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**Original Research Article**

# A study of prescribing pattern of antihypertensive drugs in hypertensive patients with co morbid diabetes in a tertiary care teaching hospital

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**ABSTRACT**

**Background:** Hypertension and diabetes mellitus are among the commonest non-communicable diseases. Co-existence of hypertension and diabetes increases morbidity and mortality. So co-existence of these diseases requires attention and rational management. Studying current prescribing pattern of drugs provide data for recommendations and decisions regarding rational practice. We undertook this study to study prescribing pattern.

**Methods:** It was cross sectional, observational, descriptive study in outdoor patients suffering from hypertension and type 2 diabetes mellitus for duration of one year. Data of 601 patients were analyzed using descriptive statistics to determine prescribing pattern of drugs.

**Results:** In this study, 71.55% patients were above 50 years age. Female patients were 56.57%. Average duration of hypertension was 4.08 years. Commonly prescribed antihypertensive drug groups were angiotensin converting enzyme (ACE) inhibitors (85.36%) followed by β receptor blockers (33.44%) and calcium channel blockers (29.95%). Enalapril (85.36%) followed by amlodipine (29.95%) and atenolol (21.46%) were commonly prescribed antihypertensive drugs. Single antihypertensive drug was prescribed in 292 (48.59%) prescriptions. The most common monotherapy drug was enalapril (82.19%). Two antihypertensive drugs were prescribed in 231 (38.43%) prescriptions. The most common two drug combination was ACE inhibitors + β receptor blockers (40.69%). Four antihypertensive drugs were prescribed in only 1.50% prescriptions.

**Conclusions:** From this study, the results suggest that the prescribing pattern of antihypertensive drugs reflects recommendations of current guidelines and practices. However, β receptor blockers were prescribed more commonly. There is room for improvement in choice of drugs.

**Keywords:** Antihypertensive drugs, Diabetes mellitus, Hypertension, Prescribing pattern

## INTRODUCTION

Hypertension and diabetes mellitus are among the most common non-communicable diseases in both developed and developing countries.[1] In 2008, worldwide, approximately 40% of adults aged 25 and above had been diagnosed with hypertension. The number of people with the condition rose from 600 million in 1980 to 1 billion in 2008.[2] In India, prevalence for hypertension was 29.8%.[3] Co-existence of hypertension and diabetes varies across different ethnic, racial and social groups. The prevalence of hypertension coexisting with diabetes appears to be increasing in industrialized nations because populations are aging and both hypertension and non insulin dependent diabetes mellitus incidence increases with age.[4] Hypertension leads to various cardiovascular complications and diabetes is an independent risk factor for cardiovascular disease. Hypertension contributes to diabetic retinopathy, one of the leading causes of blindness. An estimated 35-75% of diabetic cardiovascular

and renal complications can be attributed to hypertension.[5] Overall, morbidity and mortality increase when hypertension is coexisting with diabetes. Therefore, co-existence of hypertension with diabetes needs special attention and management. Availability of numerous antihypertensive drugs gives physicians several options to individualize the therapy.[6] Due to this fact there will be change in the prescribing pattern from patient to patient and physician to physician. The study of prescriptions can be used as an exploratory tool to assess the drug utility pattern in the society.[7] We undertook this study to understand prescribing pattern of antihypertensive drugs in hypertensive patients with coexisting diabetes mellitus and to provide recommendations regarding practices.

## METHODS

It was cross sectional, observational, descriptive study after approval from ethics committee of the institute. We used a sample consisting 601 patients. Duration of the study was from June 2015 to June 2016. Outdoor patients aged more than 12 years having hypertension with type-2 diabetes mellitus, who gave consent, were included. We excluded those patients, who had acute complication like stroke, myocardial infarction and required indoor admission.

The diagnosis and management were decided by the physician in charge. Once consultation by the physician was over, patients fulfilling study criteria were explained about research work. We interviewed such patients and reviewed their prescriptions after obtaining their written informed consent. Data like age, sex, duration of illness, concurrent diseases and ongoing treatment were recorded in predesigned and pretested case record forms. Finally, collected data were compiled and subjected to descriptive statistical analysis with the help of MS-excel software to determine prescribing pattern of antihypertensive drugs.

## RESULTS

Authors have analyzed data of 601 patients. Majority of patients (39.44%) belonged to the age group of more than 60 years. Average age of the patients was 54.63 years. Female patients were 56.57% and male patients were 43.43% in our study. Patients with history of hypertension for 2-5 years were 35.11% and that for 0-2 years were 30.61%. Mean duration of hypertension was 4.08 years. Table 1 shows demographic characteristics of patients.

In our study, commonly prescribed antihypertensive drug group was angiotensin converting enzyme (ACE) inhibitors (85.36%) followed by β receptor blockers (33.44%) and calcium channel blockers (29.95%). Telmisartan with hydrochlorothiazide and metoprolol with amlodipine were fixed dose combinations, we found in our study. Figure 1 shows prescribing pattern of antihypertensive drug groups.

**Table 1: Distribution of patients as per demographic characteristics.**

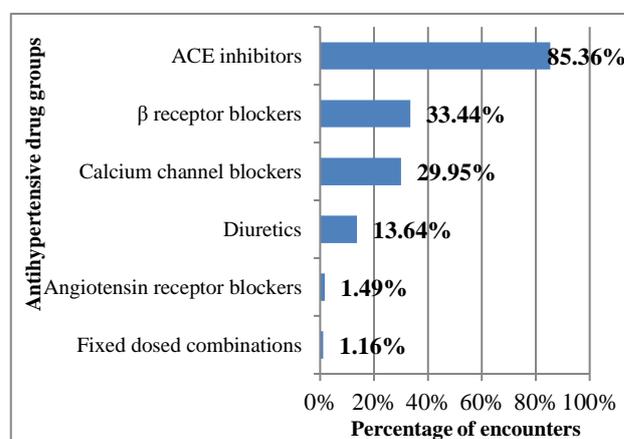| Characteristics | Number of patients | Percentage |
|---|---|---|
| **1. Age** | | |
| 20-29 years | 3 | 0.50% |
| 30-39 years | 36 | 5.99% |
| 40-49 years | 132 | 21.96% |
| 50-59 years | 193 | 32.11% |
| ≥60 years | 237 | 39.44% |
| **2. Gender** | | |
| Male | 261 | 43.43% |
| Female | 340 | 56.57% |
| **3. Duration of hypertension** | | |
| 0-2 years | 184 | 30.61% |
| 2-5 years | 211 | 35.11% |
| 5-10 years | 153 | 25.46% |
| ≥10 years | 53 | 8.82% |



**Figure 1: Prescribing pattern of antihypertensive drug groups.**

**Table 2: Prescribing pattern of antihypertensive drugs.**

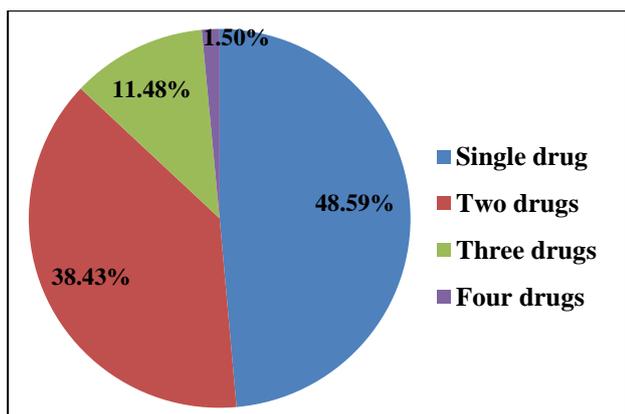| Name | Number of encounters | Percentage of encounters |
|---|---|---|
| Enalapril | 513 | 85.36% |
| Amlodipine | 180 | 29.95% |
| Atenolol | 129 | 21.46% |
| Furosemide | 77 | 12.81% |
| Metoprolol | 69 | 11.48% |
| Losartan | 5 | 0.83% |
| Chlorthalidone | 5 | 0.83% |
| Telmisartan | 4 | 0.67% |
| Telmisartan with hydrochlorothiazide FDC | 4 | 0.67% |
| Metoprolol with amlodipine FDC | 3 | 0.50% |
| Carvedilol | 2 | 0.33% |
| Propranolol | 1 | 0.17% |

**Figure 2: Distribution of patients as per number of antihypertensive drugs in a prescription.**

The commonest antihypertensive drug prescribed was enalapril (85.36%) followed by amlodipine (29.95%) and atenolol (21.46%).

Authors found carvedilol in two (0.33%) prescriptions and propranolol in only one (0.17%) prescription. Four (0.67%) prescriptions contained telmisartan with hydrochlorothiazide fixed dose combination (FDC) and three (0.50%) contained metoprolol with amlodipine fixed dose combination. Table 2 shows prescribing pattern of antihypertensive drugs.

51.41% of total prescriptions contained two or more antihypertensive drugs and 48.59% of prescriptions contained monotherapy antihypertensive regime (Figure 2).

Out of 292 (48.59%) prescriptions containing monotherapy regime, majority of prescriptions contained ACE inhibitor (82.19%) followed by calcium channel blocker (8.90%) and β receptor blocker (5.48%). Prescriptions with two antihypertensive drugs were 231 (38.43%).

**Table 3: Distribution as per number of antihypertensive drugs in a prescription.**

| Drug | Number of prescriptions | % of total prescriptions |
|---|---|---|
| **1. Single antihypertensive drug in a prescription (n=292)** | | |
| ACE inhibitor | 240 | 82.19% |
| Calcium channel blocker | 26 | 8.90% |
| β receptor blocker | 16 | 5.48% |
| Angiotensin receptor blocker | 6 | 2.05% |
| Diuretic | 4 | 1.37% |
| Total prescriptions containing single antihypertensive drug | 292 | 100% |
| **2. Two antihypertensive drugs in a prescription (n=231)** | | |
| ACE inhibitor + β receptor blocker | 94 | 40.69% |
| ACE inhibitor + calcium channel blocker | 92 | 39.83% |
| ACE inhibitor + diuretic | 20 | 8.66% |
| Calcium channel blocker + β receptor blocker | 18 | 7.79% |
| Diuretic + β receptor blocker | 3 | 1.30% |
| Angiotensin receptor blocker + diuretic | 1 | 0.43% |
| Angiotensin receptor blocker + calcium channel blocker | 1 | 0.43% |
| Calcium channel blocker + Diuretic | 1 | 0.43% |
| ACE inhibitor + angiotensin receptor blocker | 1 | 0.43% |
| Total prescriptions containing two antihypertensive drugs | 231 | 100% |
| **3. Three antihypertensive drugs in a prescription (n=69)** | | |
| ACE inhibitor + β receptor blocker + diuretic | 30 | 43.48% |
| ACE inhibitor + β receptor blocker + calcium channel blocker | 24 | 34.78% |
| ACE inhibitor + calcium channel blocker + diuretic | 11 | 15.94% |
| β receptor blocker + calcium channel blocker + diuretic | 3 | 4.35% |
| Angiotensin receptor blocker + β receptor blocker + diuretic | 1 | 1.45% |
| Total prescriptions containing three antihypertensive drugs | 69 | 100% |
| **4. Four antihypertensive drugs in a prescription (n=9)** | | |
| ACE inhibitor + β receptor blocker + calcium channel blocker + diuretic | 6 | 66.67% |
| Angiotensin receptor blocker + β receptor blocker + calcium channel blocker + diuretic | 2 | 22.22% |
| ACE inhibitor + angiotensin receptor blocker + β receptor blocker + calcium channel blocker | 1 | 11.11% |
| Total prescriptions containing four antihypertensive drugs | 9 | 100% |

In these 231 prescriptions, ACE inhibitor + β receptor blocker (40.69%) followed by ACE inhibitor + calcium channel blocker (39.83%) and ACE inhibitor + diuretic (8.66%) were commonly prescribed combinations. Prescriptions with three antihypertensive drugs were 69 (11.48%). ACE inhibitor + β receptor blocker + diuretic (43.48%) followed by ACE inhibitor + β receptor blocker + calcium channel blocker (34.78%) and ACE inhibitor + calcium channel blocker + diuretic (15.94%) were commonly prescribed combinations in such prescriptions. Nine (1.50%) prescriptions contained four antihypertensive drugs (Table 3).

## DISCUSSION

In this study, majority of patients (39.44%) belonged to more than 60 years age group. The average age of the patients was 54.63 years. This finding are in consonance with other studies.[8-10] In this study, 56.57% patients were female and 43.43% were male. Other studies showed similar findings.[8,11] In this study, duration of hypertension was less than 10 years in majority of patients (91.18%). The mean duration of hypertension was 4.08 years. The study conducted by Dhanaraj E et al, showed similar mean duration (4 years).[10] Duration of hypertension is an important factor for determining the disease progression. The co-existence of hypertension along with diabetes increases the morbidity twice the usual. Prescribing patterns of drugs are affected by duration of illness.

ACE inhibitors were prescribed in 85.36% of total prescriptions. Enalapril was the only drug prescribed from this class in this study. It was also the most common class prescribed as monotherapy. 82.19% of single antihypertensive drug (monotherapy) containing prescriptions had enalapril. This pattern of utilization is a per the Joint National Committee (JNC) 7 and JNC 8 recommendations.[12,13] The UKPDS study and HOPE trial has shown the efficacy of ACE inhibitors over other drugs in hypertensive patients with diabetes. Evidence from the CAPPP, FACET and ABCD trial has also suggested cardiovascular protection benefits of ACE inhibitors in hypertension with diabetes.[14] This was also the commonest class of drugs prescribed overall and as monotherapy in similar studies.[10,15] The most common drug class was calcium channel blockers in the study conducted by Dahal et al.[9] In this study, angiotensin receptor blocker drugs were prescribed less commonly (1.49%). Angiotensin receptor blocker drugs were prescribed more commonly in other similar studies.[9,10]

The second most common class prescribed as monotherapy was calcium channel blockers (8.90%) in this study. Other studies showed similar findings.[8,16,15] Amlodipine was the only calcium channel blocker prescribed in this study. Preference for Amlodipine in diabetics with or without nephropathy seems to relate to the positive pharmacokinetic findings which translate into convenient dosage.

The third most common class prescribed as monotherapy was β receptor blockers (5.48%). The finding is in consonance with the study findings of Naveed S et al.[16] β receptor blockers have been advised as first line antihypertensive agents for patients with known coronary artery disease by American diabetic association.[17] Among β receptor blockers, atenolol was the commonest followed by metoprolol, carvedilol and propranolol. Thus β-1 receptor selective blockers were preferred in this study. β-1 receptor selective blockers have less propensity to cause hypoglycaemic unawareness and impairment of exercise capacity. Diuretics as monotherapy were prescribed in only 1.37% prescriptions in this study.

Enalapril was the most common antihypertensive drug prescribed as monotherapy in this study. Telmisartan was the most common monotherapy drug in the study conducted by Rekha MB et al.[18] It was calcium channel blocker amlodipine in studies conducted by Alavudeen S et al. and Sandozi et al.[8,11]

In this study, single antihypertensive drug was prescribed in 48.59% of total prescriptions and multiple antihypertensive drugs were prescribed in 51.41% of total prescriptions. Table 4 shows percentage of prescriptions with single antihypertensive drug and multiple antihypertensive drugs in various studies. This variation might be due to different demographic as well as clinical presentations of the patients.

**Table 4: Comparison of mono and multi drug antihypertensive therapy in various studies.**

| Studies | % of prescriptions with antihypertensive monotherapy | % of prescriptions with antihypertensive multi drug regime |
|---|---|---|
| This study | 48.59% | 51.41% |
| Arifulla M, et al[19] | 63.6% | 36.4% |
| Dhanaraj, et al[10] | 41% | 59% |
| Dahal, et al[9] | 29% | 71% |
| Janagan, et al[15] | 23.7% | 76.3% |
| Naveed, et al[16] | 16% | 84% |

In antihypertensive multidrug regime, two drugs regime (38.43%) was the commonest in this study. This finding is in consonance with other studies.[8,9,20] In two drugs antihypertensive regime, the commonest combination was ACE inhibitor with β receptor blocker (40.69%). This was followed by ACE inhibitor with calcium channel blocker (39.83%) and ACE inhibitor with diuretic (8.66%). β receptor blockers were combined with calcium channel blockers and diuretics in 7.79% and 1.30% of patients respectively. Calcium channel blocker with diuretic

combination was found to be prescribed in only 0.43% patients. Diuretic with ACE inhibitor/angiotensin receptor blocker was the preferred combination in other studies.[8,9,19] Diuretic with ACE inhibitor/angiotensin receptor blocker have synergistic effect and adverse effect of one group of drugs is countered by other group of drugs.

In this study, three antihypertensive drugs were seen in 11.21% of the patients. The study finding is in consonance with other study.[9] The most common combination prescribed in this study was ACE inhibitors + β receptor blockers + diuretics followed by ACE inhibitors + β receptor blockers + calcium channel blockers and ACE inhibitors + calcium channel blockers + diuretics. It was ACE inhibitor/angiotensin receptor blocker + diuretic + calcium channel blockers in other studies.[10,19] There appears to be variation in frequency and prescribing patterns of three anti hypertensive drugs regime in similar studies. In this study, β receptor blockers were prescribed more commonly in combination therapy compared to other similar studies.[10,19,20]

In this study, 0.97% of prescriptions contained this drugs regime. Combination of ACE inhibitor + β receptor blocker + calcium channel blocker + diuretic was the most common fthis drugs regime. The finding is in consonance with other study.[21]

Overall, ACE inhibitors (85.36%) were commonly prescribed antihypertensive drugs followed by β receptor blockers (33.44%) and calcium channel blockers (29.95%) in this study. JNC 8 recommends use of ACE inhibitors/angiotensin receptor blockers and calcium channel blockers as preferred drug classes both in monotherapy and combination therapy.[13]

β receptor blockers were included as first line antihypertensive drugs in JNC 7. β receptor blocker reduces cardiac events in patient with diabetes. These drugs reduce blood pressure and heart rate. β receptor blocker affects metabolism of the myocardium and favours glucose utilization compared to fatty acid utilization thereby decreases the cardiac workload and reduces ischemia.[22] First and second generation β receptor blockers may lead to peripheral vasoconstriction, increase insulin resistance, decrease HDL levels, increase serum glucose and triglycerides levels. These problems can be circumvented by using third generation drugs, which have vasodilator effects, increase HDL cholesterol, reduce serum glucose and triglycerides. β receptor blocker should be used in patients with arterial hypertension and added angina pectoris, post-myocardial infarction, heart failure, tachy arrhythmias, glaucoma and/or pregnancy. In hypertensive patient without one of the added above-mentioned conditions, it is less clear whether or not β receptor blockers are among first choice drugs.[23] JNC 8 recommends β receptor blockers only for selected group of patients i.e. hypertensive patients with co morbid ischemic heart conditions.[13] In this study, β receptor blockers were commonly prescribed in monotherapy and in combination

therapy in spite of only 6.82% patient with documented history of ischemic heart diseases.

This study is single centre study with limited number of patients but it provides reasonable view of antihypertensive drugs prescribing pattern in hypertensive patients with diabetes. Recommendations of JNC 8 guideline for use of ACE inhibitors and calcium channel blockers were reflected in this study. However, use of β receptor blockers was not according to JNC 8 guidelines. There is room for improvement in choice of drugs. Further large scale and more detailed studies are recommended to study rational use.

## ACKNOWLEDGEMENTS

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