

## A Cross Sectional Study on Prescription Pattern and Combination Drug Therapy in Hypertension Among Patients Visiting Alka Hospital Kathmandu

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### Abstract

**Background:** The sources of drug usage data vary from country to country depending on the level of sophistication of medical record keeping, data collection, data analysis, reporting and the operational considerations of the health care system. In the majority of the countries, different physicians' prescribing patterns for anti-hypertensive medications widely differ from the established standards.

**Objective:** The objective of this study was to assess the prescription pattern and practice of combination drug therapy of anti-hypertensive medicines in Alka Hospital, Kathmandu.

**Method:** The medical record of patients who received anti-hypertensive drugs during their treatment periods were reviewed. Data entry was done in MS Excel data sheet and data were analyzed in SPSS. The total number of prescriptions analyzed was 112.

**Results:** The maximum percentage of males and females with hypertension was found in the age group of 40-60 years. As mono therapy Angiotensin II Receptor Blockers (ARBs) (39.28%) were the most commonly prescribed anti-hypertensive followed by Calcium Channel Blockers (CCBs) (8.92%) and Angiotensin Converting Enzyme Inhibitors (ACEIs) (0.89%). In combination therapy often two drugs combination was prescribed. The most common combination was ARBs + CCBs (24.1%), followed by ARBs + Diuretics (6.25%).

**Conclusion:** The prevalent prescribing pattern of antihypertensive in Alka Hospital seems to be in compliance with Joint National Committee VIII (JNC VIII) guidelines.

**Keywords:** Hypertension, Antihypertensive Drugs, Mono-therapy, Combination Therapy

### Introduction

Hypertension is a serious public health issue across the world, and it is a key contributor to the development of non-communicable illnesses, particularly cardiovascular disease [1]. A persistent systolic blood pressure of 140 mm Hg or a sustained diastolic blood pressure of 90 mm Hg is considered hypertension. Hypertension results from increased peripheral vascular smooth muscle tone, which leads to increased arterial resistance and reduced capacitance of venous system. Although it is not a disease in itself, it

is a significant risk factor for cardiovascular mortality and morbidity. Epidemiological studies have confirmed that higher is the blood pressure greater is the risk of cardiovascular diseases. It is linked to functional and structural cardiac and vascular disorders that could affect the heart, kidneys, brain, vasculature, and other organs, resulting in premature morbidity and mortality [2]. According to JNC VIII guidelines the Blood Pressure is classified as below [3]:

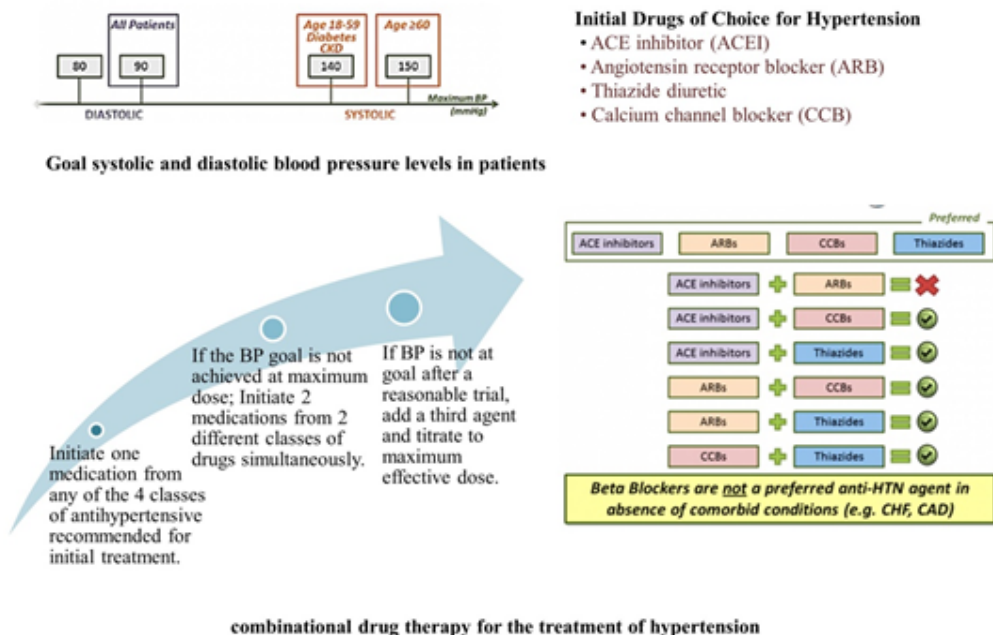
**Table 1: Blood Pressure Classification in Adults Above 18 Years**

Classification	Systolic Blood Pressure		Diastolic Blood Pressure
Normal	<120	and	<80
Prehypertension	120–139	or	80–89
Stage one HTN	140–159	or	90–99
Stage two HTN	≥160	or	≥100

Hypertension therapy has been shown to lower the cardio-vascular risks. Many studies have proven the effectiveness of therapy for major risk factors like myocardial infarction, heart failure, stroke, dementia, kidney disease, and progressive atherosclerosis [4]. As a result; several guidelines have been developed by relevant authorities in various countries to aid physicians in making the best

blood pressure (BP) control decisions. The WHO 2021 Hypertension Guidelines contain current proposals for the threshold for initiation of drug treatment for hypertension, proposed follow-up intervals, target blood pressure to be achieved for monitoring, and the number of healthcare professionals who can initiate treatment. This gives rise to the choice of whether to start treatment with monotherapy, dual therapy, or the combination of drug in one tablet [5]. To accomplish BP goal, JNC VIII guidelines recommend both changes in lifestyle and medication. Thiazide diuretics are indicated as the first choice of medication for most patients with uncomplicated hypertension, based on data from the recently completed Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) and previous studies [6]. The basic BP treatment objective, according to JNC VIII, is to decrease systolic BP to less than 140 mm Hg and diastolic BP to less than 90 mm Hg.

**Overview of JNC VIII guidelines for treatment of hypertension**



**Figure 1: The JNC 8 Hypertension Guidelines: An Overview**

The main aim of this study is to assess the prescription pattern and extent of practice of combination drug therapy of anti-hypertensive medicine in Alka Hospital, Kathmandu, Nepal.

**Methodology**

**Research Design and Study Setting**

This research was a cross sectional descriptive study. New patients along with the patients who visited for regular check up in the Alka Hospital were included.

**Data Collection Tools and Sampling Technique**

The required information was noted from the prescription of the patients in questionnaire form. Purposive non-probability sampling was done. The sample size was determined by  $n = Z_{\alpha/2}^2 * P * (1-P) / d^2$  where, n is the sample size,  $\alpha/2$  = level of significance at 95% confidence interval thus  $Z_{\alpha/2} = 1.96$ , P is the predicted prevalence of hypertension which is supposed to be 50%, thus  $p=0.5$  and d is precision ( $d=0.4$ ). The sample size was calculated and was found to be 114. For a better result, data was collected until saturation of response was observed, then repetitive and erroneous data was removed.

## Study Period and Study Population

The data was collected from Bidhya Alka Pharmacy, Alka Hospital from 20th Feb. 2019 - 3rd March 2019. Patients of age group >20 years were included in study. The visiting patients with hypertension with other ailments like cardiovascular disease, diabetes mellitus, asthma or treated with combination therapy were also included in study. However, pregnant women and patients with liver disorder or having other opportunistic infection were excluded from the study.

## Data Analysis

All the data collected from Alka Hospital was coded as per variables, entered in MS Excel data sheet and analyzed with the help of statistical software SPSS. The analyzed data was expressed through tables and graphical presentation. As this study is a cross-sectional study, the frequency and percentage distribution were being calculated for all variables.

## Ethical Approval

The study protocol was reviewed by the institutional ethical committee of Janmatri Foundation Institute of Health Science (Ref. No. 01/2019). Based on the study protocol, the Clinical Expertise Centre concluded that this research lies outside the scope of the Medical Research Involving Human Subjects Act. The verbal consent was obtained from each participant prior to data collection. The participants' anonymity was guaranteed throughout the research. There was no discrimination on the basis of cast, religion, socioeconomic status etc. The participants were informed about the purpose and objectives of the study. Participants were assured that the collected data was used only for research purpose.

## Results

### Demographic Characterization

During the study period, a total of 112 hypertensive patients fulfilled the criteria for inclusion in the study analysis. Out of the 112 hypertensive patients 49% were male and 51% female, indicating that hypertension is slightly more prevalent in the female gender (Figure 2). The average age of the patients was  $55.58 \pm 12.21$ . The age distribution of hypertensive patient was 8.05% below the age of 40 years, 60.71% were between 40 and 60 years and 31.25% were above 60 years. The maximum number of male hypertensive patients belonged to the age group of 51-60 years followed by the age group 41-50 years. The maximum number of hypertensive patients belonged to the age group of 41-50 years followed by the age group 51-60 in female patients (Figure 3).

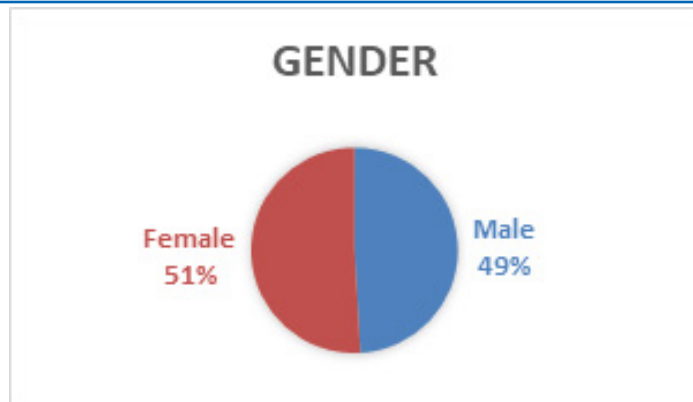


Figure 2: Demographic Characteristics of Hypertensive Patients

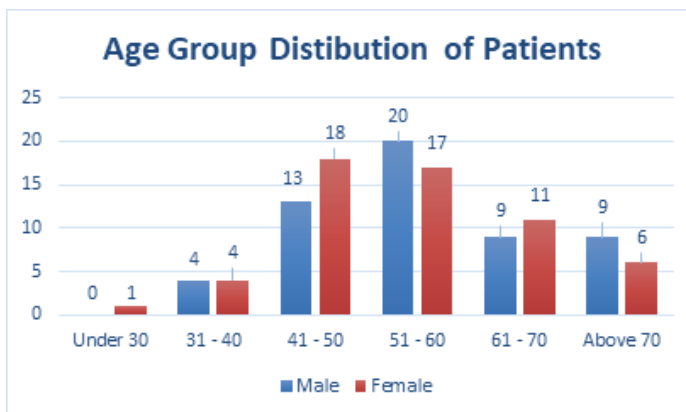


Figure 3: Age Group Distribution of Hypertensive Patients

### Patterns of Use of Various Classes of Antihypertensive Drugs

The prescription pattern and rate of antihypertensive drug prescribed for hypertensive patients both as mono-therapy and overall utilization profile (mono and combined therapies) were noticed. Among the mono-therapy category, the various classes of drugs used were as follows Angiotensin II Receptor Blockers (80%), Calcium Channel Blockers (18.18%) and ACE Inhibitors (1.82%).

Losartan Potassium (24.1%) was the most commonly prescribed antihypertensive agent as mono-therapy followed by Telmisartan (15.18%). However, in case of overall utilization pattern of antihypertensive agents, Angiotensin II Receptor Blockers (50.57%) were the most frequently prescribed class, Calcium Channel Blockers (26.44%) ranked second followed by Diuretics (13.22%),  $\beta$ -Blockers (7.47%) and ACE Inhibitors (1.73%) (Table 2).

**Table 2: Patterns of Use of Various Classes of Antihypertensive Drugs**

Antihypertensive Drugs	Overall Prescription Frequency (%)	Mono-therapy Prescription Frequency (%)
ACE Inhibitors	3 (1.73)	1 (1.81)
Angiotensin II Receptor Blockers	88 (50.57)	44 (80)
Calcium Channel Blockers	46 (26.44)	10 (18.18)
Diuretics	23 (13.22)	0
β-Blockers	13 (7.47)	0
α-Blockers	1 (0.57)	0

### Combinational Drug Therapy as Treatment of Anti-Hypertension

The result unfolds the fact that only 49% patients received mono-therapy. The majority (51%) were on the multiple drug therapy. Out of which 37.5% patients received two drug therapies, 10.7% patients received three drug therapy and 5.2% patients received four drug therapy. The average number of drugs prescribed was  $1.67 \pm 0.77$ .

The most prevalent combination of drug was a 2-drug therapy of CCBs + ARBs which was found to be 24.1% followed by ARBs + Thiazide diuretics (6.25%). Among the three drug combinations: ARBs, Diuretics and Calcium Channel Blockers comprised the most commonly prescribed combination. ARBs, Thiazide diuretics and CCBs comprise 3.57% of total prescription followed by ARBs, and two class of Diuretics (Thiazide diuretics + Spironolactone diuretics) 2.67%. (Table 3).

**Table 3: Patterns of Use of Antihypertensive Combination Therapy**

Drug Therapy Prescribed	Number of Prescriptions	Percentage (%) of Prescriptions	
Single Drug Therapy	55	49	
<b>Multiple Drug Therapy</b>			
2 Drug Therapy	42	73.68	
3 Drug Therapy	12	21.15	
4 Drug Therapy	3	5.27	
Total	57	51	
Combination Therapy Drug Regimen	No. of Prescriptions	Percentage (%) of Total Prescriptions	Percentage (%) of Receiving Combination Therapy
<b>Two Drug Combination</b>			
ARBs + CCBs	27	24.1	47.36
CCBs + β-Blockers	5	4.46	8.77
ARBs + Thiazide diuretics	7	6.25	12.28
ARBs + β-Blockers	1	0.89	1.75
Thiazide diuretics + Spironolactone diuretics	1	0.89	1.75
β-Blockers + α-Blockers	1	0.89	1.75
<b>Three Drug Combination</b>			
ARBs + CCBs + Thiazide diuretics	4	3.57	7.01
ARBs + Thiazide diuretics + Spironolactone diuretics	3	2.67	5.26
ARBs + CCBs + β-Blockers	2	1.78	3.5
ARBs + β-Blockers + Thiazide diuretics	2	1.78	3.5
ACIs + Thiazide diuretics + Spironolactone diuretics	1	0.89	1.75

## Discussion

The result of study shows that hypertension is more prevalent in females 57 (51%) than in males 55 (49%). The aforementioned tendency is consistent with a prior Indian research, which found that 54.6% percent of hypertension patients were female, while 45.4% percent were male [7].

The key causes of this growth appear to be increased salt consumption and an increase in body mass index. There is a very high frequency as well as a quick rise in HTN prevalence in Nepali society as a result of changing lifestyle, which is most likely due to socioeconomic transformation [8].

For age group distribution of patients, most of hypertensive patients were in the age group of between 40-60 years was 42.85%. Likewise, in the age group of below 40 years were 8.03%, and patients in the age group above 60 years were 31.25%. In a systematic research of the prescription pattern of antihypertensive medicines in a tertiary care hospital in Bangalore, the study also found that the majority of hypertension patients were between the ages of 40 and 60. It also reveals a greater prevalence of hypertension in elderly (those above the age of 40) [9]. The main reason for this might be that as one gets older, there is a greater probability of acquiring HTN and having a high coronary risk [10].

In our analysis, the average number of antihypertensive medications administered per prescription is only  $1.67 \pm 0.77$ , which is close to the 1.8 reported before. During the research period, no generics were prescribed because the hospital does not have its own formulary and the medicines are acquired from an in-house retail pharmacy. The majority of antihypertensive prescriptions in Alka Hospital appear to be in accordance with JNC VIII and the WHO 2011 Hypertension guidelines [5, 7].

It was observed that 51% of the patients were prescribed combination therapy (i.e. more than one antihypertensive in the prescription) which is lower than the recommendations. Assessment from several other researches demonstrated that combination therapy was required in at least 70% of the study population to achieve optimal blood pressure control.

Single drug therapy was recommended for 49% patients in Alka Hospital. Higher risk of adverse drug responses from the combination of antihypertensive and concomitant medications, as well as pharmacoeconomic considerations, may be the reasons for physicians' reluctance to use combination treatment in general at Alka Hospital.

In a survey done in Nigeria, 73 % of hypertension patients were administered an antihypertensive combination [11]. Another African research, this time in Ghana, found that two third of hypertension patients were given combination medication, whereas just 1/3 were given monotherapy [12]. In an Indian research, 60% patients were given combination medication, whereas 40 % were given monotherapy [13].

In a large Japanese research of 12,437 hypertension patients, around two third were given monotherapy, 35% were given combination treatment, and non-pharmacological measures were indicated for the other 3% of the patients [14].

Another study done in India found that 59% of the patients were administered monotherapy, which supports the preceding pattern. Among the combination therapies 2- drug treatment was preferred for 75% of the hypertensive patients with CCB and  $\beta$ -blocker being the most frequent drug combination [15].

## Conclusion

In this prospective study, it was observed that the age group of patients which are more affected by hypertension was 40-60 whose percentage was 60.71%. It was found that hypertension is slightly more prevalent in females 51% than in males 49%. The most frequently used antihypertensive drugs group were Angiotensin II Receptor Blockers 50.57%, followed by Calcium Channel Blockers 26.44%, Diuretics 13.22%,  $\beta$ -Blockers 7.47% and Angiotensin Converting Enzyme Inhibitors 1.73% respectively. The number of drugs prescribed in which 49% patients received monotherapy and rest 51% combination therapy although 37.5% of total received two drugs, 10.71% three drugs & 2.67 % received four or more drugs. Diabetes mellitus was found to be the most affected comorbidity disease.

## Implication

The finding may be useful guideline for organizing the health education programs and hypertension reduction modality planning in future. This study finding might be helpful for researcher to use this study as reference.

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