

## DRUG UTILIZATION PATTERN OF ANTIHYPERTENSIVE MEDICATIONS IN A TERTIARY CARE HOSPITAL, SOUTH INDIA

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### ABSTRACT

**Objective:** The objective of the study is to assess drug use pattern of antihypertensive medications in hypertensive patients.

**Methods:** It is a prospective cross-sectional study conducted in the outpatient dispensary, Government Medical College, Thiruvananthapuram for the period of 6 months from January 2019 to June 2019. About 500 prescriptions of patients visiting outpatient dispensary with an antihypertensive prescription were enrolled for the study. Drug use patterns of different classes of antihypertensive medications were analyzed from individual prescriptions.

**Results:** A total of 500 patients were included in this study, among which 281 were male (56.2%) and 219 (43.8%) were female. In 500 patients, 133 patients were treated with monotherapy. In that 42.1% of patients were treated with amlodipine, 28.57% of patients were treated with losartan. In combination therapy most commonly used was double therapy (42.8%) followed by triple therapy (24.2%). Calcium Channel Blockers (56.2%) was most prescribed class of drug followed by Angiotensin Receptor Blockers.

**Conclusion:** This study reveals that calcium channel blockers as most prescribed class of antihypertensive and Amlodipine was the most prescribed antihypertensive. In our study, most of the patients were treated with combination therapy in that double drug therapy was most common. There is a chance of various medication errors, development of adverse drug reaction as majority (290) of patients belong to age above 60 and chances of getting error also increases as combination therapy is most used. Therefore close monitoring is required for such patients.

**Keywords:** Antihypertensives, Combination therapy, Drug use pattern, Hypertension, Monotherapy.

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### INTRODUCTION

Hypertension affects around one billion individuals worldwide and about 234 million adults are effected by the same in India by 2019 [1,2]. It is usually asymptomatic, chronic disorder needing lifelong treatment. Hypertension is defined as a sustained blood pressure greater than 90 mm Hg accompanied by an elevated systolic blood pressure 140 mm Hg [3].

Now a day's hypertension remains poorly controlled. It is due to multiple factors including low antihypertensive efficacy of single-drug therapy, reluctance of primary care physicians to modify or titrate initially chosen therapy to obtain target blood pressure, and poor compliance with medication [3,4]. Drug prescribing patterns vary from country to country and within various regions of individual countries [5]. It is, therefore, important to understand current antihypertensive medication patterns and their impact on blood pressure control. Drug utilization research can increase our understanding of how drugs are being used as follows. It can determine the pattern or profile of drug use and the extent to which alternative drugs are being used to treat particular conditions [6,7]. It can be used to compare the observed patterns of drug use for the treatment of a certain disease with current recommendations or guidelines [7]. The aim of this study was to detect the drug utilization pattern of antihypertensive prescribed.

### METHODS

#### Study design

Prospective cross sectional study.

#### Study site

Tertiary care hospital.

#### Study period

6 months (January 2019-June 2019)

#### Study population

Patients visiting outpatient dispensary with an antihypertensive prescription, Government Medical College, Thiruvananthapuram, Kerala.

#### Sample size

425 patients prescribed with antihypertensive medications.

#### Inclusion criteria

- Patient clinically diagnosed with hypertension with or without comorbidities, both genders included.
- Patients who are willing to participate in the study are included in the study.

#### Exclusion criteria

- Patients aged above 80 years old are excluded from the study.

#### Data collection technique

- Details will be obtained from the patients through structured questionnaire by direct interview
- Drugs use pattern assessed from individual prescription.

#### Ethical consideration

- Ethical clearance was obtained from Institutional Research/ Human Ethics Committee of Government Medical College, Thiruvananthapuram. Informed consent was obtained from the patient and caregiver before commencing the study. Permission for checking case sheets of patients was obtained from the hospital authorities. All data will be kept confidential and was used for the purpose of this study only.

### Statistical analysis

- Data obtained was entered into Microsoft Excel Sheet and analyzed using Statistical Package for the Social Sciences trial version 18.0. Qualitative variables will be expressed in percentages. Quantitative variables will be expressed in mean and standard deviation (SD) and its confidence interval.

### RESULTS

In this prospective study, a total of 500 patients were enrolled and among these patients, 281 (56.2%) patient were males and 219 (43.8%) patients were females. Mean age in the study population from the Table 1 was found to be 59.69 ( $\pm 9.738$ ) years. Results from the table showed that among 500 patients 58% were in the age group of  $\geq 60$  years and 42% were of age group of  $< 60$  years.

This study also showed that 30% of patients have a family history of Hypertension and 70% does not have any family history of hypertension. In case of social habits, 14 patients were smokers, 10 patients were alcoholic, 63 were ex-alcoholic, and 104 were ex-smokers (Table 1).

The enrolled patients were categorized, based on blood pressure level as per the Joint National Committee guideline (JNC-8). Among 500 patients, most of the patients belong to stage 1 hypertension (31.8% having systolic blood pressure and 36.4% having diastolic blood pressure). In stage 2 hypertension 23.4% have systolic blood pressure and 14.6% have diastolic blood pressure (Table 2).

Hypertension is usually associated with co-morbidities such as heart diseases, diabetes, stroke, and kidney failure. In 500 patients about 452 patients (90.4) where with comorbidity. Above Table 3 showed that 53% of patients had Coronary artery disease (CAD), followed by diabetes (46.6%), dyslipidemia (42%), hypothyroidism (13.4%), chronic kidney disease (CKD) (5.8%), and Stroke (5.2%).

**Table 1: Baseline characteristics of all hypertensive patients**

Characteristics	Frequency (n)	Percentage
Gender		
Males	281	56.2
Females	219	43.8
Age group		
$< 60$	210	42.0
$\geq 60$	290	58.0
Family history		
Yes	150	30.0
No	350	70.0
Social habits		
Alcoholic	10	2.0
Non-alcoholic	407	81.4
Ex-alcoholic	63	12.6
Occasional alcoholic	20	4.0
Smoking		
Smoking	14	2.8
Non-smoking	375	75.0
Ex-smoking	104	20.8
Occasional smoking	7	1.4

**Table 2: Distribution of patients according to blood pressure**

Blood pressure	SBP (mmHg)	DBP (mmHg)	SBP		DBP	
			Frequency	Percentage	Frequency	Percentage
Normal	$< 120$	$< 80$	77	15.4	235	47.0
Pre-hypertension	120–139	80–89	147	29.4	10	2.0
Stage 1 hypertension	140–159	90–99	159	31.8	182	36.4
Stage 2 hypertension	$\geq 160$	$\geq 100$	117	23.4	73	14.6
Total			500	100	500	100

SBP: Systolic blood pressure, DBP: Diastolic blood pressure

Fig. 1 indicates that 367 (73.4%) patients were receiving combination therapy and only 133 (26.6%) patients were receiving monotherapy.

In this study, 133 patients were treated with monotherapy in that 42.1% patients were treated with amlodipine, followed by Losartan (28.57%), Telmisartan (9.77%), Metoprolol (9.77%). Ramipril, Enalapril were used less frequently (Table 4).

In combination therapy most commonly used was double therapy (42.8%) followed by triple therapy (24.2%), four-drug therapy (5.6%), and five drug therapy (0.6%) (Table 5).

Table 6 showed that Calcium Channel Blockers (281) either alone or in combination were the most commonly prescribed antihypertensive class of drug and in this class Amlodipine (84.34%) was frequently prescribed followed by Clinidipine (15.37%) and Diltazem and Nifedipine (0.71). Two hundred and forty-nine patients were prescribed with Angiotensin Receptor Blockers as antihypertensive drug; In that Losartan (67.06%) was commonly prescribed and which is followed by Telmisartan (31.22%) and Olmesartan (0.16%).

Among angiotensin-converting enzyme inhibitors most prescribed was Enalapril (58.49%), followed by Ramipril (38.67%) and Captopril (1.88%). The Diuretics prescribed preferably Thiazides are first-line agents for most patients with hypertension, especially in combination therapy. The result showed that Furosemide (54.05%) was the most prescribed Diuretic, followed by Hydrochlorothiazide (23.42%), Spironolactone, and Chlorthalidone 17.11%, last Torsemide (3.60%).

Beta-blockers are now considered as first-line drug when having compelling indications like coronary disease risk and myocardial infarction. It was seen that 82.18% were treated with Metoprolol, 12.55% patients were treated with Nebivolol, 4.04 with atenolol, and least with Bisoprolol and Propranolol (Table 6).

### DISCUSSION

This study was conducted in the outpatient dispensary, Government Medical College Hospital, Thiruvananthapuram, Kerala, and a total of 500 patients were enrolled. The study duration was a period of 6 months. In the study, among the 500 patients, 281 (56.2%) patients were males and 219 (43.8%) patients were females, which was similar to another study conducted by Amit Sharma *et al.* in his study 55.3% were male and 44.7% were female [8]. Majority of patients (58%) in the study were in the age group of greater than or equal to 60 and 42% were in the age group less than 60. The mean  $\pm$  SD age in the study population was 59.69  $\pm$  9.738 years. Dhanaraj *et al.* also reported that mean SD age as 56.5  $\pm$  10.1 in the study conducted in Chandigarh [9].

In our study, 30% (150) of patients have a family history of hypertension. This observation was in accordance with another study conducted at outpatient department of tertiary care hospital in Andhra Pradesh in which 23.7% had family history of hypertension [10]. The enrolled patients were categorized based on blood pressure level in adults as per JNC-8 [11]. Among 500 patients, most of the patients belong to stage 1 hypertension this was similar to the study of Cidda [12]. Hypertension is usually associated with

co-morbidities such as heart diseases, diabetes, stroke, and kidney failure [11]. The analysis of this study population shows that 53% had CAD, 46.6% had diabetes, 42% had dyslipidemia, 13.4% had hypothyroidism, 5.8% had CKD, and 5.2% had Stroke. Akintunde *et al.* also found similar result in their study [13].

**Table 3: Distribution of patients according to comorbidities**

Comorbidities	Frequency	Percentage
CAD	265	53.0
Diabetes mellitus	233	46.6
Dyslipidemia	210	42.0
Hypothyroid disease	67	13.4
CKD	29	5.8
Stroke	26	5.2
Heart failure	9	1.8
Post MI	4	0.8
No co-morbidities	48	9.6

CAD: Coronary artery disease, CKD: Chronic kidney disease

**Table 4: Patients on monotherapy**

Monotherapy drug	Frequency	Percentage
Amlodipine	56	42.10
Losartan	38	28.57
Telmisartan	13	9.77
Metoprolol	13	9.77
Cilnidipine	4	3.0
Olmesartan	2	1.5
Enalapril	2	1.5
Ramipril	2	1.5
Nebivolol	1	0.75
Carvedilol	1	0.75

**Table 5: Distribution of patients according to combination drug therapy**

Combination therapy	Frequency	Percentage
Double-therapy	214	42.8
Triple-therapy	121	24.2
Four drug therapy	28	5.6
Five drug therapy	3	0.6

**Table 6: Distribution of prescription according to various class of antihypertensive drug prescribed**

Antihypertensive class	Name of the drug	Frequency	Percentage
Calcium channel blocker (n=281)	Amlodipine	237	84.34
	Cilnidipine	43	15.30
	Diltiazem	2	0.71
	Nifedipine	2	0.71
Angiotensin receptor blocker (n=249)	Losartan	167	67.06
	Telmisartan	78	31.32
	Olmesartan	4	1.60
Angiotensin converting enzyme inhibitor (n=106)	Enalapril	62	58.49
	Ramipril	41	38.67
	Captopril	2	1.88
Diuretics (n=111)	Furosemide	60	54.05
	Hydrochlorothiazide	26	23.42
	Spironolactone	19	17.11
	Chlorthalidone	19	17.11
	Torsemide	4	3.60
Beta blocker (n=247)	Metoprolol	203	82.18
	Nebivolol	31	12.55
	Atenolol	10	4.04
	Bisoprolol	2	0.80
	Propranolol	1	0.40
Centrally acting drugs (n=32)	Clonidine	32	100
Alpha blocker (n=17)	Prazosin	17	100
Alpha and beta blocker (n=8)	Carvedilol	8	100

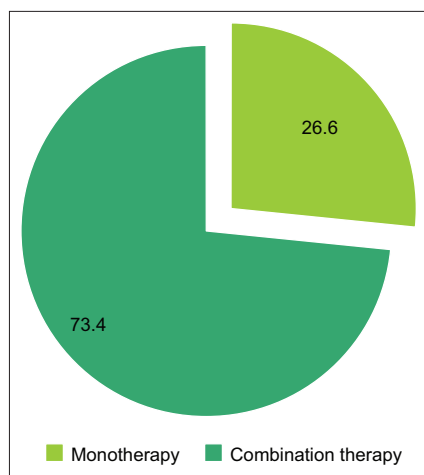
The analysis of the present study indicates that 73.4% of patients were treated with combination therapy and only 26.6% of patients were treated with monotherapy. A similar report was established in another different studies [14-16]. In patients those who received monotherapy, 42.1% patients were treated with Amlodipine, 28.57% patients were treated with Losartan, and 9.77 % were receiving Telmisartan and Metoprolol followed by Cilnidipine (3%), Olmesartan, Ramipril, and Enalapril (1.5%). Monotherapy is able to normalize blood pressure in less than a quarter of patients with Hypertension. This was similar to the result of Varakantham *et al.* and Jarari *et al.* studies were Amlodipine was the most common drug used [17,18].

In combination therapy most commonly used was double therapy (42.8%) followed by triple therapy (24.2%), four drugs (5.6%), and five drug therapy (0.6%). In the study conducted by Rakesh *et al.* also double drug therapy was the most preferred combination therapy [19].

The study revealed that Calcium Channel Blocker (281) either alone or in combination was the most commonly prescribed class of drug, in that majority patients were prescribed with Amlodipine as first-line Calcium Channel Blocker (84.34%) followed by Cilnidipine (15.37%) and Diltiazem and Nifedipine (0.71%). In the study, Varakantham *et al.* and Sandeep *et al.* also found that Calcium Channel blocker was the most common class of drug used [17,20].

Among angiotensin-converting enzyme inhibitors most prescribed was Enalapril (58.49%), followed by Ramipril (38.67%) and Captopril (1.88%). Beta-blockers are now considered as first-line drug when having compelling indications like coronary disease risk and myocardial infarction. It was seen that 82.18% were treated with Metoprolol, 12.55% patients were treated with Nebivolol, 4.04 with atenolol, and least with Bisoprolol and Propranolol. This was accordance with the study conducted by Abdulameer *et al.* and Metha *et al.* were Enalapril was major ACE inhibitor and Metoprolol was the most common Beta blocker given to patients [15,21].

The Diuretics prescribed preferably Thiazides, are first-line agents for most patients with hypertension, especially in combination therapy. The result showed that Furosemide (54.05%) was the most prescribed Diuretic, followed by Hydrochlorothiazide (23.42%), Spironolactone, and Chlorthalidone 17.11%, last Torsemide (3.60%). In the study conducted by Abdulameer SA *et al.* majority of patients were given with Furosemide and Spironolactone [21].



**Fig. 1: Distribution of patients according to monotherapy and combination therapy**

## CONCLUSION

In most cases, hypertension will lead to several other diseases including cardiovascular and renal diseases. In our study population most frequently observed comorbidity was CAD and Diabetes Mellitus. Majority were having stage 1 hypertension and 30% had family history of hypertension. Most of the patients were treated with combination therapy in that double drug therapy was most common. Combination therapy was preferred as majority of patients were having comorbidities. On analysis of drug use pattern calcium channel blocker was most prescribed class of antihypertensive and drug was Amlodipine.

Most geriatric patients were on combination therapy so avoiding polypharmacy and promoting rational use of drug should be considered while prescribing. Fixed-dose combinations can be preferred for geriatric patients with proper monitoring.

Limitations of the study include single centered and limited time period for follow-up. If the study was conducted in larger sample size for long duration more significant results would have been obtained.

## AUTHOR CONTRIBUTION

All authors contributed equally.

## CONFLICT OF INTEREST

None.

## FUNDING

Nil.

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