

## Research Article

## Drug Utilization Pattern of Antihypertensive Drugs at Tertiary Care Teaching Hospital

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**Abstract : Background:** Hypertension is a global public health issue. It is a significant contributor to rising morbidity and mortality because of its associations with cardiovascular, renal and cerebrovascular complications. A drug utilization review on antihypertensive drugs should be done to determine different classes of antihypertensive medications with respect to diagnosis. Aim was to study drug utilization pattern of antihypertensive medication in a tertiary care teaching hospital. **Methods:** This is a prospective, observational and descriptive study conducted between September 2020 to February 2021 at outpatient Department of General Medicine, Dr. VRK Women's Medical College Teaching Hospital & Research Center. Prescriptions of 130 patients of either sex and age >18 years who have been diagnosed with hypertension as per JNC-8 guidelines and patients receiving or prescribed with antihypertensive medications were included. **Results:** The highest age group patients were between 51-60 years accountable 27.4 % and least age group patients were between 18-30 years 8.1 %. The gender ratio of the patients' male: female was found to be 1.2:1. Out of the 135 patients, 64.4 % (83) of patients were male and 38.5 % (52) of patients were female. Test of proportion showed that the male patients were slightly more than the female patients. Most of the patients 53 (39.2%) were significantly higher systolic blood pressure ranging between 160-179 mmHg (Stage 2 HTN) and least patients were emergency hypertensive were 5.1 %. Most of the patients 73 (54.0%) were on Mono therapy significantly higher than dual therapy, triple therapy and poly therapy, 36 (26.6%), 17 (12.5%), 9 (6.6%) respectively. Calcium channel blocker was the frequently used class of drug for monotherapy (17.0 %). In dual drug therapies were CCB+ARB accounting for 13.3 %, and 8.1% of patients were on triple drug therapy with CCB+ARB+Diuretic. Causality assessment of ADRs was done using WHO-UMC scale shows that type of reactions and their percentage are as certain (19.3 %), Probable/ Likely (67.7%), Possible (9.6 %) and Unlikely (3.2 %). **Conclusion:** Large differences in utilization of different groups of antihypertensive agents were noted in this study. This type of studies gives the base line idea of prescription pattern and ADRs of antihypertensive drugs. These helps to design policy for rational use of drugs and motivation of physician for rational use of drugs.

**Keywords:** Antihypertensive, Drug utilization, Adverse drug reaction.

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### INTRODUCTION

Hypertension is a highly prevalent chronic health condition with its devastating consequences on the heart and cardiovascular system. Blood pressure varies from person to person, and from time to time for individuals, however, if the blood pressure is constantly elevated above 140/90 mmHg at different times of measurement, it is regarded as high blood pressure (hypertension) [2]. In the year 2000 hypertension was estimated to affect almost one billion patients worldwide. Prevalence is predicted to increase by approximately 60% by 2025 [3].

A number of national and international guidelines for the treatment of hypertension have been published. The most recent JNC 8 guideline recommends diuretics as the first-line treatment in hypertension [4, 5]. Due to high prevalence of hypertension and the requirement of medications for prolonged periods, the drug treatment cost poses a major issue in health economics. In developed countries, the expenditure on antihypertensive therapy has increased sharply in recent years due to increasing use of newer and more expensive drugs such as calcium-channel blocking agents, angiotensin-converting enzyme inhibitors and angiotensin-receptor antagonists [6].

Changes over time in terms of recommended guidelines and innovations in drug formulations have resulted in modifications to the prescription patterns of antihypertensive drugs. Availability of numerous antihypertensive gives physicians several options to individualize the therapy [7]. Due to this fact there is change in the prescribing pattern from patient to patient and physician to physician. The reason for this variation in the prescribing pattern is due to the conflict of interest of physicians [8].

The World Health Organization (WHO) defines drug utilization research as “the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences” [9]. Thus, inherent in the definition, such studies provide logical background for determining the rationality of drug use as well as providing evidence based guidance for making policy decisions at various levels of healthcare [10]. Drug utilization research studies conducted in the inpatient settings are effective tools that help in evaluating the drug prescribing trends, efficiency, and cost-effectiveness of hospital formularies. There is always a variation in drug utilization among different countries and even among health institutions within a country and sometimes within the same institute at different point of time probably because of changing disease trends over a period of time [11].

## MATERIALS AND METHODS

This is a prospective, observational and descriptive study conducted between September 2020 to February 2021 at outpatient Department of General Medicine, Dr.VRK Women's Medical College Teaching Hospital & Research Center. Prescriptions of 130 patients of either sex and age >18 years who have been diagnosed with hypertension as per JNC-8 guidelines and patients receiving or prescribed with antihypertensive medications were included. Patients in emergency, life threatening medical or surgical conditions, pregnant and lactating women and patients with incomplete data were excluded. The patient's sociodemographic profile, receiving or current prescribing patterns of antihypertensive medications were recorded in a predesigned data collection record form. Those receiving or with prescription of a one active principle medication was considered as monotherapy and those receiving or prescription of a more than one active principle medications were defined as a polytherapy.

The main aim of study was evaluating the different classes of antihypertensive medications with respect to diagnosis and to carry out the drug utilization review in hypertension with its different combinations. Patient's demographics, type of antihypertensive drug prescribed, lab reports, detailed medical history, concomitant medications for co morbid diseases were

recorded. Frequency of drug prescription among different age groups, frequency of administration of individual drugs, frequency of prescribing combination drugs, frequency of prescribing fixed drug combinations, number of prescriptions per drug, number of drugs prescribed per total number of prescription, percentage of patients in the treatment of hypertension with comorbidities, percentage of economic difference, percentage of expenditure cost, and average drug acquisition cost (ADAC) were calculated.

## ADVERSE DRUG REACTIONS

In the present study, causality assessment between the drug and suspected reaction was determined by using WHO-UMC Scale, Naranjo Scale and Hartwig and Siegel scale. According to Naranjo Criteria, the ADRs are analysed on the basis of a questionnaire comprising 10 questions in which each question is given a score of +2, +1, 0 or -1 depending on the analysis. When total if the score is >9 – labelled as definite ADR, if 5-8 – probable ADR, if 1-4 – possible ADR, if 0 – doubtful ADR.

## STATISTICAL ANALYSIS

Data was analysed using the software, Statistical Package for Social Sciences (SPSS for windows. Version 25 software. Percentage describes categorical data mean±standard deviation (SD) describes continuous data Subjects were recruited in the study. All drug related adverse events were evaluated according to the “WHO causality Assessment Scale” was used to describes causality of adverse drug event into adverse drug reaction.

## RESULTS

### Age distribution of patient

In table 1, the highest age group patients were between 51-60 years accountable 27.4 % and least age group patients were between 18-30 years 8.1 %.

**Table-1: Distribution of age group**

Age group in years	No. of patients (n=135)	Percent
18-30	11	8.1
31-40	31	22.9
41-50	33	24.4
51-60	37	27.4
>61	23	17.0

**Table-2: Distribution of gender**

Gender	No. of patients	Percent
Male	83	61.4
Female	52	38.5

### Gender distribution of patient

In table 2, the gender ratio of the patients' male: female was found to be 1.2:1. Out of the 135 patients, 83 (61.4%) of patients were male and 52 (38.5%) of patients were female. Test of proportion showed that the male patients were slightly more than the female patients.

**Table-3: Duration of hypertension**

Duration in years	No. of patients	Percent
< 3 years	69	51.1
4-6 years	41	30.3
> 7 years	25	18.5

### Duration of hypertension

In table 3 shows that 69 (51.1%) patients were between < 3 years, 41 (30.3%) patients were between 4-6 years and 25 (18.5%) were having history of >7 years.

**Table-4: Distribution of Systolic blood pressure**

Systolic blood pressure (mmHg)	No. of patients	Percent
120-139 (Pre HTN)	34	25.1
140-159 (Stage 1 HTN)	41	30.3
160-179 (Stage 2 HTN)	53	39.2
>180 (HTN emergency)	7	5.1

### Systolic blood pressure distribution in patients

In table 4 depicts most of the patients 53 (39.2%) were significantly higher systolic blood pressure ranging between 160-179 mmHg (Stage 2 HTN) and least patients were emergency hypertensive were 5.1 %.

**Table-5: Distribution of Diastolic blood pressure**

Diastolic blood pressure (mmHg)	No. of patients	Percent
80-89 (Pre HTN)	31	22.9
90-99 (Stage 1 HTN)	37	27.4
100-119 (Stage 2 HTN)	59	43.7
>120 (HTN emergency)	8	5.9

### Diastolic blood pressure distribution of patients

In table 5, test of proportion showed most of the patients 59 (43.7 %) were significantly higher diastolic blood pressure ranging between 100-119 mmHg and least patients were emergency hypertensive were 5.9 %.

**Table-6: Distribution of drug therapy**

Drug Therapy	No. of patients	Percent
Monotherapy	73	54.0
Dual therapy	36	26.6
Triple therapy	17	12.5
Poly therapy	9	6.6

### Drug therapy distribution among patients

In table 6 shows most of the patients 73 (54.0%) were on Mono therapy significantly higher than dual therapy, triple therapy and poly therapy, 36 (26.6%), 17 (12.5%), 9 (6.6%) respectively.

**Table-7: Utilization pattern of different antihypertensive drugs**

Treatment	No. of patients use antihypertensive drug	Percent
<b>Monotherapy</b>		
Calcium channel blocker	23	17.0
ARB	17	12.5
ACE Inhibitor	9	6.6
Beta Blocker	19	14.0
Alpha Blocker	2	1.4
Diuretics	3	2.2
<b>Dual therapy</b>		
CCB+ARB	18	13.3
CCB+Beta Blocker	11	8.1
CCB+ Diuretic	5	3.7
ARB+ Diuretic	2	1.4
<b>Triple therapy</b>		
CCB+ARB+Diuretic	11	8.1
CCB+B Blocker+Diuretic	6	4.4

### Utilization pattern of different antihypertensive drugs

In table 7, Calcium channel blocker was the frequently used class of drug for monotherapy (17.0 %). In dual drug therapies were CCB+ARB accounting for 13.3 %, and 8.1% of patients were on triple drug therapy with CCB+ARB+Diuretic.

**Table-8: WHO causality assessment of ADRs**

Type of reaction	No. of patients reported ADR (31)	Percent
Certain	6	19.3
Probable/likely	21	67.7
Possible	3	9.6
Unlikely	1	3.2
Conditional/unclassified	-	-
Unassessable/unclassifiable	-	-

In table 8, among 135 patients only 31 patients experienced ADRs. Causality assessment of ADRs was done using WHO-UMC scale which categorizes ADRs as "certain", "probable", "possible" and "unlikely". Table 8 shows that type of reactions and their percentage are as certain (19.3 %), Probable/ Likely (67.7%), Possible (9.6 %) and Unlikely (3.2 %).

**Table-9: Severity of reported ADRs by modified Hartwig and Siegel scale**

Type of reaction	No. of patients reported ADR (43)	Percent
Lethal	-	-
Severe	1	3.2
Moderate	7	22.5
Mild	23	74.1

In table 9, it was found that from all ADRs, reported (74.1 %) were mild, (22.5 %) moderate and only (3.2 %) was classified as severe.

**Table-10: Common ADR Reported**

Class of drugs	Adverse events experienced	No of patients (31)	%
CCB	Pedal edema, giddiness, headache, abdominal pain, bradycardia	8	25.8
ARB	Anxiety, Nausea and Vomiting, Headache, Abdominal pain, Restlessness, Itching and inflammatory swelling	6	19.3
ACE Inhibitor	Dry cough, dizziness, headache, drowsiness, diarrhea, hypotension, weakness, cough, rash, metallic or salty taste.	11	35.4
Beta Blocker	Constipation, nausea and vomiting, headache, hypoglycemia, postural hypotension	3	9.6
Diuretics	Hypotension, muscle cramps, headache vertigo, pain in legs, dysuria	2	6.4
Other	Skin reaction	1	3.2

Total 31 patients were reported ADR. 35.4% patients were on ACE inhibitors. 25.8 % patients receiving Calcium channel blocker reported side effect.

## DISCUSSION

The WHO defines drug utilization studies as “the marketing, distribution, prescription and the use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences.” Prescription pattern surveys are an important methodological instrument of drug utilization studies, which help provide an in-depth insight into the disease profile of patients and prescribing behaviour of clinicians. Hypertension is a serious public health problem worldwide [12]. It is the leading cause of death in the world and is the most common cause for outpatient visits to physicians [13].

In this study, the maximum number of patients, were from the age group of 51-60 (27.4%) years followed by 41-50 (24.4%) and least number in 18-30 (8.1%) years of age of patients are from this age group. Whereas, total 135 patients were there, including 83 (61.4%) males and 52 (38.5%) females (Table 2) and showing a predominance of male population. The hypothetical cause of higher number of male patients is elevated levels of androgen such as testosterone as they play a role in elevation of blood pressure [14]. A similar study was also conducted by Paradkar SG, et al, which is supporting this study [15].

The present study observed that single-drug therapy (54.0 %) as a CCBs was more commonly employed than multiple-drug therapy. These results

support the work of Adake P et al. which showed blood pressure could be adequately controlled with the help of single-drug therapy [16]. This might be attributed to patient’s compliance, good response, and less incidence of adverse effects. In a study by Kale A et al, CCBs were found to be the most frequently used group of drugs which is parallel to findings of our study [17]. In our study, BBs were prescribed most frequently next to CCBs the findings of which are similar to the study performed in a tertiary care hospital of India by Shah J PR et al [18].

In this present study, it was observed that there was a significant change in antihypertensive prescribing pattern with a considerable increase in the frequency of intake of CCBs, ARBs, ACEIs and BBs. These observations line with other study [19]. CCBs and ARBs constitute the most frequently prescribed antihypertensive drug class. Increased prescription of ARBs and CCBs probably suggest that clinicians are more aware of the long term cardiovascular and renovascular benefits. The prescriptions were also in accordance with the evidence and the guidelines, as these medications will reduce the chance of occurrence of diabetic nephropathy, retinopathy and other related complications in diabetes patients. When calcium channel blockers were concerned the most commonly prescribed drugs were the dihydropyridine type of calcium channel blockers (ie., Amlodipine), whereas the prescription of non-dihydropyridine type of calcium channel blockers was very less.

Observations on combination therapy reflect that the most commonly prescribed drugs in combination were diuretics (i.e., Thiazide and

potassium sparing diuretic groups). The joint national committee on prevention, detection, evaluation and treatment of High blood pressure (JNC-8) report notes that volume overload due to inadequate diuretic therapy is one of the commonest reason for resistance observed in HTN treatments [20]. So, there is a paradigm shift towards increased prescribing of combination therapy. The present observational study depicts that the patients with co-morbidity were prescribed one or two antihypertensive along with other medications to treat their associated diseases such as diabetes mellitus, IHD, CVA and Bronchial asthma. In a study by Hussain IM et al, the most commonly prescribed antihypertensive among elderly patients was Amlodipine [21]. This is also in consonance with the recommendations of the JNC on Prevention, Detection, Evaluation, and Treatment of high blood pressure guidelines which state that low dose of different classes of antihypertensive drugs is more beneficial than a high dose of one [22].

According to WHO-UMC Scale maximum number of ADRs in probable class followed by possible, unlikely and certain class. Moreover, as per the modified Hartwig and Siegel's scale maximum number of ADRs was mild category and lowest in severe type of reaction was observed in this study. No ADRs were found in lethal type of reaction. These findings were consistent with the literature reported by Rachana PR et al, Total 31 patients were reported ADR [23]. In our study, 35.4 % patients were on ACE inhibitors. 25.8 % patients receiving Calcium channel blocker reported side effect.

Finally, the strength of this study lies firstly in the unparalleled period of consideration (8 months). Earlier studies have been characterized by a relatively short period of consideration (usually not exceeding 3 months) with a tangible majority of them having comparatively smaller sample sizes [24]. It is noteworthy also that there is no prior study of this kind in a secondary healthcare setting. Furthermore, the result of this study represents a much more recent (and arguably more reliable) assessment of the subject matter and, as such, is hoped to not only merit publication but also attract attention as a renewed, data-driven basis for further research in the management and control of hypertension, ultimately.

## CONCLUSION

In conclusion, our study analysed the drug utilization of antihypertensive medication and found that the prescribing pattern was totally consistent with the JNC 8 (the Eighth Report of the JNC on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) guidelines for the treatment of hypertension. Monotherapy was consistently more recommended in the early stages of hypertension to achieve target goal of blood pressure, and CCBs were the drugs of choice for hypertensive patients.

The knowledge and prescription of drug was concluding to be the base line idea of ADRs of antihypertensive drugs in hypertensive patients visiting OPD of tertiary teaching care hospital in India. In this study, we can say that all of the prescriptions found were rational; furthermore, more changes are needed to be done in prescription of antihypertensive drugs are needed in drug prescribing practices in hypertensive patients. Patients are needed to provide information and proper counselling regarding the ADRs of drugs; this would refine the quality of life.

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