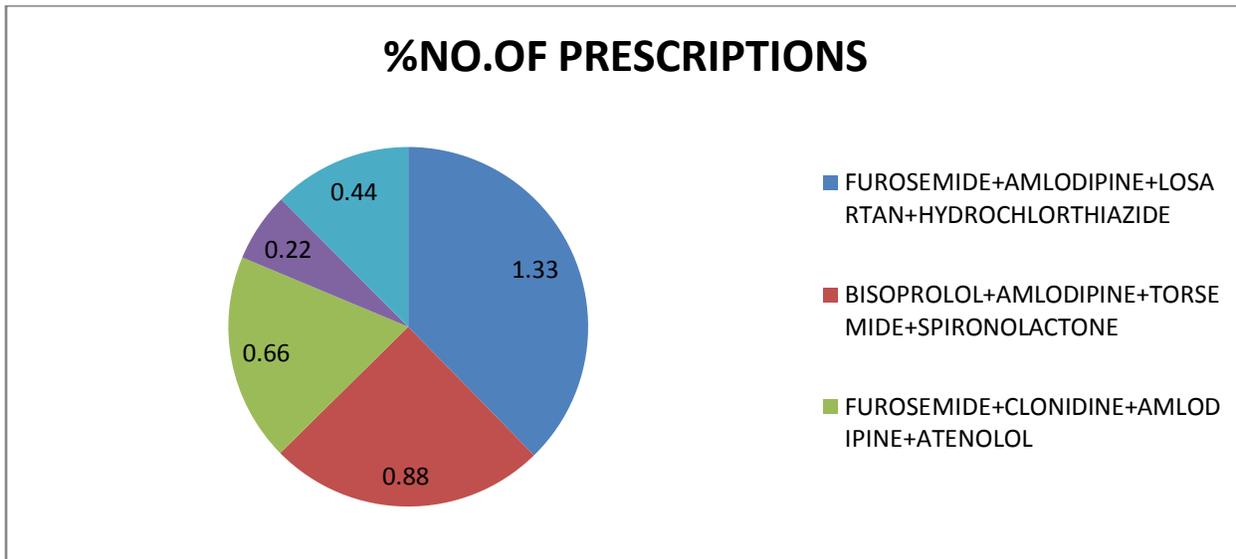


Figure 9:four Drug Regimen Prescribed for Hypertensive Patients

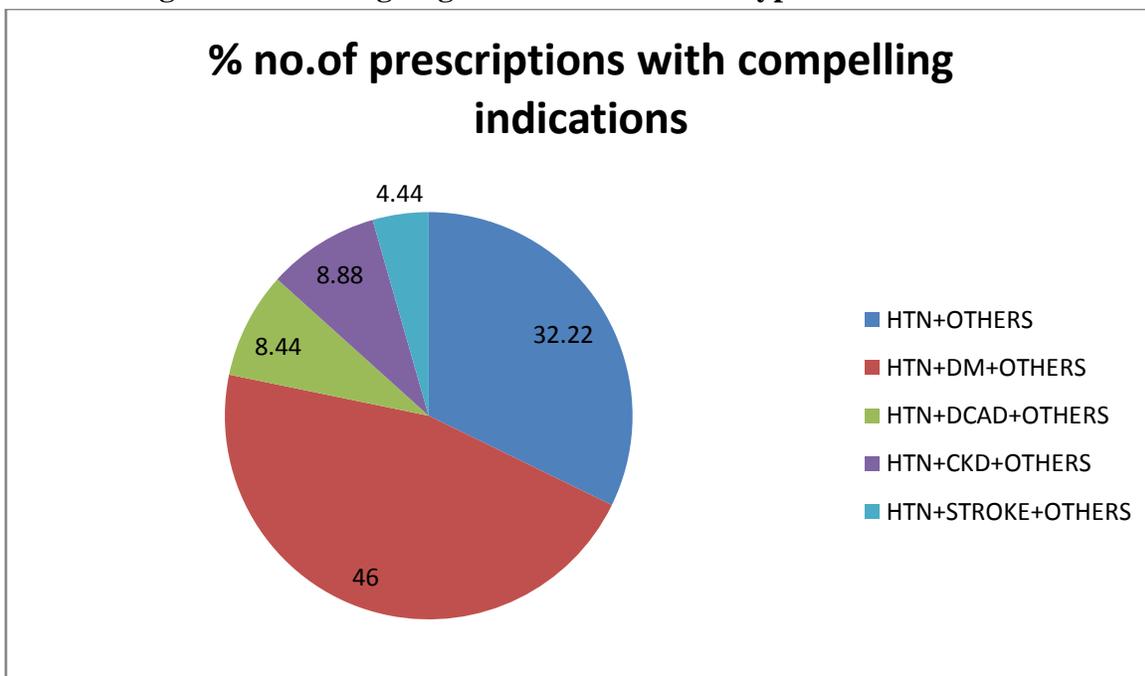
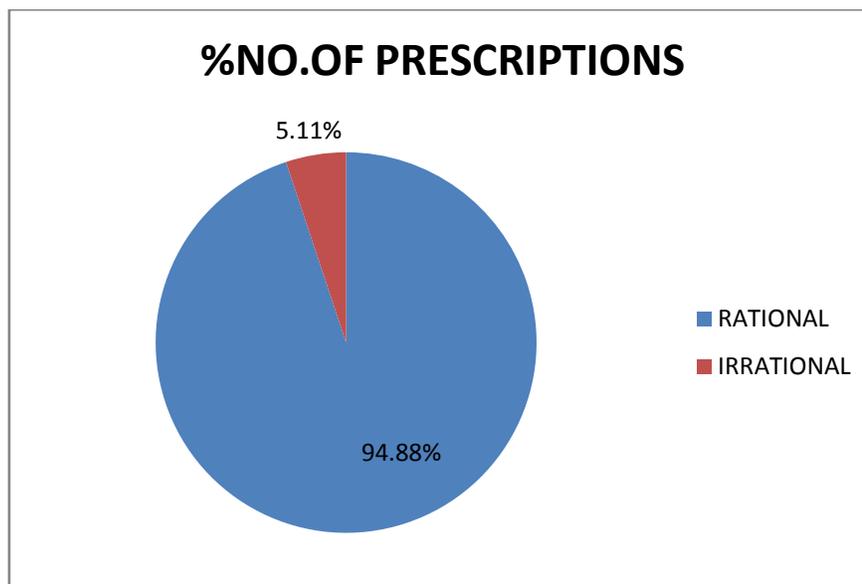


Figure 10: Number of prescriptions with compelling indications



**Figure 11: Rationality of antihypertensive drug prescribed for patients**

**Table 1: Efficacy of Monotherapy Antihypertensive Drugs in Patients in A Tertiary Care Hospital:**

BLOOD PRESSURE MEAN±SEM	ON ADMISSION	ON DISCHARGE	P-VALUE	T-VALUE
<b>ATENOLOL</b>				
SBP	152±6.268	130±2.981	0.116	<b>2.561</b>
DBP	86.75±5.126	80.26±2.45	0.0138	<b>2.135</b>
<b>METOPROLOL</b>				
SBP	150±6.268	124±3.910	0.0034	2.520
DBP	83.45±5.425	80.12±1.231	0.44	2.152
<b>LOSARTAN</b>				
SBP	148±6.761	130.5±2.589	0.0286	2.506
DBP	82.75±5.126	76.25±1.830	0.2522	1.194
<b>ENALAPRIL</b>				
SBP	137.1 ± 13.22	128.4 ± 1.601	0.5253	0.6543
DBP	85.36±12.22	82.29±2.012	0.8561	0.4561
<b>OLMESARTAN</b>				
SBP	148.8±6.417	130.1±2.948	0.1156	2.756

DBP	84.29 ± 6.117	84.29 ± 6.117	0.9678	0.04120
<b>NEBIVOLOL</b>				
SBP	137.6±6.561	125.3±3.847	0.0236	2.404
DBP	80.71±3.225	77.57±2.517	0.4493	0.7682

**Table 2: Efficacy of Monotherapy Antihypertensive Drugs in Patients in A Tertiary Care Hospital:**

BLOOD PRESSURE MEAN±SEM	On Admission	On Discharge	p-VALUE	t-VALUE
<b>AMLODIPINE</b>				
SBP	155±6.268	132±2.881	0.216	2.861
DBP	85.75±5.126	80.26±2.45	0.238	2.235
<b>FUROSEMIDE</b>				
SBP	152±6.268	124±3.910	0.0034	2.520
DBP	86.45±5.425	80.12±1.231	0.44	2.152
<b>TORSEMIDE</b>				
SBP	146±5.761	132.5±2.589	0.286	2.606
DBP	85.75±5.126	78.25±1.830	0.1522	1.294
<b>RAMIPRIL</b>				
SBP	138.1 ± 13.22	125.4 ± 1.601	0.6253	0.7543
DBP	83.36±12.22	80.29±2.012	0.6561	0.3561
<b>LOSARTAN</b>				
SBP	145.8±5.417	132.1±2.948	0.2156	2.756
DBP	82.29 ± 5.117	85.29 ± 6.117	0.8678	0.0312
<b>CLINIDIPINE</b>				
SBP	135.6±6.561	128.3±3.847	0.1236	2.504
DBP	82.71±3.225	78.57±2.517	0.6493	0.8682

**Table 3: Efficacy Of two drug therapy Antihypertensive Drugs In Patients In A Tertiary Care Hospital:**

BLOOD PRESSURE MEAN±SEM	ON ADMISSIO N	ON DISCHARG E	P- VALU E	T- VALU E
<b>ATENOLOL±AMLODIPINE</b>				
SBP	178±8.268	132±2.981	0.4516	2.891
DBP	92.75±8.126	80.26±2.45	0.4138	2.035
<b>METOPROLOL±AMLODIPINE</b>				
SBP	175±6.268	125±3.910	0.034	2.620
DBP	88.45±5.425	82.12±1.231	0.144	2.352
<b>LOSARTAN±HYDROCHLORTHAZI DE</b>				
SBP	176.2±6.761	130.5±2.589	0.0286	2.506
DBP	89.75±5.126	76.25±1.830	0.2522	1.194
<b>RAMIPRIL±AMLODIPINE</b>				
SBP	167.1 ± 13.22	128.4 ± 1.601	0.6253	0.6843
DBP	85.36±12.22	82.29±2.012	0.8561	0.4561
<b>FUROSEMIDE±RAMIPRIL</b>				
SBP	168.8±6.417	130.1±2.948	0.1156	2.756
DBP	89.29 ± 6.117	84.29 ± 6.117	0.8678	0.04120
<b>AMLODIPINE±FUROSEMIDE</b>				
SBP	177.6±6.561	125.3±3.847	0.1236	2.5104
DBP	87.71±3.225	78.57±2.517	0.5493	0.1682

**Table 4: Comparison of efficacy between mono and combination therapy of amlodipine:**

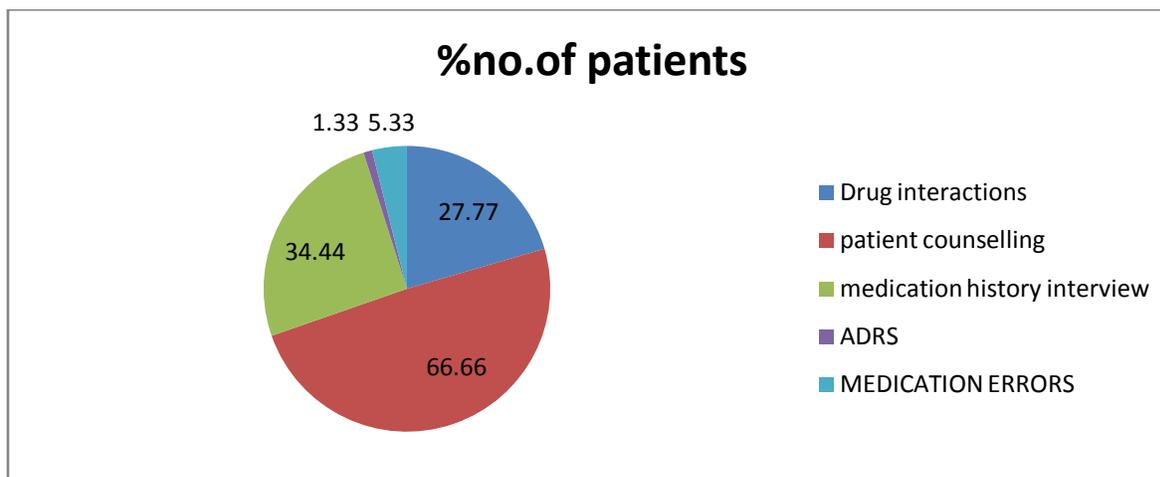
Blood Pressure	Mono Amlodipi	Combination 1 Amlodipine+losar	p - valu	t - val	Combiantion 2 Amlodipine+Atenol	p- value	t- value
Blood Pressure	Mono	Combination 1	P- Value	t- Value	Combination	P-Value	T- Value
	Furose mide [ N=47]	Furosemide+Ramipril [N=10]			FUROSEMIDE+LOSARTAN [N=5]		
Mean Reduction in SBP	7.58±5.36	20.52±8.00	0.08488	50.57322	9.05±22.0	0.82945	10.220200
Mean Reduction in DBP	5.143±4.036	5.215±4.85	0.4585	1.0374	42.50±27.50	0.0039	3.449

**Table 5. Comparison of efficacy between mono and combination therapy of furosemide:****Table 6. Comparison of efficacy between mono and combination therapy of Metoprolol:**

Blood pressure	mono	Combination	p-value	t-Value
	Metoprolol [N=10]	Amlodipine+metoprolol [N=2]		
Mean Reduction in SBP	25.15±8.255	8.0±18.0	0.6633	0.8639
Mean Reduction in DBP	6.50±5.369	2.5±1.0	0.5788	0.6785

**Table 7: Comparison of efficacy between mono and combination therapy of Losartan:**

Blood Pressure	Mono	Combination 1	P- Value	t- Value	Combination	p-Value	t- Value
	Losartan [ N=47]	Losartan+Ramipril [N=10]			Losartan+Hydrochlorothiazide [N=5]		
Mean Reduction in SBP	18.29±5.535	22.0±30	1.056	1.3227	55.0±25.0	0.0451	2.200
Mean Reduction in DBP	4.143±3.036	7.0±4.0	0.675	1.0374	42.50±27.50	0.0039	3.449



**Figure. 12. Clinical Pharmacy Services Provided in Antihypertensive Patients.**

### DISCUSSION:

A prescription-based study is considered to be one of the most effective methods to assess and evaluate the prescribing attitude of physicians<sup>2</sup> and dispensing practice of pharmacists. With increasing economic growth rate, India is not only facing the epidemic coronary artery diseases but also of obesity, diabetes mellitus and hypertension. Prevalence of hypertension is dramatically increasing in India.<sup>3</sup> Age probably represents an accumulation of environmental influences & body stresses. The prevalence of HTN in India is highest in age group 50-59 yrs in males & 60-64 yrs in females in urban areas whereas in rural areas an age-related increase is seen in both the sexes in the age group 60-64 yrs.<sup>4</sup> This is in occurrence with our study where maximum number of patients were found in age group 50-70 yrs. This represents that increasing in age is a risk factor to develop HTN in India. Pharmacist intervention can significantly increase disease-related knowledge, blood pressure control and medication adherence in patients with hypertension. However, further research is needed to address the decreased health-related quality of life after completion of the study.

In our study most prescribed class of antihypertensive drugs were diuretics followed by calcium channel blockers and  $\beta$  blockers. A similar study in Nigeria had reported a comparable results<sup>5</sup> and also diuretics was constituted the most frequently prescribed drug class in other studies<sup>6,7,8</sup> and according JNC VII guidelines the diuretics are choice of first line of antihypertensive.

In our study it was observed that 57.11% of prescription containing combination therapy which was lower than recommendations<sup>9</sup> and observations of several other studies demonstrated that the combination therapy was necessary in at least 70% the study population prescriptions to attain optimal blood pressure control.<sup>10,11</sup> Mono drug therapy was recommended in 42.88% prescription in our hospital. Higher probability of 27.77% DDI, due to combination drugs and Pharmacoeconomic consideration might be the reason which can be attributed to lesser inclination of physicians to go for combination therapy in our tertiary care hospital for comparison.

73% of HTN patients prescribed antihypertensive combination in survey conducted in Nigeria.<sup>12</sup> In an Indian study 60% and 40% of patients reviewed combination & mono therapy

respectively.<sup>13</sup> On contrary, mono therapy was preferred for 51% of the patients in a Hongkong study.<sup>14</sup>

In our study rationality were assessed by using Joint National Committee -VII and Indian guidelines of hypertension. These guidelines are intended to provide practitioners with a standard approach to the rational, safe, and effective use of antihypertensive for prevention of hypertension based on currently available clinical evidence and emerging issues. Rational recommendations of antihypertensive were very high for the hypertension patients in our study that is 427(94.88%) rationally recommended by our physicians and remaining 23(5.11%) were recommended antihypertensive irrationality to hypertension patient according to JNC-7 guidelines. Finally, this assessment indicate in our hospital physicians are well adhered to both JNC 7 and IGH guidelines which was a good sign to control hypertension for patients visiting our hospital.

While studying efficacy of mono and combination therapy in our study it was observed that combination therapy shown significant raise in mean reduction in SBP and DBP. This once again proving using combination therapy will have good control on hypertension which already proved worldwide. In contrast of these some combination therapy failed to show significant reduction in BP.

As we discussed above in our study combinations also used more than 50% thus there were more possibility to DDI's in prescriptions and also various studies have shown that potential drug - drug interactions are frequent when patients receive multiple prescriptions.<sup>15</sup>

In present study we found 387 DDI's in prescriptions of 450 hypertension patients in our tertiary care hospital. The similar study was done in hospital of Jimma in which they found 297 DDI's out of 332 hypertension patients.<sup>16</sup> These potential DDI's can be reduced in presence of clinical pharmacists and understand about DDI by physicians which was already proved in study conducted in Thailand.<sup>17</sup>

Finally, we concluded that with time, there happened to be change in the treatment strategies and there by the prescription pattern. Our results were showed that the choice of anti-hypertensive drugs reasonably comply with the JNC 7 and IGH guidelines on the management of hypertension. Which was confirms a fairly good degree of compliance by clinicians with JNC 7 and IGH guidelines for the treatment of hypertension. This study concludes the preferred use of diuretics, calcium channel blockers and  $\beta$  blockers as 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> choice of drugs for hypertension. However, there is a need for improve patient education on adherence to therapy and greater attention by clinicians to issues of life style modifications, so as to improve BP control rate in this hospital.

This study also reveals how the clinical pharmacy services are impacting in the hypertension patients by providing counselling about their disease, drugs and their life style modifications. This study reveals the effect of anti-hypertensive drugs in mono and combination therapy and the values are expressed as mean $\pm$ SEM, \* $p$ <0.05, \*\* $p$ <0.01 and \*\*\* $p$ <0.001 [Unpaired Student  $t$  test] as compared to blood pressure on admission and discharge of patients in a tertiary care hospital. and also, the efficacy of anti-hypertensive drugs in mono and combination therapy and all the values are expressed as mean $\pm$ SEM, \* $p$ <0.05 [Unpaired Student  $t$  test] as compared to blood pressure of patients treated with mono

therapy as compared to blood pressure on admission and discharge of patients in a tertiary care hospital.

### CONCLUSION:

In the present study we have concluded that in future study to develop and implement strategies in order to minimize the drug related problems associated with use of antihypertensive drugs which can be attained by recruiting clinical pharmacists. The study may be extended to other departments of the hospital to assess the prescribing pattern and rational use of antihypertensive drugs. Training programs should be included for hospital pharmacists for investigating the prescribing pattern in the hospital for assuring the rational prescribing practice. Training class for the medical staff regarding the use of rational combination of the HTN drugs. Medication adherence monitoring for all the patients admitted in tertiary care hospital.

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