

Prescribing Pattern and Effectiveness of Antihypertensives in Patients Suffering from Hypertension to Diabetes Mellitus with and without Compelling Indications in Tertiary Care Hospital

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Abstract: ***Aim:** The prevalence of hypertension (HTN) and diabetes mellitus (DM) is increasing worldwide, and their coexistence is well-documented. Managing both conditions is challenging due to shared pathophysiological mechanisms and the need to balance blood pressure (BP) control with glycemic management. The objective of this protocol was to consider the prescribing pattern and effectiveness of antihypertensive agents in hypertensive and diabetic patients, with and without compelling indications, at tertiary care hospital. **Materials and methods:** A prospective, observational study was conducted over 6 months in total 226 diabetic hypertensive patients from a tertiary care hospital. Demographic and medication history data were collected using a self-designed patient profile form. Descriptive statistics were used to analyze the data, and the results were expressed as percentages or means with standard deviations. **Results:** A total of 226 patients were included in the study, with 62% males and 38% females. 73% of patients were classified as stage 1 and 27% as stage 2 HTN. Among the prescribed antihypertensive agents, β -blockers (BBs) were the most prescribed, followed by angiotensin receptor blockers (ARBs), calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), diuretics, and other classes. Combination therapy was predominantly used, with dual-drug therapy being the most common. Compelling indications for antihypertensive treatment included ischemic heart disease (IHD) (38.49%), chronic kidney disease (CKD) (12.38%), and stroke (6.63%). The choice of antihypertensive agents varied based on the presence of compelling indications, with BBs and ARBs being frequently prescribed. BP control was achieved in 93% of the patients, with 85.96% of patients with HTN + DM, and 82.84% of patients with additional compelling indications having controlled BP. **Conclusion:** Therefore, it can be concluded that the antihypertensive medications prescribed to the study adhered to guidelines and that long-term use of these combinations proved to be more effective, safe, and well-tolerated for patients with HTN and DM with or without convincing indications. Adopting the best approach to managing HTN in people with diabetes is crucial for ameliorating patient outcomes and enhancing overall quality of life.*

Keywords: hypertension, diabetes, ARB, ACEIs

1. Introduction

Diabetes mellitus (DM) and hypertension (HTN) appear as key global health concerns, with both conditions serving as significant risk factors for cardiovascular diseases (CVD) and cerebrovascular diseases. The incidence of DM is rising rapidly across the globe. The World Health Organization (WHO) reports that the global occurrence of DM in adults was approximately 4.0% in 1995 and is expected to grow to 5.4% by 2025. This increasing trend suggests that the individuals with DM worldwide are anticipated to grow from 135 million in 1995 to 300 million by 2025.¹ Moreover, HTN is a widespread condition, impacting approximately one billion individuals globally. Furthermore, projections suggest that by the year 2025, the number of hypertensive adults worldwide could reach as high as 1.56 billion.² The coexistence of DM and HTN is well documented. There is a clear correlation between lifestyle changes and the rising prevalence of both conditions. The etiology behind this association can be attributed to shared pathophysiological mechanisms, including insulin resistance, oxidative stress, and endothelial dysfunction. Effectively managing DM and HTN presents challenges at multiple levels, including the patient, healthcare provider, and healthcare system. Addressing these challenges is crucial for improving the

overall management and outcomes of individuals with both DM and HTN.³ Antihypertensive medications are pivotal in the treatment of HTN, aiming to lower blood pressure (BP) and lessen the threat of CVD. However, the choice of antihypertensive agent in diabetic hypertensive patients should be guided by its efficacy in BP reduction without adversely affecting glycemic control. The selection of appropriate antihypertensives becomes a delicate balance, as some medications may worsen glucose levels, potentially leading to suboptimal diabetes management.⁴ Various antihypertensive medications, such as angiotensin-converting enzyme inhibitors (ACEIs), diuretics, β -blockers (BBs), calcium channel blockers (CCBs), and angiotensin receptor blockers (ARBs) are available for the management of HTN.⁵ The choice of drugs should always include an ACE inhibitor (ACEI) or an angiotensin II receptor blocker (ARB) if ACEI cannot be tolerated and should usually include a diuretic. If additional therapy is needed, a CCB, BB, or α -blocker may be used. The first-line approach in managing high BP in diabetic hypertensive individuals involves the use of ACEIs. While ACEIs can be used alone to lower BP, their effectiveness is significantly enhanced when combined with a thiazidetype diuretic or other antihypertensive medications.⁶ For diabetic hypertensive individuals, β -1 selective BBs offer benefits as part of a multidrug therapy

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regimen. These medications have fewer adverse effects such as hypoglycemic unawareness and decreased sensitivity compared to their nonselective counterparts. In the context of controlling BP, CCBs can be particularly useful for diabetic hypertensive patients, especially when used in combination therapy. They were shown to reduce CVD events in diabetics.^{7,8} Understanding the prime therapy of HTN in individuals with diabetes is vital for improving patient outcomes, reducing the burden of complications, and enhancing overall quality of life. Thus, in this regard, the current study was carried out with the objective to study prescribing pattern and effectiveness of antihypertensives in patients suffering from HTN with DM, with and without compelling indications in a tertiary care hospital. This study will also aid the physician in realizing the effectiveness of various antihypertensives, making a faster decision related to therapy, to provide better treatment to the patients, and thereby restore their health.

2. Materials and Methods

Study Design and Ethical Approval

A prospective, observational study was conducted for a duration of 6 months in the diabetic hypertensive patients, enrolled from inpatient department (IPD) of medicine. The demographic and medication history of the diabetic hypertensive patients was collected through a self-designed patient profile form to study the influence of various antihypertensives on BP and glucose level, to evaluate which therapy (mono/dual/triple therapy/poly-drug therapy) is more effective in controlling BP and to evaluate the effectiveness of antihypertensive agents in patients with or without other compelling indications like diabetes/stroke/ myocardial infarction (MI)/chronic kidney disease (CKD).

Inclusion Criteria

- Patients between the age of 18 and 80 years.
- Patients having HTN with diabetes.
- Diabetic hypertensive patients having other comorbidities like ischemic heart disease (IHD)/stroke/CKD/HFrEF.
- Patients willing to participate in the study and those who have signed the informed consent form.^{9–11}

Exclusion Criteria

- Patients below 18 years of age and above 80 years of age.
- Pregnant and lactating women.
- Patients on chemotherapy.
- Patients with sepsis.

Data Collection, Assessment, and Analysis

Descriptive statistics was used to summarize the data which included demographic characteristics (like age at onset, gender, etc.), antihypertensive agents used with their dose, frequency, duration, and different etiologic factors. Microsoft Excel was used to calculate and interpret the data, all the values were expressed in percentages, mean, and standard deviation.

3. Results

The study included 226 patients to evaluate the efficacy of antihypertensive treatments in diabetic hypertensive patients. Out of 226 patients included, 62% of patients were males and

38% were females. The majority of patients were in the 60–80 years of age-group, followed by 45–60 years, 30–45 years, and only 1% of patients belong to the age-group of 18–30 years. The social history of the patients was analyzed. It was observed that although most of the patients were found to be nonalcoholic, nonsmokers, and nontobacco chewers, their sedentary lifestyle was responsible for the diabetic hypertensive condition. Similarly, diet restrictions analysis revealed that most patients were on salt and sugar-restricted diets, followed by salt-restricted diets, sugar restricted diets, mixed diets, soft diets, and only 1% of patients were consuming a normal diet. As per American Heart Association, the enrolled patients were classified as suffering from stage 1 and stage 2 HTN. Out of 226 patients, 73% patients were suffering from stage 1 HTN and 27% patients were suffering from stage 2 HTN. It was observed that BBs were found to be most prescribed antihypertensives followed by ARBs, CCBs, ACEIs, diuretics and α -1 blockers, and centrally acting α -2 agonists, while direct arterial vasodilators were least prescribed. Among ACEIs, the most prescribed drug was ramipril followed by enalapril. Among ARBs, telmisartan was the most frequently used drug followed by valsartan, losartan, and olmesartan. Amlodipine was the most widely prescribed drug among CCBs followed by cilnidipine, nifedipine, and nicardipine, and azelnidipine was least prescribed. Among the BBs, metoprolol was the most frequently prescribed antihypertensive drug followed by bisoprolol, while labetalol and nebivolol, atenolol, carvedilol, and propranolol were least prescribed. Hydrochlorothiazide was the most frequently used thiazide diuretic followed by chlorthalidone. Hence, we analyzed the enrolled patient population for the type of combination drug therapy prescribed. In the present study, it was observed that dual (43.81%) and mono (38.94%) drug therapy was mostly prescribed while triple and poly-drug therapy was prescribed occasionally. Among the 39% of patients who were prescribed with mono-drug therapy, ARBs and BBs were the most prescribed antihypertensive drugs, followed by CCBs. While ACEIs, direct arterial vasodilators and centrally acting α -2 agonist were prescribed intermittently. Among the 44% of patients prescribed with dual drug therapy, the most prescribed drug combination was ARB + BB (28.28%) and ARB + CCB (26.26%), followed by CCB + BB (21.21%), ACEI + BB (8.08%), BB + α -1 blockers (7.07%). ACEI + CCB, ARB + diuretics, ARB + α -1 blockers, and BB + diuretics were prescribed occasionally. Among the 15% of patients prescribed with triple-drug therapy, ARB + BB + CCB (47.06%) was the single most frequently prescribed triple-drug combination followed by ARB + BB + diuretics (17.65%). Among the 2% of patients prescribed with poly-drug (>3 drugs) therapy, ARB + CCB + BB + diuretics (60%) was the single most prescribed combination drug therapy (Fig. 3). Hypertension may occur in association with many other pathological conditions, namely HF, IHD, CKD, recurrent stroke, etc., in which there are convincing symptoms for use of a particular treatment. In the present study, we investigated patients diagnosed with HTN with DM for such associated compelling indications. Among the patient population with HTN + DM, the most common compelling indication was IHD, followed by CKD, stroke, and CKD–IHD.

Drug treatment in such patients with compelling indications should be focused on tailored drug management strategies for specific compelling indications as well as HTN. It was observed that among the 25% of patients diagnosed with only HTN + DM, ARBs (57.89%) were the commonly used drugs followed by BBs (54.39%), CCBs (36.84%), ACEIs (10.53%). Diuretics (7.02%) and α -1 blockers (3.51%) were prescribed very occasionally. Among the 38% of patients diagnosed with HTN + DM + IHD, BBs (68.96%) and ARBs (51.72%) were the most prescribed drugs, followed by CCBs (31.03%) and ACEIs (16.09%). Diuretics (10.34%), α -1 blockers (3.45%), and direct arterial vasodilators (1.15%) were prescribed less frequently. Among the 12% of patients diagnosed with HTN + DM + CKD, BBs (64.29%) were the most frequently used drugs followed by CCB (46.43%), ARB and α -1 blockers (28.57%), centrally acting α -2 agonist (17.85%), and ACEI (7.14%). Among the 6.6% of patients diagnosed with HTN + DM + stroke, ARBs and CCBs (73.73%) were the most frequently used drugs followed by BB (46.66%) and diuretics (13.33%). With the main aim to study effectiveness of antihypertensives in patients suffering from HTN + DM with and without compelling indications, control of HTN was defined as per standard treatment guidelines.⁹ It was observed that, out of 226 patients, BP was found to be controlled in most patients with HTN + DM, as well as HTN + DM with additional compelling indications. Further, it was revealed that, among patients receiving mono-drug therapy or dual-drug therapy, better BP control was observed as compared to triple-drug therapy or multi-drug therapy. Furthermore, all patients in the 18–30 years age-group had their BP under control. For other age-groups, >80% of patients had controlled BP. These results indicate that BP control rates varied across different agegroups, with generally higher rates of control observed in younger age-groups. The choice of antihypertensive agent in diabetic hypertensive patients should lower BP without loss of blood glucose control. Hence, we evaluated 226 patients overall for blood glucose control and it was found to be controlled in 80% of patients and uncontrolled in 20% of patients.

4. Discussion

The aim of current study was to explore the prescribing pattern and efficacy of antihypertensive medications in patients with both HTN and DM, with and without compelling indications. The study included a diverse population of patients diagnosed with both HTN and DM. The prescribing pattern of antihypertensive medications was assessed, focusing on the utilization of different drug classes. Additionally, the effectiveness of these medications was evaluated by observing BP and blood glucose control. The findings of this study provide valuable insights into the demographic characteristics of the patients enrolled to assess the effectiveness of antihypertensive therapy in diabetic hypertensive individuals. Numerous studies consistently indicate that males experience a higher occurrence of HTN compared to females, at least until the age of 60. A rise in BP with aging is commonly associated with alterations in arterial and arteriolar stiffness. The higher prevalence rates of HTN in males compared to females can be attributed to several factors including biological, genetic, hormonal, behavioral, and sociocultural influences. The results of current study were aligned with the incidence rates of HTN, which tend to be

higher in males compared to females. Strong evidence demonstrates that modifiable risk factors, including alcohol consumption, body mass index (BMI), cigarette smoking, poor diet, and physical inactivity, contribute to over two-thirds of the incidence of cancer, CVD like HTN, chronic respiratory diseases, and diabetes. Lifestyle analysis of the patients included in the present investigation is aligned with the evidence till date as revealed by more hypertensive patients having a sedentary lifestyle. Diet analysis revealed most patients on salt and sugar-restricted diets. However, social history of the patients appeared controversial as more patients were nonalcoholic, nonsmokers, and nontobacco chewers. Thus, it can be concluded that most diabetic hypertensive patients in the present study are associated with physical inactivity and unhealthy diet, which are modifiable risk factors to prevent complications. The three main preferences for antihypertensive treatment in most patients are an ACEI (or ARB), a calcium channel blocker (CCB), or a thiazide diuretic (preferably a thiazide-like diuretic). In the current study patient population, BBs were found to be the most prescribed class, followed by ARBs, CCBs, ACEIs, diuretics, α -1 blockers, centrally acting α -2 agonists, and direct arterial vasodilators. It has been suggested that BBs should not be used as first drug of choice in patients above 60 years if there are no compelling indications. However, BBs are recommended for patients who have experienced an MI within the past 3 years. In the study population with HTN + DM, the most common compelling indication was IHD, which rationalizes BBs as the most prescribed drug in study population. All classes of drugs, namely CCBs, ACEIs/ARBs, diuretics, BBs are roughly equivalent in their effectiveness at lowering BP and improving results. However, BBs have been linked to a lower level of protection against strokes. Considering factors such as availability and affordability, the recommended antihypertensive options include amlodipine (a long-acting calcium channel blocker), enalapril or lisinopril (ACEIs), low-dose hydrochlorothiazide (a thiazide diuretic), and if necessary, losartan (a cost-effective ARB). Among ACEIs, ramipril was the most prescribed drug, followed by enalapril. This finding is supported by clinical evidence demonstrating the efficacy of ramipril. Amlodipine was the most widely prescribed CCB, consistent with its status as a firstline agent for HTN management due to its efficacy and tolerability. Hydrochlorothiazide emerged as the most frequently used thiazide diuretic, reflecting its established role in BP control. Telmisartan was found to be the most frequently used medication among ARBs. These results align with the effectiveness and safety profiles of telmisartan as mentioned in the 2019 Indian guidelines for hypertension-IV

Overall, >80% of the total patient population had controlled BP, and only <20% had uncontrolled BP with the prescribed antihypertensive therapies, which were as per guidelines. In addition, overall blood glucose was found to be controlled in 80% of patients and uncontrolled in 20% of patients. In conclusion, the antihypertensive medications prescribed to the study group adhered to established guidelines. Long-term use of these drug combinations was found to be more effective, safe, and well-tolerated for patients with HTN and DM, whether or not there were additional compelling indication.

5. Conclusion

Diabetes mellitus and HTN are significant global health concerns and important risk factors for CVD. The incidence of both DM and HTN is growing globally. Managing these conditions are challenging due to common pathophysiological mechanisms and the need to balance BP control along with glycemic control. The main objective of this study is to estimate the prescribing pattern and effectiveness of antihypertensive medications in diabetic hypertensive patients with and without compelling indications. The results showed that the most prescribed antihypertensive agents were BBs, followed by ARBs, CCBs, ACEIs, diuretics, and other classes of drugs. Among ACEIs, ramipril was the most prescribed, and among ARBs, telmisartan was the most frequently used. Amlodipine was the most prescribed CCB, and metoprolol was the most frequently prescribed BB. Hydrochlorothiazide was the most used diuretic. Combination therapy was common, with dual-drug therapy being the most prescribed. Ischemic heart disease, CKD, and stroke were the most common compelling indications for treatment in a significant number of patients. The choice of antihypertensive agents varied depending on the compelling indication. ARBs and BBs were commonly prescribed in patients with HTN + DM, while BBs and ARBs were frequently prescribed in patients with HTN + DM + IHD. BBs and CCBs were commonly used in patients with HTN + DM + CKD, and ARBs and CCBs were frequently prescribed in patients with HTN + DM + stroke. Overall, 83.62% of the patients had controlled BP, while 16.37% had uncontrolled BP. The study suggested that the selection of antihypertensive agents must be tailored to the individual needs, considering the presence of diabetes, compelling indications, and the impact on BP and glycemic control. The results highlight the importance of individualized treatment approaches in managing HTN in diabetic patients. The findings suggest that a combination therapy approach, including BBs and ARBs, is commonly employed and can successfully regulate BP in this patient population. However, further research is needed to evaluate the long-term effects and safety of these medications in diabetic patients. Understanding the ideal therapy of HTN in individuals with DM is crucial for refining patient follow-up, decreasing problems, and augmenting overall quality of life.

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