

# Anti Hypertensive Prescribing Patterns and Cost Analysis for Primary Hypertension: A Retrospective Study

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## ABSTRACT

**Objective:** The present study was conducted to analyze the current prescription pattern and cost analysis of antihypertensive drugs in hypertensive patients in a tertiary care hospital.

**Materials and Methods:** A retrospective cross-sectional study was conducted in tertiary care hospital, Bangalore for three months and utilized 300 prescriptions for the analysis. The data analysed from the prescription included patients demographics, stage of hypertension according to JNC VII guidelines, type of drug therapy, class of anti-hypertensive, and cost effectiveness of therapy. Drug acquisition costs was calculated, using the cost of the cheapest available drug and the most commonly prescribed dosage, for each drug on a daily and annual basis.

Total annual drug expenditure on buying required doses of all antihypertensive prescribed in the study population for a year was calculated.

**Results:** Monotherapy (48.94%) was leading trends of antihypertensive therapy followed by fixed dose combination (35.04%) and polytherapy (16.01%). The most frequent antihypertensive class to be prescribed were CCBs (38.59%) followed by beta blockers (24.07%). The ranking in terms of cost utilized per year from the highest to the lowest found in this study was: alpha blockers> ACE-inhibitors> ARBs> CCBs> beta blockers > diuretics. The diuretics were most cost-effective (Cost per day: 5.89 ± 2.87; Cost per year: 2129.02 ± 1080.49) in relation to the other antihypertensive prescribed.

**Keywords:** Antihypertensive drugs, Cost analysis, Hypertension, Prescription-pattern

## INTRODUCTION

Hypertension has been reported to be the strongest modifiable global risk factor for cardiovascular morbidity, mortality as well as health burdens [1,2]. Epidemiological studies conducted in many parts of the world have consistently identified an important and independent link between hypertension and various disorders, especially coronary heart disease, stroke, congestive heart failure and impaired renal function [3].

Hypertension is currently the leading risk resulting in considerable death and disability worldwide and accounted for 9.4 million deaths and 7% of disability adjusted life years in 2010 [4]. In India, the situation is more alarming as hypertension attributes for nearly 10% of all deaths [5]. Prevalence of hypertension in India is reported to vary from 4-15% in urban and 2-8% in rural population [6]. It is estimated that the worldwide prevalence of hypertension would increase from 26.4% in 2000 to 29.2% in 2025 [7]. Epidemiological studies also demonstrate that prevalence of hypertension is increasing rapidly among Indian urban and rural populations[8].

Antihypertensive pharmacotherapy effectively reduces hypertension-related morbidity and mortality [9]. Over the past decade a range of clinical guidelines on antihypertensive treatment have been published with contributions from multiple clinical trials and studies [10,11]. The Joint National Committee (JNC) in 2003 published a series of guidelines recommend the appropriate antihypertensive therapy based on the best available evidence. The guidelines recommend Thiazide diuretics to be prescribed alone or as part of combination therapy for most hypertensive patients without compelling indications [11]. However, most recent published data showed an increasing use of the more expensive Calcium Channel Blockers (CCBs) and Angiotensin Converting Enzyme Inhibitors (ACEIs) despite the lack of evidence to support that they are superior to diuretics and beta blockers in reducing morbidity and mortality of cardiovascular diseases [12]. Despite broad dissemination of the JNC guidelines, prescribing practices have long remained discrepant with recommendations [13].

The cost of medications has always been a barrier in effective treatment. The increasing prevalence of hypertension and the continually rising expense of its treatment influence the prescribing patterns among physicians and compliance to the treatment by the patients.

The objective of the present study was to analyse the prescription pattern of antihypertensive drugs and adherence to JNC VII guidelines as well as to study the cost incurred during the treatment. Cost of the drug was obtained from current index of medical specialties (CIMS) [14].

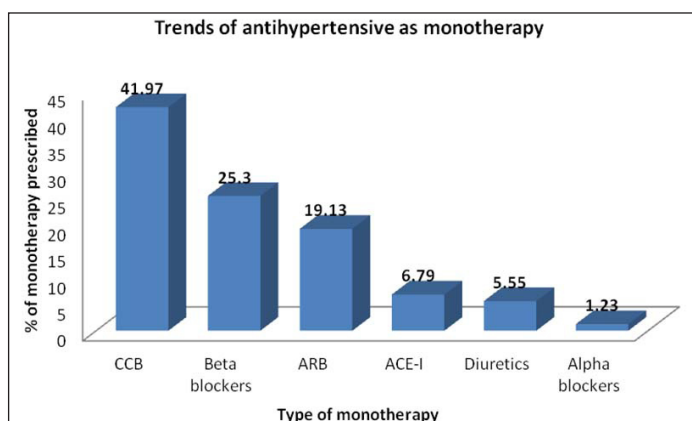
## MATERIALS AND METHODS

This was a retrospective cross-sectional study conducted on patients attending the out-patient department of General Medicine of a Tertiary Care Hospital, Bangalore. The duration of the study was over three months from September to November 2013. Total 300 prescriptions were collected and data was analysed using SPSS version 20. Patients aged ≥ 18 y and diagnosed with hypertension were included in this study. We excluded patients with serious co morbid illness like congestive heart failure, chronic kidney disease, stroke, dementia, cognitive/ sensory deficits and also pregnant, lactating mothers.

The information collected from each prescription included the name, gender, age, recorded blood pressure (both systolic and diastolic), name of drugs (generic as well as brand name), dosage, frequency, type of therapy (monotherapy, polytherapy and fixed dose combination) and cost of the drugs. For brand-name and combination antihypertensive agents, each generic name (active ingredient) component of the agent was counted separately. Subsequently, each generic name was categorized into its major antihypertensive drug class. The drug costs were obtained from CIMS and universally applied to clinical facilities regardless of their size. Cost of drugs was obtained from the Current Index of Medical Specialties (CIMS) [14]. Drug acquisition costs was calculated, using the cost of the cheapest available drug and the most commonly prescribed dosage, for each drug on a daily and annual basis. Total

Total No. of Prescriptions		300
<b>Gender</b>	<b>N</b>	<b>%</b>
Male	164	54.66
Female	136	45.33
<b>Age</b>	<b>Mean ± SD</b>	
Male	58.06±12.94	
Female	62.09±14.27	
Total	59.89 ± 13.68	
<b>Systolic Blood Pressure (SBP) - mm Hg</b>	<b>Mean ± SD</b>	
Male	148.23±25.03	
Female	146.45±23.52	
Total	140 ± 16.32	
<b>Diastolic Blood Pressure (DBP) - mm Hg</b>	<b>Mean ± SD</b>	
Male	86.48±18.19	
Female	86.18±13.15	
Total	104.4 ± 8.93	
<b>Stage of Hypertension (JNC VII guidelines)</b>	<b>N</b>	<b>%</b>
Normal	26	8.66
Prehypertension	75	25
Stage 1	109	36.33
Stage 2	90	30
<b>Type of therapy</b>	<b>N</b>	<b>%</b>
Monotherapy	162	48.94
Polytherapy	53	16.01
Fixed Dose combination	116	35.04

[Table/Fig-1]: Characteristics of the studied patients., N= Frequency; %= Percentage



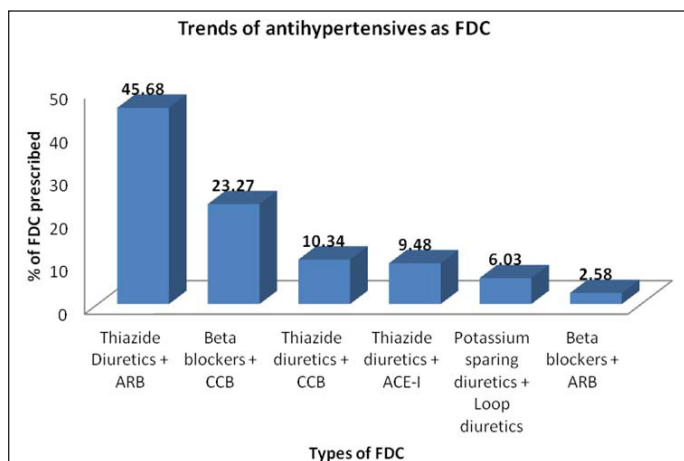
[Table/Fig-2]: Percentage of antihypertensive medication as monotherapy

annual drug expenditure (money spent on buying required doses of all antihypertensive prescribed in the study population for a year) was calculated. Drug expenditure due to a single drug was expressed as a percentage of total drug expenditure [15].

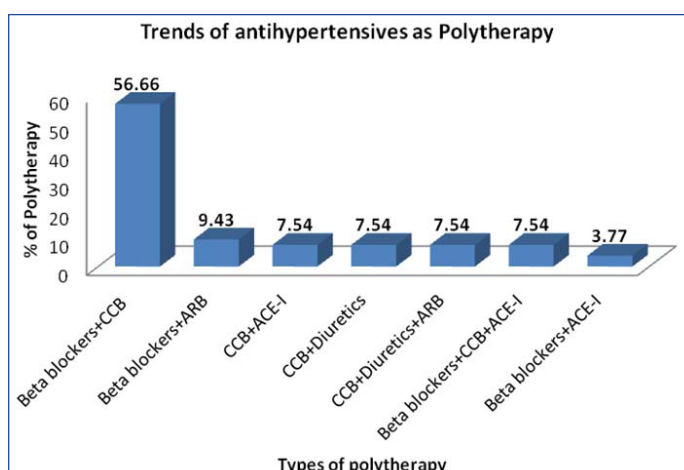
The JNC VII guideline was used to classify the stages of hypertension among the patients. Patients who were on antihypertensive medication with only one active ingredient were defined as receiving monotherapy; those taking two active ingredients in a combination pill were defined as receiving fixed dose combination (FDC) therapy and those who had been prescribed with two or more active ingredients were considered to be on polytherapy. The study protocol was approved by the Institutional Review Board and Ethics Committee of the hospital.

### STATISTICAL ANALYSIS

Data collected from patients prescriptions were transferred to data entry format for evaluation. Continuous variables are presented as mean values ± standard deviation (SD) and categorical variables are presented as percentages. Cost analysis was done using ANOVA.



[Table/Fig-3]: Percentage of antihypertensive medication as FDC



[Table/Fig-4]: Percentage of antihypertensive medication as polytherapy

## RESULTS

The data were expressed as mean ± standard deviation. 300 prescriptions were included in the analysis. The demographics of the patients are given in [Table/Fig-1]. The patients were grouped according to the stages of hypertension as per the JNC VII guidelines. Based on the blood pressure recorded at the time of visit to the OPD, 8.66% of patients were found to have normal blood pressure, 25% were pre-hypertensives, 36.33% were at Stage 1 and 30% were at Stage 2 hypertension. The percentage corresponding to number of hypertensive patients, who received the type of medication is shown in [Table/Fig-1].

The trends of antihypertensive medication prescribed as monotherapy are shown in [Table/Fig-2]. Total of 116 prescriptions were found to have FDCs, trends of antihypertensive combination is been depicted in [Table/Fig-3]. In polytherapy [Table/Fig-4] beta blockers with CCBs were mostly prescribed (56.66%) followed by beta blockers with ARBs (9.43%).

The frequencies of the six antihypertensive drug classes prescribed by physicians are described in [Table/Fig-5]. Among the different classes of antihypertensives Amlodipine (37.3%) was the most prescribed drug followed by Atenolol (19.43%), and Telmisartan (8.03%).

**Cost-effectiveness of the pharmacological agents:** The ranking in terms of cost per year from the highest to the lowest found in this study was: alpha blockers > ACE-I > ARBs > CCBs > beta blockers > diuretics. Drug utilization and costs of different antihypertensive agents incurred per day as well as per year are represented in [Table/Fig-6]. Thus, the diuretics were most cost-effective (Cost per day: 5.89 ± 2.87; Cost per y: 2129.02 ± 1080.49) in relation to the other antihypertensive prescribed.

**Cost-effectiveness of Different Therapy:** In the comparison for antihypertensive therapy, lower costs were incurred with

Type of Antihypertensive prescribed	N	%
<b>Beta blockers</b>		<b>24.07</b>
Atenolol	75	19.43
Metoprolol	14	3.62
Bisoprolol	3	0.77
Carvedilol	1	0.25
<b>CCB</b>		<b>38.59</b>
Amlodipine	144	37.3
Nifedipine	5	1.29
<b>Diuretics</b>		<b>13.2</b>
Hydrochlorothiazide	19	4.92
Furosemide	29	7.51
Spironolactone	3	0.77
<b>ARB</b>		<b>17.35</b>
Losartan	26	6.73
Olmesartan	10	2.59
Telmisartan	31	8.03
<b>ACE-I</b>		<b>6.21</b>
Ramipril	18	4.66
Enalapril	6	1.55
<b>Alpha -blockers</b>		<b>0.51</b>
Prazosin	2	0.51
<b>Total</b>	<b>386</b>	

[Table/Fig-5]: Types of antihypertensive medications prescribed overall

monotherapy followed by FDC while polytherapy proved to be the most expensive. Cost analysis of different therapy prescribed is also represented in [Table/Fig-6]. One-way ANOVA analysis on yearly expenditure on medication suggested the difference in cost of medication prescribed within a type of therapy was not significant at the  $p < 0.05$  level for all three mode of therapy { $df = (2, 297) = 0.32964$ ;  $p = 0.7194$ }.

## DISCUSSION

Appropriate antihypertensive drug therapy is important as the prevalence of hypertension has risen dramatically in last three decades [16]. Any deviation from evidence-based guidelines in hypertension treatment contributes to the high cost of medications and creates difficulties in providing affordable prescription drugs [17].

In our study, the prevalence of hypertension was seen more in males compared to females (1.2:1), which corresponds to the findings of Gupta R et al., [18] and Guang Hui Dong et al., [19].

Out of six classes of drugs prescribed as monotherapy in our study, CCBs were found to be prescribed most frequently followed by beta blockers and ARBs, though diuretics are the first line of medication for the management of hypertension according to the JNC VII guideline. Diuretics were prescribed more often as FDC in our study which is comparable to studies conducted in several countries including India and USA [20,21].

JNC VII guidelines advocate initiating therapy with two drugs, either as individual doses or in fixed-dose combinations, when either the SBP is  $>20$  mmHg or DBP is  $>10$  mmHg above the recommended goal of  $<140/90$  mmHg [22]. The fixed combination of beta blockers and CCBs was the second most prescribed in this study because of its efficiency and cost effectiveness [23]. Use of FDC has an advantage over polytherapy as it enhances compliance to the treatment regimen. It has also been suggested that FDC are often less expensive than multiple dosage regimen or high dose monotherapy [24].

Prescription with polytherapy reflected the major use of beta blockers and CCBs (56%) which was in line with multiple other

Class	N	CPD (mean $\pm$ SD)	CPY (mean $\pm$ SD)
Diuretics	93	5.89 $\pm$ 2.87	2129.02 $\pm$ 1080.49
Beta blockers	149	6.01 $\pm$ 2.80	2184.23 $\pm$ 1069.49
CCB	51	9.02 $\pm$ 4.27	3293.32 $\pm$ 1603.22
ARB	67	10.23 $\pm$ 4.21	3748.54 $\pm$ 1552.29
ACE-I	24	9.33 $\pm$ 5.62	3780.41 $\pm$ 2501.14
$\alpha$ blockers	2	13.08 $\pm$ 3.23	4776.05 $\pm$ 1179.48
Type of therapy	N	CPD (mean $\pm$ SD)	CPY (mean $\pm$ SD)
Monotherapy	162	6.30 $\pm$ 3.71	2362.69 $\pm$ 1521.67
Polytherapy	53	6.87 $\pm$ 2.37	2525.72 $\pm$ 853.33
FDC	116	7.16 $\pm$ 3.70	2576.48 $\pm$ 1399.47

[Table/Fig-6]: Drug acquisition (daily and annual) costs of the different antihypertensive drugs prescribed in the outpatient clinic., CPD= Cost per Day; CPY= Cost Per Year. ( $df=2$ ;  $p=0.7194$ ) (Both CPD and CPY in Indian Rupees).

studies conducted previously [15,25-27]. The result of cost evaluation showed that diuretics had the lowest cost per day (CPD) -INR (5.89  $\pm$  2.87) and cost per year (CPY) -INR (2129.02  $\pm$  1080.49) followed by other classes; these results were comparable with other studies which evaluated the cost effectiveness of the available antihypertensives [28-30]. Analysis of the comparative cost effectiveness of the therapies showed that monotherapy was least costly followed by FDC and polytherapy. This finding was supported by results of other studies which observed that patients on three or four drug regimens had significantly higher treatment costs [31].

In a developing country like India, one of the smart ways to reduce the prescription costs is to use the generics. Even though the Medical Council of India have insisted on prescribing the generic drugs as far as possible, doctors are reluctant to write prescriptions containing only generic or unbranded chemical name of drugs. All too often, the physicians and the patients prefer the expensive brand name drugs because they believe that the generic equivalent is inferior. The present study was undertaken after the implementation of drug price control order act (DPCO) 2013. According to the DPCO 2013, medication price are calculated taking simple average of all brands which have more than one percent market share [32]. Out of 652 drugs under price control, we found that only seven antihypertensives prescribed by our hospital physicians were included in the DPCO list 2013. These included atenolol, metoprolol, amlodipine, nifedipine, hydrochlorothiazide, losartan and enalapril. Previous randomized controlled trials have proven that these agents prevent recurrent myocardial infarction, stroke and decrease the overall cardiovascular mortality. Therefore by including these medications in the revised price list of DPCO 2013, they are more affordable for the patients. Medication cost are the highest proportion of the overall cost of managing hypertension. We can now hope that these price changes would improve the patient compliance and their adherence to the treatment regimen.

Our study had few limitations. Firstly, the main challenge with cross sectional study design in general. We could not assess the patients adherence to the treatment. Patients with severe co morbid illness like congestive heart disease, chronic kidney disease were not included in this study. Having these limitations, treatment pattern of anti hypertensive drugs were relatively uniform.

## CONCLUSION

Our retrospective cross-sectional study analysed the prescription pattern of antihypertensive drugs and found that the prescribing pattern was not totally consistent with the JNC VII 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 calcium channel blockers were the drugs of choice for hypertensive patients as a single drug therapy and overall utilization.

The cost analysis showed monotherapy to be more economical. The under utilization of diuretics in monotherapy is the most important drawback of the present prescribing pattern as they are available at lower cost. But in combination therapy diuretics are being utilized in combination with angiotensin receptor blocker (45.68 %) and the pattern supports JNC VII guidelines. Higher percentage of patients (56.66%) was found to be on polytherapy. The DPCO 2013 has overcome the problem of fixation of prices of drugs.

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