A PROSPECTIVE STUDY ON DRUG UTILITY PATTERNS OF ANTIHYPERTENSIVE DRUGS IN MONOTHERAPY AND COMBINATION THERAPY AT A TERTIARY CARE HOSPITAL IN DAKSHINA KANNADA

Dr. A. R. Shabaraya[1] and Lathika A. Nayak[2]*

[1]Principal and HOD, Department Pharmacy Practice, Srinivas College of Pharmacy, Srinivas College of Pharmacy, Manglore-574143.

[2]Pharm D, Department of Pharmacy Practice, Srinivas College of Pharmacy, Manglore-574143.

*Corresponding Author

Lathika A. Nayak

Pharm D, Department of
Pharmacy Practice, Srinivas
College of Pharmacy,
Manglore-574143.

ABSTRACT

Hypertension, persistent increase in systolic and diastolic blood pressure is one of the diseases that has severe impact on body and economy. Rational drug prescribing is the use of the least number of drugs to attain the maximum effect in the smaller period at minimum cost. Main aim and objective of our study was to find out the prescribing patterns of antihypertensives. A prospective observational study was conducted at a tertiary care hospital in Dakshina Kannada for period of 6 months.150 hypertensive patients who were on at least one antihypertensive medication, admitted to in-patient department were included for drug utilization study during the study period. According to the study, 54% of hypertensive subjects were above 60-75 years of age. 86% of prescription had more than 6 drugs. As per the study, the most frequently prescribed antihypertensive drug was calcium channel blocker (36.10%) - Amlodipine.

KEYWORDS: Antihypertensive drugs, prescription, Amlodipine, Calcium channel blocker.

INTRODUCTION

Systemic hypertension is a worldwide general health problem influencing presently more than one billion of the world's population with an alarming protrusion to 1.56 billion by year 2025.[1]

Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure. It is the paramount risk factor for cardiovascular morbidity and mortality due to target organ damage to blood vessels of the heart, brain, kidney, and eyes.[2] The WHO has gauged that high blood pressure is a crucial public health issue and lead to one in eight death.[3]

However, recently published evidence indicated an increase in use of Calcium Channel Blockers (CCBs) and Angiotensin Converting Enzyme Inhibitors (ACEIs) are noted compared to diuretics and beta blockers in lowering morbidity and mortality of cardiovascular diseases.[4]

MATERIALS AND METHODS

- **STUDY DESIGN**: A prospective observational study to evaluate drug utilization and pharmacoeconomic analysis of antihypertensive drugs.
- **STUDY SITE**: The study was conducted at Srinivas Institute of Medical Science and Research Centre, Mukka-574146.
- **STUDY DURATION**: The study was conducted for a duration of 6 months from March 2022 – August 2022.
- **SAMPLE SIZE**: The sample taken for the study was 150.
- **ETHICAL CLEARANCE**: The study protocol was approved by the Institutional Ethics Committee (IEC) of Srinivas Institute of Medical Science, Mukka, Mangaluru.

(Ref. No.: SIEC/SIMS & RC/2022/10/04)

- **STUDY CRITERIA**

Inclusion criteria

● Hypertensive patients

● Patients above 18 years of age

● Patient with comorbid conditions: Stroke, CKD, DM, Hyperlipidemia, CHF and others

● Patient on at least one oral antihypertensive drug

Exclusion criteria

● Out-patients

● Patients below 18 years of age

- **SOURCE OF DATA**

Data(s) for the study were collected using data collection form from the in-patient case files.

- **STUDY METHOD**

The study period was divided into three phases

Phase 1

Preparation for the study:

- Data(s) were collected using data collection form with the aid of medical records of in-patients in a tertiary care hospital, Manglore.
- Data collected include patient name, gender, age, diagnosis, drugs prescribed.
- Institutional Ethics Committee approval: Ethical clearance was obtained from the Institutional Ethics Committee (IEC) of Srinivas Institute of Medical Science and Research Centre (SIMS & RC), Mangaluru.

Phase 2

1) Data Collection from in-patient case files: Initially 200 in-patient case files with hypertension containing equal proportions of male and female were collected, maintaining confidentiality. This was done to avoid bias.

2) Selection of case files: 150 cases were filtered out based on the inclusion and exclusion criteria.

3) Collection of data from selected case files: Data were collected using data collection form from the in-patient case files of SIMS & RC, Mangaluru.

4) Filling information in data collection form:

The information includes the patient's demographic details, blood pressure level, comorbidities, final diagnosis, drug generic name, brand name, dose, frequency, route of administration, number of days of hospitalization.

The collected data(s) were analysed for drug utility pattern using number of antihypertensive drugs given as monotherapy and fixed dose combinations and number of antihypertensive drugs per prescription.

Phase 3

Data analysis: The obtained results after the application of suitable tools were analyzed in Microsoft excel and all the data(s) were kept confidential.

- **STATISTICAL ANALYSIS**

Statistical analysis involves collecting and scrutinizing of every data sample in a set of items from which samples were drawn and a suitable statistical test was applied to analyse the data. The collected data(s) were analysed using Microsoft excel.

RESULT

1. **Demographic Characteristics of Participants**

a) **Age group**

The study on drug utility patterns of antihypertensive drugs in monotherapy and combination therapy was conducted with sample size of 150 and the subjects were all hypertensive patients above 18 years of age. Among the 150 subjects, 54% were of age group 61 to 75 years [N=81, Male-49, Female-32]. 30% of sample were from age group of 41 -60 years [N=45, Male-18, Female-27]. 12% of subjects were from age group above 75 years [N18, Male-8, Female-10]. 4% of sample were of age group 18-40 years and all were male[6], as shown in the Figure 1
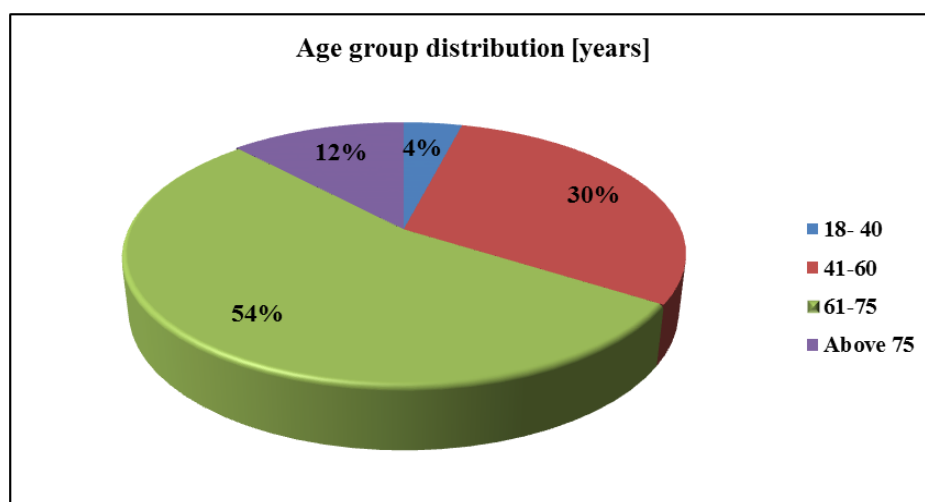
Figure: 1 Age group distribution.

b) **Gender and BMI**

This study was carried out by analysing the inpatient case files and confidentiality was maintained. In this study 54% of the participants were male patients among them 14.81% were underweight and 40.7% were of normal weight, 32.09% over weight, 12.34% were obese and out of 46% of the female patients, 5.79% were found to have underweight, 33.33% had normal weight, 43.47% were overweight and remaining 17.39% were obese, as per the Figure 2 and Table 1.
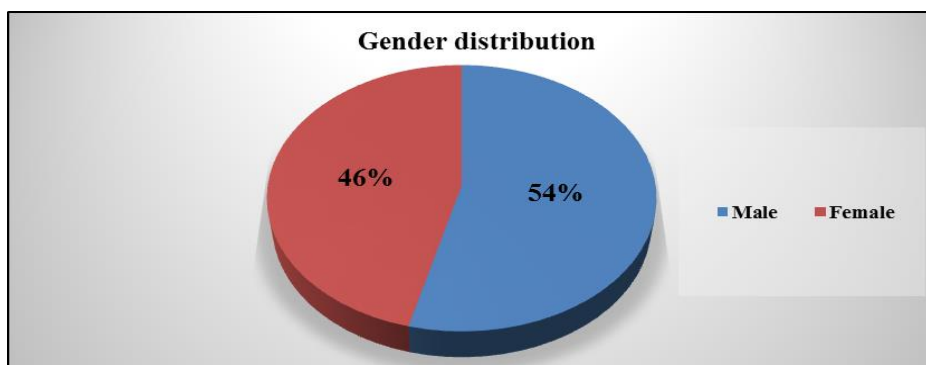
Gender distribution

46%   54%   ■ Male ■ Female

Figure: 2 Gender distribution.

BMI Classification	Male	Female	Total	%
Under weight - <18.50kg/m^2	12	4	16	10.67
Normal weight-18.50-24.99 kg/m^2	33	23	56	37.33
Over weight - 25.0- 29.99 kg/m^2	26	30	56	37.33
Obese - >/= 30 kg/m^2	10	12	22	14.67
Total	81	69	150	100

c) HTN Classification

Data showed that in male patients, 33.33% had stage 1 HTN, 23.45% had stage 2 hypertension and hypertensive crisis, 9.87% had elevated BP and the remaining had normal BP, and in female 34.78% had stage 1 hypertension, 27.53% had stage 2 hypertension, 14.49% had hypertensive crisis, 13.04% had elevated BP and the rest were normal, as per Table 2.

Table 2: HTN Classification.

Blood pressure (mmHg)	Male	Female	Total	%
Normal <120/80	8	7	15	10
Elevated 120-129/<80	8	9	17	11.33
Stage 1 HTN 130-139/80-89	27	24	51	34
Stage 2 HTN 140 or </90 or <	19	19	38	25.33
Hypertensive Crisis 160</120<	19	10	29	19.33
Total	81	69	150	100

2. Antihypertensive drug utility pattern as in monotherapy and Fixed Dose Combinations

a) Antihypertensive drug class prescribed in monotherapy

According to the study, out of 150 prescriptions, 36.10% of people were prescribed calcium channel blockers, 17.07% of people were prescribed ARB, 15.12% of the prescription had beta blockers, and 13.17% were given diuretics. Alpha blockers, centrally acting

sympatholytics, vasodilators and ACE inhibitors contributed 8.78%, 5.85%, 1.95% and 1.95% respectively, as per Figure 3.
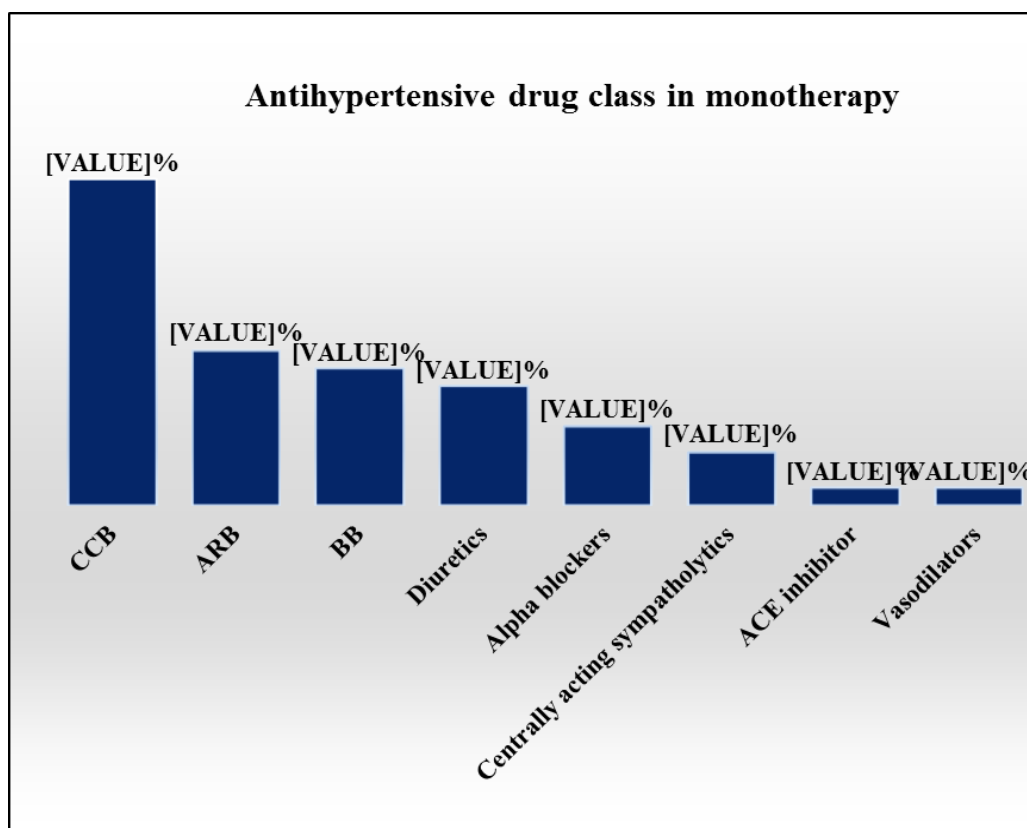
Figure: 3 Antihypertensive drug class prescribed in monotherapy.

b) Antihypertensive drugs prescribed in monotherapy

Among calcium channel blockers Amlodipine was the most commonly prescribed (51.81%) followed by Cilnidipine (19.28%), Nifedipine (15.66%), Diltiazem (7.23%), Verapamil and Benidipine both constituting 2.41% and Lecarnidipine 1.2%

Among ARBs Telmisartan was the most commonly prescribed (71.42%) followed by Losartan (25.71%) and Olmesartan 2.85%

Out of 31 Beta blockers, 24.24% was constituted by Metoprolol, 18.18% by Propranolol, followed by Atenolol, Bisoprolol, Labetolol constituting 15.15% each and Nebivolol 1%, Carvedilol 9.09% and Nebivolol 3.03%

Among Diuretics, Furosemide was the most commonly prescribed (43.33%), followed by Torsemide (26.67%), Spironolactone (16.67%), Mannitol, Hydrochlorthiazide, Lasilactone, Indapamide constituting 3.33% each.

It was observed that only Prazosin was prescribed among Alpha blockers.

Among Centrally acting sympatholytics, Clonidine was the most commonly prescribed (69.23%) followed by Moxonidine (30.77%)

Nitroglycerine (60%) followed by sodium Nitroprusside and Dihydralazine both constituting 20% each were prescribed among Vasodilators.

In this study, among the least prescribed ACE inhibitors (1.95%), Enalapril constituted 75% followed by Ramipril 25%, according to Table 3.

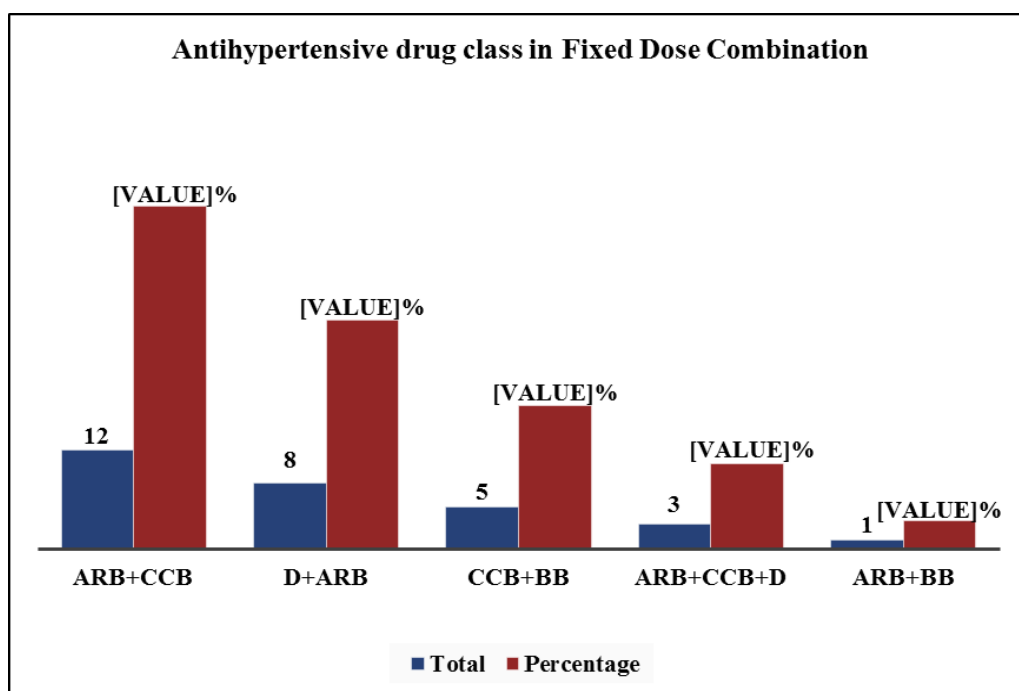**Table 3: Antihypertensive drugs prescribed in monotherapy.**

DRUG	NUMBER OF DRUGS PRESCRIBED	PERCENTAGE (%)
CCB (36.14%)		
Amlodipine	43	51.81
Cilnidipine	16	19.28
Nifedipine	13	15.66
Diltiazem	6	7.23
Verapamil	2	2.41
Benidipine	2	2.41
Lercanidipine	1	1.2
ARB (17.07%)		
Telmisartan	25	71.42
Losartan	9	25.71
Olmesartan	1	2.85
BB (15.12%)		
Metoprolol	8	24.24
Propranolol	6	18.18
Atenolol	5	15.15
Bisoprolol	5	15.15
Labetalol	5	15.15
Cavedilol	3	9.09
Nebivolol	1	3.03
DIURETICS (13.17%)		
Furosemide	13	43.33
Torsemide	8	26.67
Spironolactone	5	16.67
Mannitol	1	3.33
Hydrochlorthiazide	1	3.33
Lacilactone	1	3.33
Indapamide	1	3.33
ALPHA BLOCKERS (8.78%)		
Prazosin	18	100
CENTRALLY ACTING SYMPATHOLYTICS (5.85%)		
Clonidine	9	69.23
Moxonidine	4	30.77
VASODILATORS (1.95%)		
Nitroglycerine	3	60

Dihydralazine	1	20
Sodium Nitroprusside	1	20
ACEI (1.95%)		
Enalapril	3	75
Ramipril	1	25

c) Antihypertensives prescribed in Fixed Dose Combination

This study shows that out of 150 prescriptions, 29 of them had antihypertensive Fixed Dose Combination. 26 prescriptions had dual drug combination, and the remaining 3 prescriptions had triple drug combinations. Out of 29 prescriptions with combination antihypertensives, 41.38% (12) of them had ARB+CCB, 27.59% (8) had D+ARB, 17.24% (5) had CCB+BB, 3.45% (1) had ARB+BB and 10.34% (3) prescriptions had triple drug combination of ARB+CCB+D, as depicted in Figure 5.

The antihypertensive drugs used in fixed dose combinations are as shown in Figure 5.

Figure: 5 Antihypertensive drug class prescribed in Fixed Dose Combination therapy.
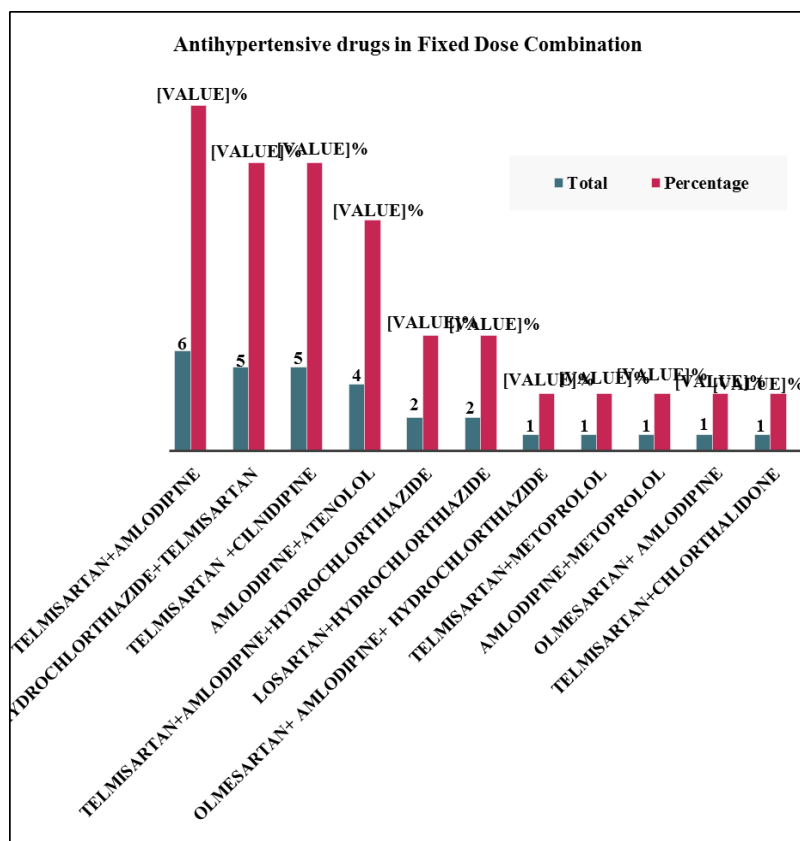
Figure: 6 Antihypertensive drugs in Fixed Dose Combination.

d) Number of antihypertensive drugs per prescription

On the basis of data collected for prescribing patterns for antihypertensive drugs, 48.67% of prescriptions were prescribed with one antihypertensive, 29.33% of prescriptions had two antihypertensives, 13.33% of the prescriptions had three antihypertensives and 8.67% had 4 antihypertensives, as illustrated in Figure 7.
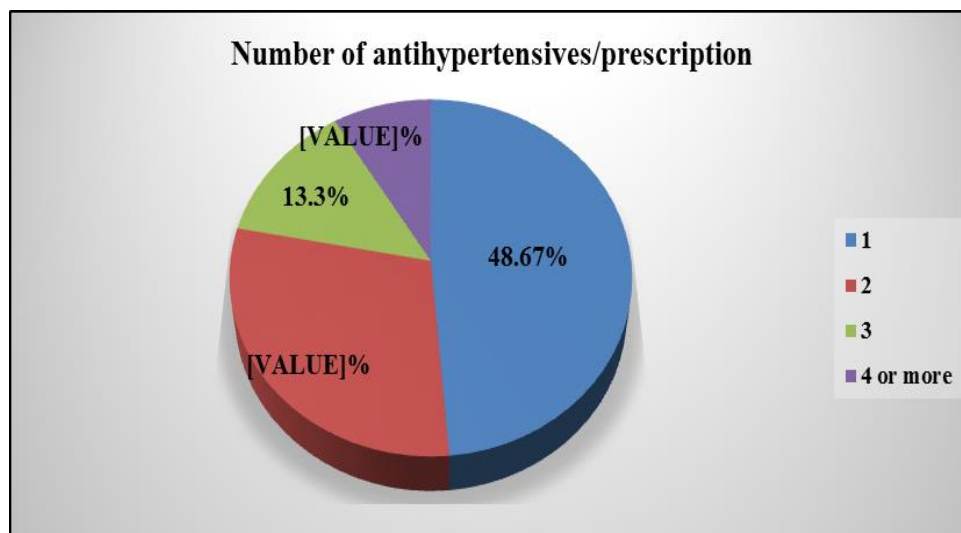
Figure: 7 Number of antihypertensives per prescription.

e) Class of drugs prescribed other than antihypertensive

Out of 150 prescription, 15.42% of the drugs were gastroprotectant, 14.01% were antibiotics, 11.31% were analgesics, 9.25% antidiabetics, 6.56% multivitamins, 6.04% antiemetics, 5.66% antiplatelet, 5.27% lipid lowering agents, 4.76% electrolytes, followed by anxiolytics/ antidepressants, thyroid preparations, anticholinergics constituting 3.08%, 1.80%, 0.51% respectively, as in Figure 8.

Figure: 8 Class of drugs prescribed other than antihypertensives.

DISCUSSION

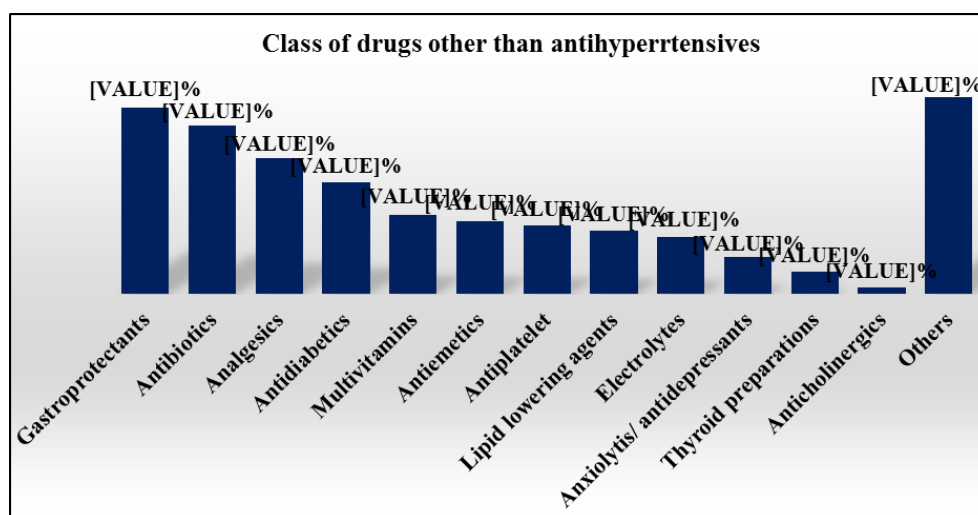According to the study, 66% [N=99, M=57, F=42] of hypertensive subjects were of above 60 years of age, which was similar to the study conducted by Ramakrishnan S *et al.*, where prevalence increased with age; especially in those with age ≥65 years.[5] The specific underlying mechanisms of HTN in older persons, includes mechanical hemodynamic changes, arterial stiffness, neurohormonal and autonomic dysregulation, and the aging of kidney.[6]

As stated in the study, the prevalence of hypertension was seen more in males (54%) compared to females (46%) which corresponds to the findings of similar study performed by Connelly PJ *et al.,* where the prevalence of hypertension was more in men (34.6%) than in women (30.8%). In reference to the study, prevalence of HTN in male was seen more compared to female, particularly with the age group below 40 years [male- 4%[N=6], female- 0%] where all were male, but during the fourth decade of age, the rate of developing HTN in female was high compared to male. Similar result was found in a study where males continue to have higher rates of this condition (18–39 years: 31.2 vs 13.0%; 40–59 years: 59.4 vs

49.9%; over 60 years: 75.2 vs 73.9%); however, the rate at which females develop hypertension is much steeper compared to males.[7] The older the participants were, the more likely they were to have hypertension.[8]

Observed gender differences in hypertension, which exist in human and animal populations, are due to both biological and behavioural factors.[9] The biological factors include sex hormones, chromosomal differences, and other biological sex differences that are protective against hypertension in women.[10] Nevertheless, with increasing age, the females' advantage of protection against hypertension is lost and the development of hypertension accelerates when compared to males.[11]

According to a study carried out by Moges B *et al.,* the prevalence of overweight based on calculated body mass index (BMI) was 32.4% (22/68) while the prevalence of obesity was 16.2% (11/68).[12] Similarly, in conforming to the present study, 37.3% of sample were overweight and 14.67% were obese.

Even though the mechanisms of obesity-induced hypertension are still being meticulously scrutinized, research in experimental animals and humans recommend vital roles for impaired renal-pressure natriuresis due to physical compression of the kidneys and activation of the Renin Angiotensin Aldosterone System and Sympathetic Nervous System. As obesity and its metabolic and hemodynamic consequences are sustained during many years, renal injury gradually makes the hypertension more severe and more resistance to therapy.[13]

A study by Shukrala F *et al.,* reported that out of 400 samples, most of the patients had Stage 1 hypertension (69%), followed by Stage 2 hypertension (31%).[14] Similarly, in accord with this study, 34% had Stage 1 HTN, 25.33% had stage 2 HTN, 19.33% had Hypertensive Crisis, 11.33% had prehypertension and 10% of the subjects had their blood pressure under control.

As per the study, CCBs were the most prescribed drugs, which correlates with the study by Anuradha VP *et al.,* where out of 1070 prescribed drugs, CCBs were the most prescribed drugs (26.26%), followed by ARBs (23.27%), followed by Beta blockers, Diuretics, ACE inhibitors, Centrally acting sympatholytic and vasodilators.[15]

The most frequently prescribed antihypertensive drug as monotherapy and in Fixed Dose Combination was calcium channel blocker-Amlodipine (51.81%) which correlates to the

study done by Naik HG *et al.,* where it was found, Amlodipine (49%) is the most frequently prescribed antihypertensive.[16]

Tolerance and compliance will also be elevated with the help of fixed low dose combination resulting in fewer side effects. However, recently published evidence indicated an increase in use of Calcium Channel Blockers (CCBs) and Angiotensin Converting Enzyme Inhibitors (ACEIs) are noted compared to diuretics and beta blockers in lowering morbidity and mortality of cardiovascular diseases.[16]

CONCLUSION

Present study concludes that, multiple individual drugs among hypertensive subjects were more prevalent hence polypharmacy was observed. This can be reduced by prescribing Fixed Dose Combinations. Prescribing drugs using generic names, decreases medical confusion and allows selection of better alternatives.

MERITS OF THE STUDY

- The study was conducted among hypertensive subjects, chosen according to inclusive criteria, hence providing sufficient data.
- This study provides information regarding the most commonly used antihypertensive drugs in monotherapy and combination.

LIMITATIONS OF THE STUDY

- Limited duration of the study.
- Relatively small number of samples.
- Data was collected only from inpatients case files.
- As the study has focused on a specific institution, it may be difficult to generalize the findings.

ACKNOWLEDGEMENTS

REFERENCE

1. Olanrewaju TO, Aderibigbe A, Busari OA, Sanya EO. Antihypertensive drug utilization and conformity to guidelines in a sub-Saharan African hypertensive population. Int J Clin Pharmacol Ther., 2010 Jan; 48(1): 68-75.

2. Solanki ND, Patel P. drug utilization pattern and pharmacoeconomic analysis of antihypertensive drugs prescribed in secondary care Hospital in Gujarat, India. Asian J Pharm Clin Res., 2017 Mar. 1; 10(3): 120-4.

3. Jainaf NRAM, Parimalakrishnan S, Ramakrishna RM. Study on drug utilization pattern of antihypertensive medications on out-patients and inpatients in a tertiary care teaching hospital: A cross sectional Study. Afr J Pharm Pharmacol, 2015 Mar 22; 9(11): 383–96.

4. Geetha S, Aithal S, Balaji V, Swetha ES. Analysis of drug utilization pattern among hypertensive patients admitted to medical intensive care unit of a tertiary care hospital. World J. Pharm. Res., 2015; 4(3): 1320-30.

5. Oliveros E, Patel H, Kyung S, Fugar S, Goldberg A, Madan N, et al. Hypertension in older adults: Assessment, management, and challenges. Clin Cardiol, 2020 Feb; 43(2): 99–107.

6. Connelly PJ, Currie G, Delles C. Sex differences in the prevalence, outcomes and management of hypertension. Curr Hypertens Rep., 2022; 24(6): 185–92.

7. Choi HM, Kim HC, Kang DR. Sex differences in hypertension prevalence and control: Analysis of the 2010-2014 Korea National Health and Nutrition Examination Survey. Spracklen CN, editor. PLOS ONE., 2017 May 25; 12(5): e0178334.

8. Sandberg K, Ji H. Sex differences in primary hypertension. Biol Sex Differ., 2012 Mar 14; 3(1): 7.

9. Everett B, Zajacova A. Gender Differences in Hypertension and Hypertension Awareness Among Young Adults. Biodemography and Social Biology, 2015 Jan 2; 61(1): 1–17.

10. Moges B, Amare B, Fantahun B, Kassu A. High prevalence of overweight, obesity, and hypertension with increased risk to cardiovascular disorders among adults in northwest Ethiopia: a cross sectional study. BMC Cardiovasc Disord., 2014 Nov 5; 14(1).

11. Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity-Induced Hypertension. Circ. Res., 2015 Mar 13; 116(6): 991–1006.

12. Shukrala F, Gabriel T. Assessment of prescribing, dispensing, and patient use pattern of antihypertensive drugs for patients attending outpatient department of Hiwot Fana Specialized University Hospital, Harar, Eastern Ethiopia. Drug Des Devel Ther., 2015 Jan 17; 9: 519-23.

13. Shrestha B, Dixit SM. The Assessment of Drug Use Pattern Using WHO Prescribing Indicators. J Nepal Health Res Counc., 2018 Oct 30; 16(3): 279-284.

14. Satish S, Rose AJ, Shabaraya AR. A study to assess the impact of comorbidities and polypharmacy in nonadherence to antihypertensives. International Journal of Research and Review, 2021; 8(2): 222-227.

15. Naik HG, Harshitha CS. Study on antihypertensive drug utilization in a tertiary care hospital. Natl J Physiol Pharm Pharmacol, 2019; 9(11): 1063-7.

16. Nguyen TP, Nguyen TB, Nguyen TT, Vinh Hac V, Le HH, Schuiling-Veninga C, Postma MJ. Direct costs of hypertensive patients admitted to hospital in Vietnam- a bottom-up micro-costing analysis. BMC Health Serv Res., 2014 Oct 28; 14: 514.