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Original Article

Internal Medicine Section

Management Strategies for Hypertension in Patients with Diabetes and Other Co-morbidities: Insights from the HYDIA Cross-sectional Survey

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ABSTRACT

Introduction: The simultaneous rise of hypertension and diabetes in Indian patients necessitates effective management strategies to prevent severe complications. The study addresses the limited understanding of hypertension management in diabetic patients within the Indian clinical context, highlighting gaps in region-specific data on expert perceptions and preferred strategies.

Aim: To assess Indian physicians' perceptions and practices regarding the impact of hypertension in patients with diabetes and the most appropriate strategies for managing it.

Materials and Methods: The present study was a cross-sectional, questionnaire based electronic survey. A total of 1618 physicians throughout India were invited to participate in an online survey and virtual meetings. The study questionnaire had two sections. Section 1 consisted of four questions focusing on the detrimental effects of hypertension on diabetes. Section 2 included seven questions regarding appropriate management approaches for hypertension. The data collected was analysed using Microsoft Excel 2019 and presented as frequency.

Results: Majority of the physicians (39.9%) were from Western region. The majority of participants in this survey had 10-20 years of experience (n=504, 41.2%) and practiced in their clinic (n=541, 44.3%). The expert panel reported that cardiac events (48.22%) were the most common consequence of hypertension in diabetic patients. They recommended telmisartan (85.9%), amlodipine (64.7%), and metoprolol (76.0%) as preferred treatments for managing diabetes with hypertension and cardiovascular Co-morbidities. For patients with diabetes, hypertension, and Chronic Kidney Disease (CKD), telmisartan (84.0%), amlodipine (63.4%), and hydrochlorothiazide (63.1%) were favoured. Additionally, 51.3% of diabetologists did not recommend the use of dual RAAS inhibitors (ACE inhibitors+ARB). In a patient with diabetes, hypertension and a history of stroke, if Blood Pressure (BP) remains uncontrolled on an optimal ARB dose, Calcium Channel Blockers (CCBs) should be added as a second-line therapy.

Conclusion: Appropriate management strategies, such as enhancing medication adherence, patient education, and selecting effective treatments, can prevent the detrimental effects of hypertension in patients with diabetes and Co-morbidities. Indian diabetologists typically prefer ARBs as the first-line therapy and CCBs, beta-blockers, or diuretics as second-line options. The most commonly chosen medications include telmisartan, amlodipine, metoprolol, and hydrochlorothiazide. As a second-line treatment, CCBs are particularly preferred for patients who have both diabetes and CKD.

Keywords: Angiotensin 2 receptor blockers, Beta blockers, Calcium channel blockers, Cardiac events, Type 2 diabetes mellitus

INTRODUCTION

The simultaneous occurrence of hypertension with diabetes among Indian patients is constantly rising, leading to the development of a dual disease epidemic. Despite hyperglycaemia being the most common attributable factor for cardiovascular morbidity and mortality, the vital role of uncontrolled BP in the development of microvascular and macrovascular complications cannot be ignored. A vast array of clinical studies indicates that the reduction in elevated BP in patients with diabetes was associated with improved clinical outcomes in terms of reduction in stroke, cardiovascular events, and diabetes-related as well as cardiovascular mortality [1-5]. Therefore, it is noteworthy that an appropriate management strategy should be applied for adequate BP control in patients with diabetes to prevent severe clinical outcomes linked to diabetes-associated complications [6,7].

During decision-making about the management approach of hypertension in patients with diabetes, clinicians need to consider a few critical factors, including individual risk factors, co-morbidities, and patient preferences, mainly when the target BP is optimally minimal. In achieving lower BP, there is a risk of developing unwanted adverse events such as hypotension or hypokalaemia in elderly patients or patients with CKD or multiple co-morbidities [7]. Furthermore, lack of awareness about disease course, risk of complications, and impact of medicine non-adherence on long-term prognostic outcomes among patients with diabetes and hypertension portray a dire need for patient education and a change of focus of healthcare systems towards an accurate diagnosis of hypertension and control with appropriate drug therapies [6]. The existing gaps in the literature that prompted this study revolve around the limited understanding of how hypertension is perceived and managed specifically in diabetic patients within the Indian clinical context. There is a lack of region-specific data on how Indian healthcare experts perceive the detrimental effects of hypertension in this population. Additionally, the literature does not comprehensively cover the strategies that Indian clinicians believe to be most appropriate for managing hypertension in diabetic patients. This gap in knowledge, particularly regarding local practices, clinical experiences, and expert insights in India, encouraged to conduct this survey to gain a clearer understanding of current perceptions and practices in this area. The present survey report aims to evaluate the Indian clinical

experience on the perception and practices of physicians regarding the detrimental effect of hypertension in patients with diabetes and the most appropriate hypertension management strategies for patients with diabetes and hypertension with different co-morbid conditions.

MATERIALS AND METHODS

The present cross-sectional, comprehensive electronic survey was conducted among 1222 Indian physicians across four regions of India: north, east, west, and south, between May 2022 and August 2022. Indian physicians having >10 years of experience in managing diabetes and hypertension were invited to participate in the survey. Responses of all the participants were recorded. A total of 396 experts were invited for round table meetings across Pan India sites (between 26th May 2022 and 20th August 2022) to discuss the survey responses and understand their opinions. The entire session was recorded and feedback was taken from expert panelists. This study was conducted according to the Declaration of Helsinki principles and followed the guidelines for Good Epidemiology Practice. The study was approved by an Independent Ethics Committee.

Study Procedure

A survey questionnaire with questions related to the detrimental effect of hypertension in diabetes and clinical Co-morbidities was designed by a collaborative team of physicians, who worked on the following points:

- Section 1: The detrimental effect of HTN on diabetes (number of questions=04).
- Section 2: Appropriate management approaches were used for HTN (number of questions=07).
- There were six single-choice questions and five multiple-choice questions. Each multiple-choice question had one correct option for each sub-question.

A panel of eight experts participated in the questionnaire validation process. The panelists, highly qualified and experienced in the field, provided their insights to ensure the questionnaire's relevance and clarity. The expert review was conducted virtually via Zoom, where the panel discussed, evaluated, and finalised the questionnaire for validation. The questionnaire was rolled out for a year in 2021. Based on the discussion with the expert panelists and the collected opinions of the participating physicians, clinical insights were derived and compiled to prepare this expert opinion related to the clinical experience on perception and practices of healthcare practitioners in Indian patients with diabetes and hypertension about the detrimental effect of hypertension in diabetes and the most appropriate management strategies.

STATISTICAL ANALYSIS

All responses to the survey questionnaires were analysed and entered into a suitable spreadsheet. The data was analysed using Microsoft Excel 2019. Qualitative variables were represented as frequency and percentage.

RESULTS

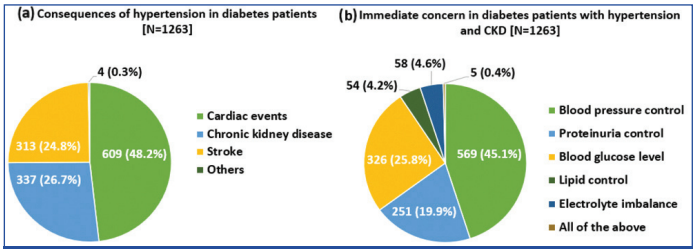
A total of 1618 physicians throughout India were invited to participate in an online survey and virtual meetings. A total of 1222 physicians participated in this survey, and 396 delegates participated in the regional meetings. Majority (39.9%) of the physicians were from Western region Physicians. The majority of participants in this survey had 10-20 years of experience (n=504, 41.2%) and practiced in their clinic (n=541, 44.3%) [Table/Fig-1].

Parameters	Total (n=1222) (%)
Region	
East	202 (16.5)
West	487 (39.9)
South	179 (14.6)
North	354 (28.9)
Experience (Years)	
<10	412 (33.7)
10-20	504 (41.2)
>20	306 (25.0)
Practice setting	
Hospital	339 (27.7)
Individual clinic	541 (44.3)
Both	342 (28.0)

[Table/Fig-1]: Demographic characteristics of the participants.
Data presented as n (%)

Detrimental Effect of Hypertension in Diabetes

Common consequences: The panel of experts opined that the occurrence of cardiac events (48.2%) was the most common consequence of hypertension in diabetes patients, followed by CKD (26.6%) and stroke (24.8%) [Table/Fig-2a]. A panel of experts commented that the most immediate concern is BP control (45.0%) in patients with diabetes along with hypertension and CKD [Table/Fig-2b].



[Table/Fig-2]: Detrimental effects of hypertension in diabetes.

Signs of cardiac end organ damage: A panel of experts (46.0%) observed LVH as a sign of cardiac organ damage in <20% of patients with diabetes and hypertension. Most of the experts observed (48.3%) exertional angina followed by admission for myocardial infarction reported by 20-40% of patients as a sign of cardiac end organ damage. Admission for heart failure as the most common sign of cardiac organ damage reported in 40-50% of patients with diabetes and hypertension reported by 36.4% of experts [Table/Fig-3].

Signs of cardiac end organ damage	Participants response, n (%) (N=1150)			
	<20%	20-40%	40-50%	>50%
LVH	529 (46.0)	368 (32.0)	176 (15.3)	77 (6.7)
Exertional angina	315 (27.3)	556 (48.3)	229 (19.9)	50 (4.3)
Admitted for MI	367 (31.9)	407 (35.3)	261 (22.7)	115 (10.0)
Admitted for HF	381 (33.1)	138 (12.0)	419 (36.4)	212 (18.4)

[Table/Fig-3]: Proportion of diabetes patients with hypertension and signs of cardiac end organ damage.
HF: Heart failure; LVH: Left ventricular hypertrophy; MI: Myocardial infarction

Adherence: In patients with multiple co-morbid conditions, the panel of experts ranked side-effects (46.1%) as the most common factor responsible for the issue of medication adherence, followed by the cost of therapy (41.2%) and polypharmacy (31.3%) [Table/Fig-4].

The most Appropriate Management Strategies for Hypertension in Diabetes

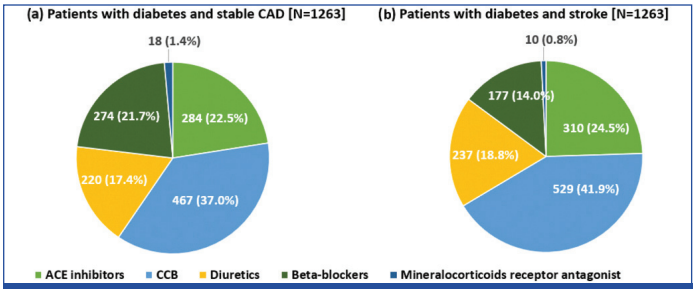
Hypertension with cardiac complications: A panel of experts recommended telmisartan (85.9%) among ARBs, amlodipine (64.7%) among CCBs and metoprolol (76.0%) among beta-blockers as the preferred drug of choice for the management of patients with diabetes along with hypertension and cardiovascular Co-morbidities {Coronary Artery Disease (CAD) and angina}. In the case of a patient with diabetes with uncontrolled BP and stable CAD receiving an optimal dose of

ARB, panelists (36.9%) recommended using CCBs as the preferred 2nd line of therapy [Table/Fig-5a].

Hypertension with stroke: In a patient with diabetes, hypertension, and a history of stroke receiving an optimal dose of ARB, if BP is not controlled, CCBs (participants responded 41.8%) should be used as 2nd line of therapy with ARB [Table/Fig-5b]. The majority of participants recommended telmisartan (86.1%) among ARBs and amlodipine (71.0%) among CCBs as the preferred drug of choice for the management of patients with diabetes along with hypertension and history of stroke [Table/Fig-6].

Rank	Reason for poor medication adherence, n (%)				
	Side-effects	Cost of therapy	Polypharmacy	Lack of regular follow-up	Asymptomatic nature of the disease
1	583 (46.1)	357 (28.2)	282 (22.3)	323 (25.5)	350 (27.7)
2	283 (22.4)	521 (41.2)	412 (32.6)	390 (30.8)	359 (28.4)
3	219 (17.3)	225 (17.8)	396 (31.3)	251 (19.8)	222 (17.5)
4	80 (6.3)	122 (9.6)	111 (8.7)	208 (16.4)	127 (10.0)
5	98 (7.7)	38 (3.0)	62 (4.9)	91 (7.2)	205 (16.2)

[Table/Fig-4]: Ranking of the factors responsible for poor medication adherence (N=1263).



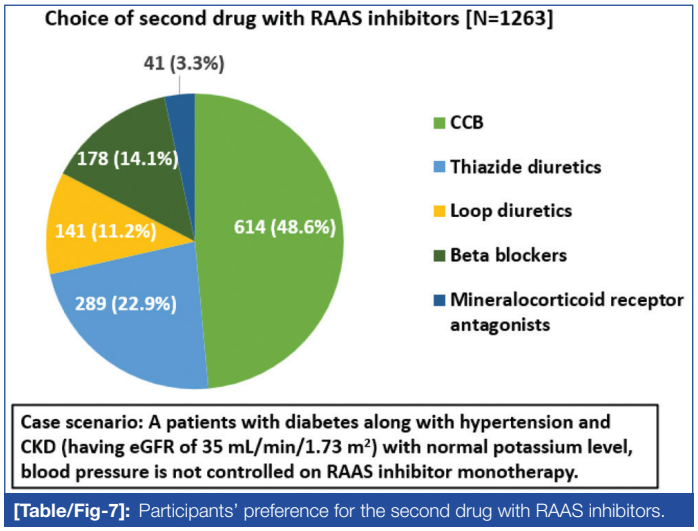
[Table/Fig-5]: Participants opinion about the choice of drug in second-line of therapy in a diabetes patient with uncontrolled blood pressure with various clinical co-morbidities.

Disease	Class	Drug	Participant response, (N=1263) n (%)
DM+HTN+CVS Co-morbidities (CAD, angina)	ARB	Telmisartan	1086 (85.9)
		Olmesartan	115 (9.1)
		Losartan	26 (2.0)
		Azilsartan	14 (1.1)
		Valsartan	22 (1.7)
	CCB	Amlodipine	818 (64.7)
		Cilnidipine	386 (30.5)
		Azelnidipine	37 (2.9)
		Benidipine	12 (0.9)
		Nifedipine	10 (0.7)
	BB	Metoprolol	961 (76.0)
		Bisoprolol	191 (15.1)
		Carvedilol	60 (4.7)
		Atenolol	24 (1.9)
		Nebivolol	27 (2.1)
DM+HTN+CKD	ARB	Telmisartan	1061 (84.0)
		Olmesartan	144 (11.4)
		Losartan	36 (2.8)
		Azilsartan	15 (1.1)
		Valsartan	7 (0.5)
	CCB	Amlodipine	801 (63.4)
		Cilnidipine	404 (31.9)
		Azelnidipine	33 (2.6)
		Benidipine	14 (1.1)
		Nifedipine	11 (0.8)
	Diuretics	Hydrochlorothiazide	797 (63.1)
		Chlorthalidone	421 (33.3)
		Indapamide	25 (1.9)
		Metolazone	20 (1.5)
DM+HTN+Stroke	ARB	Telmisartan	1088 (86.1)
		Olmesartan	123 (9.7)
		Losartan	31 (2.4)
		Azilsartan	10 (0.7)
		Valsartan	11 (0.8)
	CCB	Amlodipine	897 (71.0)
		Cilnidipine	317 (25.1)
		Azelnidipine	27 (2.1)
		Benidipine	11 (0.8)
		Nifedipine	11 (0.8)

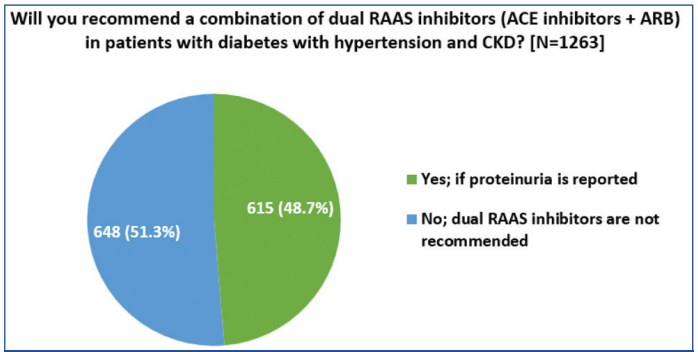
[Table/Fig-6]: Participants' opinions about preferable drugs of choice in different clinical scenarios.
ARB: Angiotensin receptor blockers; BB: Beta-blockers; CCB: Calcium channel blocker; CKD: Chronic kidney disease; CVS: Cardiovascular system; DM: Diabetes mellitus; HTN: Hypertension

Hypertension with chronic kidney disease: During the survey and virtual meetings, recommended telmisartan (84.0%) among ARBs, amlodipine (63.4%) among CCBs and hydrochlorothiazide (63.1%) among diuretics as the preferred drug of choice for the management of patients with diabetes along with hypertension and CKD [Table/Fig-6].

According to the majority of experts (48.6%), in the case of a patient with diabetes along with hypertension and CKD (having eGFR of 35 mL/min/1.73 m^2) with normal potassium level, if BP is not controlled with RAAS inhibitor monotherapy, CCBs should be used as 2nd line of therapy [Table/Fig-7]. In patients with diabetes along with hypertension and CKD, a combination of dual RAAS inhibitors (ACE inhibitors+ARB) was not recommended by 51.3% of physicians; whereas remaining physicians recommended the use of this combination therapy if proteinuria is reported in these patients [Table/Fig-8].



[Table/Fig-7]: Participants' preference for the second drug with RAAS inhibitors.



[Table/Fig-8]: Participants opinion about use of combination of dual RAAS inhibitors.

DISCUSSION

The strong wall of evidence suggests the co-occurrence of diabetes and hypertension is the key contributory factor to the elevated risk of a wide range of complications (such as cardiovascular, cerebrovascular, and renal) and associated mortality [8,9]. A panel of experts opined that cardiac events are the most common consequence of hypertension in patients with diabetes. Analysis of data from a cross-sectional study demonstrated similar findings wherein patients with diabetes and hypertension had a significantly higher risk of myocardial infarction, stroke, and albuminuria than those without hypertension [6,8-10]. Moreover, a few of the participating experts opined that the duration of hypertension and other co-morbid risk factors also affect the consequences of hypertension. Therefore, regular monitoring of BP and other vital parameters (eGFR, potassium levels, lipid levels, and ECG) is necessary to prevent further target organ damage in these patients.

In the present survey, a panel of experts opined that the signs of LVH and exertional angina are relatively seen among patients with diabetes and hypertension in routine clinical practice. Furthermore, they opined that hospitalisation for heart failure (40-50% of patients) and myocardial infarction (20-40% of patients) is also commonly observed in this patient population. Though the survey response and regional meetings discussion suggest the prevalence of LVH is low (<20%) in patients with diabetes and hypertension, the literature indicates the opposite trend wherein a higher prevalence of LVH (around 25%) is reported. Moreover, evidence suggests that the severity of hypertension influences LVH prevalence which ranges from <20% for patients with mild hypertension and >50% for patients with severe hypertension [11].

Overall, these responses portray a comprehensive picture of the detrimental effects of hypertension in patients with diabetes in real-world clinical practice. Therefore, physicians suggested that patients with diabetes having hypertension should be carefully screened for the development of cardiovascular complications to avoid any poor prognostic outcomes. In this survey, the most common reason for medication non-adherence issues was the side effects of treatment, followed by the cost of therapy and polypharmacy. Further, a few experts also highlighted other reasons, including the asymptomatic nature of the disease and lack of regular follow-up for medication non-compliance. A recent review by Dalal JJ et al., described similar factors impacting medication adherence in hypertension [12]. A meta-analysis comparing adherence rates of various drugs demonstrated a relatively low adherence rate to any cardiovascular drug, antihypertensive medications, and statins compared to aspirin and antidiabetic agents, indicating lower adherence rates for cardiovascular medications [13]. In summary, experts agreed that educating and counselling patients about the importance of regular follow-up and the consequences of non-adherence to medication are the key approaches to improve adherence.

A vast array of evidence suggests that a reduction in systolic BP is associated with a higher reduction rate of cardiovascular events as compared to the reduction rate achieved by a decrease in blood glucose levels [8,14-16]. Therefore, apt treatment strategies with drugs that effectively reduce BP with a good safety profile are necessary for patients with diabetes and hypertension. Several guidelines recommended to avoid combination therapy of ARB and ACE inhibitors [17,18]. In line with this, a panel of experts highlighted that the use of combination therapy of ACE inhibitors with ARBs is not preferred in patients with diabetes, hypertension, and CKD due to the high-risk of hyperkalemia and acute kidney injury. Based on their clinical practice, experts suggested that ARB is the preferred drug class among ARB and ACE inhibitors, as ACE inhibitors lead to the development of dry cough in around 30% of patients.

As per the opinion of a panel of experts, telmisartan was the most preferred drug of choice among ARBs for managing hypertension in patients with diabetes and various Co-morbidities such as CAD, angina, history of stroke, and CKD. Observations from multiple clinical trials support the significant benefits of telmisartan in the prevention of stroke and composite vascular endpoints [19].

The present survey responses indicate amlodipine as the most preferred CCB for the management of patients with diabetes along with hypertension and different clinical Co-morbidities such as CAD, angina, history of stroke, and CKD. In parallel with the survey response, a systematic review and meta-analysis revealed the potential benefit of amlodipine in reducing the risk of stroke and myocardial infarction among patients with hypertension [20]. A recent Indian data from the retrospective observational study reported a prescription pattern of commonly used antihypertensive drugs that included amlodipine (57%), telmisartan (55%), chlorthalidone (30%), hydrochlorothiazide (29%), and metoprolol (25%) [21]. This usage pattern concordes with the present survey responses. A cross-sectional observational survey determining Indian clinician's perspectives on management strategies for hypertension suggested the use of telmisartan among ARBs and metoprolol among beta-blockers as the most preferred drug for young adults [22]. A real-world study from India involving patients with hypertension and CAD indicated telmisartan and metoprolol were the drugs of choice for patients aged >65-year-old and those aged <65-year-old, respectively [23]. For patients with diabetes and co-morbid CKD or cardiac ailments, a multidisciplinary consensus report from Indian healthcare experts recommended the use of ARBs/ACE inhibitors (most preferred), beta-blockers, CCB or diuretics as first-line therapy for BP control; CCBs and beta-blockers as second- and third-line options; alpha-blockers can be added if target BP is not achieved with an optimal dose of previous therapies [24]. However, the perception of experts from the present study slightly differed from the above-mentioned literature. Beta-blockers, hydralazine, and nitrates have also shown mortality benefits in congestive heart failure and exert antihypertensive effects, and thus should be used as first-line agents to treat hypertension in patients with congestive heart failure. However, clinical evidence regarding the true potential of the combination of hydralazine and nitrate therapy in terms of mortality benefit among different ethnicities is uncertain and thus might not be preferred by clinicians for heart failure management [25-27].

Limitation(s)

Although the present survey report portrays a comprehensive picture of the perception of Indian healthcare physicians from pan India locations regarding hypertension management in patients with diabetes and clinical co-morbidities, there are several limitations that need to be considered while interpreting the data. One limitation of this survey is the reliance on self-reported data, which may introduce response bias, as participants could provide socially desirable or inaccurate answers. The study's demographic reach is another limitation, as it may not capture regional or cultural differences. Non-response bias is also a concern, as individuals who chose not to participate might hold different perspectives that are not reflected in the findings.

CONCLUSION(S)

Detrimental effects of hypertension in patients with diabetes and clinical Co-morbidities can be prevented with appropriate management strategies such as improving medication adherence, patient education, and judiciously selecting an apt treatment approach having maximum benefits and tolerable safety profile. For the management of hypertension, use of ARBs as first-line therapy and CCBs, beta-blockers, or diuretics as second-line therapy are the most preferred approaches practiced by Indian physicians in patients with diabetes and clinical Co-morbidities. Telmisartan, amlodipine, metoprolol, and hydrochlorothiazide were the standard choice of drugs among ARBs, CCBs, beta-blockers, and diuretics, respectively. The use of CCBs as second-line therapy is the preferred approach in patients with diabetes and CKD.

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