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Expert opinion on the prescription pattern of telmisartan and its combination for the management of Hypertension in the Indian setting

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Abstract
Objective: The survey was intended to gather expert opinion on the prescription patterns of telmisartan and its combinations for the management of Hypertension.
Methodology: The cross-sectional, multi-response questionnaire-based survey involving 24 questions collected perspectives of experts across various India settings regarding the usage of telmisartan and its combinations for the management of Hypertension in their clinical practice.
Results: The survey, which included 651 experts, revealed that the majority of clinicians (82%) favored angiotensin receptor blockers (ARBs) as the primary choice for treating Hypertension. Among ARBs, telmisartan was the predominant choice in clinical practice, preferred by 97% of the respondents. Most of the experts (85%) preferred fixed-dose combination (FDC) therapy for Hypertension management with two or more drugs. According to 30% and 28% of clinicians, FDC therapy reduced pill burden and enhanced patient adherence, respectively. Additionally, 60% favored FDC therapy for patients with uncontrolled Hypertension. Sixty-one percent of clinicians preferred telmisartan combined with amlodipine as the preferred calcium channel blocker (CCB), while 60% favored chlorthalidone as the preferred diuretic alongside telmisartan. In patients with Hypertension and coronary artery disease (CAD), 62% of the clinicians preferred the combination of telmisartan with metoprolol. Most of the experts (63%) preferred the triple-drug combination of telmisartan, a CCB, and a beta-blocker for managing Hypertension in young patients at risk of cardiovascular disease (CVD). Additionally, 47% of clinicians favored a triple-drug combination comprising telmisartan, a CCB, and a diuretic in their clinical practice.
Conclusion: Telmisartan emerged as the favored first-line treatment among clinicians due to its enhanced efficacy and widespread utilization. Specific combinations, such as telmisartan with amlodipine or chlorthalidone, and telmisartan combined with metoprolol were preferred for patients with Hypertension and CAD. Clinicians preferred the triple-drug combination of telmisartan, a calcium channel blocker, and a beta blocker for managing Hypertension in young patients at risk of cardiovascular disease, and a significant proportion of clinicians also favored telmisartan, a calcium channel blocker, and a diuretic triple-drug combination in clinical practice.

Keywords: Hypertension, cardiovascular disease, angiotensin receptor blockers, telmisartan, fixed-dose combination

Introduction
Hypertension, affecting approximately 1.28 billion individuals aged 30 to 79 worldwide, is a significant contributor to premature mortality rates [1]. On a global scale, it emerges as the foremost risk factor for cardiovascular (CV) mortality, surpassing all other modifiable risk factors combined. Alarmingly, Hypertension is implicated in over fifty percent of fatalities attributed to coronary heart disease and stroke, underscoring its profound impact on CV health outcomes [2, 3]. Hypertension poses a substantial health burden in India, affecting an estimated 200 million individuals and emerging as the foremost noncommunicable disease risk factor in the country. Despite its pervasive nature, only approximately 12% of those afflicted maintain their blood pressure (BP) within recommended levels. This prevalence underscores Hypertension's status as the primary health risk factor in India, contributing significantly to both disease burden and mortality rates. It is implicated in approximately 1.6 million deaths annually, primarily attributable to ischemic heart disease and stroke [4-6].

Angiotensin receptor blockers (ARBs) are effective in reducing BP by inhibiting the renin-angiotensin system and are recommended as the first-line treatment for Hypertension. According to the current US and European guidelines, ARBs, along with calcium channel blockers (CCBs) and thiazide diuretics, are the most suitable first choice for treating Hypertension [7, 8]. Telmisartan, a highly selective angiotensin II (AII) type 1 (AT1) receptor antagonist, has been approved by regulatory agencies such as the U.S. Food and Drug Administration (FDA), the European Medicines Agency (EMA), and others for the treatment of Hypertension. Its extended elimination half-life ensures sustained BP reduction throughout the entire 24-hour dosing period. Robust evidence from meticulously designed clinical trials and real-world clinical practice underscores enduring antihypertensive efficacy and favorable tolerability profile of telmisartan across diverse hypertensive populations, including elderly individuals and those with comorbidities such as type 2 diabetes mellitus, metabolic syndrome, and renal impairment [9].

One promising avenue for simplifying the pharmacologic management of Hypertension involves the utilization of fixed-dose combination (FDC) agents. The 2018 European Society of Cardiology (ESC)/European Society of Hypertension (ESH) guidelines emphasize the significance of FDCs in Hypertension treatment, advocating for initial single-pill combination therapy in nearly all patients. Similarly, the Japanese Society of Hypertension (JSH) guidelines endorse FDCs to enhance medication adherence and improve BP control [10-13]. The present survey was aimed to gather expert opinion regarding the prescription patterns of telmisartan and its combinations in Hypertension management in Indian settings.

Methods

We carried out a cross sectional, multiple-response questionnaire based study among clinicians specialized in treating Hypertension patients in the major Indian cities from June 2023 to December 2023.

Questionnaire

The questionnaire booklet titled FiDoCO-HY (Fixed Dose Combination in Hypertension Management) study was sent to the physicians who were interested to participate. The FiDoCO-HY study questionnaire comprised 24 questions addressing current feedback, clinical observations, and specialists' experiences with the use and prescription patterns of antihypertensive medications in managing Hypertension. The study was conducted after receiving approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

Participants

An invitation was sent to leading clinicians in managing Hypertension in the month of March 2023 for participation in this Indian survey. About 651 clinicians from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provided necessary data. Clinicians were given the option to skip any questions they did not want to answer and were instructed not to discuss the questionnaire with their colleagues, answering it independently. Before the study began, each doctor provided written informed consent.

Statistical analysis

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to provide a clear understanding of their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, pie, and bar charts were created using Microsoft Excel 2013 (version 16.0.13901.20400).

Results

The survey included 651 experts. According to 51% of the respondents, primary Hypertension is observed in 26-50% of patients in their clinical practice. Nearly 54% of clinicians reported that 6-15% of patients have secondary Hypertension in their clinical practice. More than half (58%) of the clinicians reported that 11-20% of patients have BP variability in patients with known cases of essential Hypertension. Approximately 49% of clinicians preferred home BP monitoring. According to a significant proportion (63%) of clinicians, the most challenging aspect of managing Hypertension is patient compliance with regular medication consumption. According to 37% of the clinicians, a multiple-dose regimen is one of the major factors associated with patient non-adherence to oral antihypertensive medication.

Based on the survey, nearly 33% of the experts preferred one-on-one sessions (33%) to educate patients with Hypertension. Nearly 43% of clinicians moderately agreed that telemedicine or teleconsultation is an integral part of Hypertension management. A significant proportion (82%) of clinicians preferred ARBs as the first-line drug in patients with Hypertension (Table 1). Telmisartan emerged as the most commonly prescribed ARB in clinical practice, as it is preferred by almost all clinicians (97%) (Fig. 1).

Table 1: Distribution of response to preferred first-line drug in patients with Hypertension

First-line drug	Response rate (n = 651)
ARBs	537 (82.49%)
ACE inhibitors	35 (5.38%)
Beta blockers	29 (4.45%)
CCBs	47 (7.22%)
Not attempted	3 (0.46%)

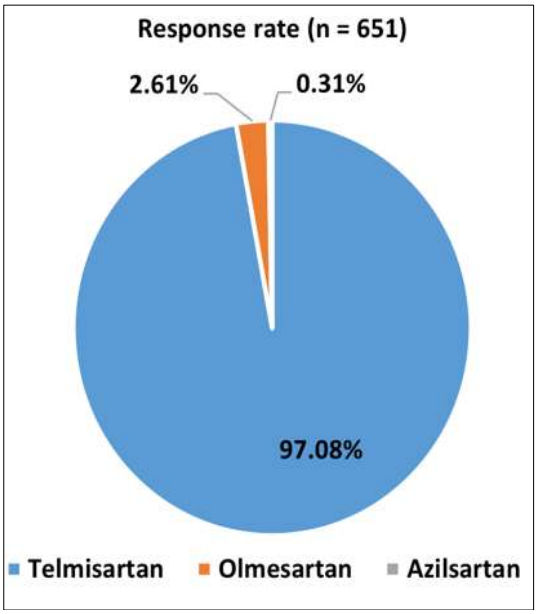

Fig 1: Distribution of response to most commonly prescribed ARB in clinical practice

Approximately 34% indicated that 21-30% of newly diagnosed hypertensive patients require two drugs. A significant proportion of clinicians (85%) preferred FDC therapy in the management of Hypertension when two or more drugs are required (Fig. 2). According to 30% and 28% of clinicians, FDC therapy helps reduce pill burden and improve patient adherence in Hypertension treatment. The majority of clinicians (62%) preferred prescribing this FDC therapy to middle-aged patients aged 35-50 years. The majority of the respondents (60%) preferred FDC therapy for patients with uncontrolled Hypertension.

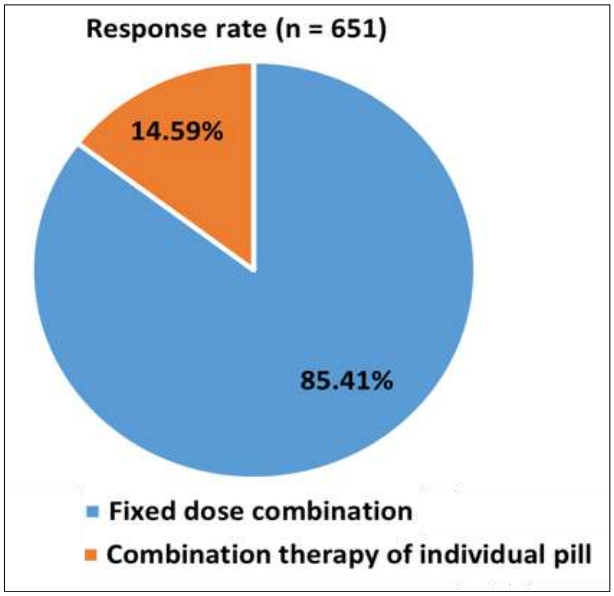

Fig 2: Distribution of response to preferred treatment strategy for managing Hypertension with 2 or more drugs

According to 50% of the clinicians, beta blockers were the preferred second-line drugs for young patients with Hypertension. Nearly 38% each preferred CCBs and beta blockers as the preferred second-line drug in elderly patients with Hypertension. According to 48% of the respondents, beta-blockers are the preferred commonly prescribed add-on 3rd drug for Hypertension management. Among the surveyed clinicians, 36% followed the ACC/AHA guidelines, while 32% reported adhering to the Indian Hypertension IV guidelines.

A significant majority (61%) of clinicians preferred amlodipine as the preferred CCB for combining with telmisartan (Table 2). Majority of the clinicians (60%) favored chlorthalidone as the preferred diuretic in combination with telmisartan (Fig. 3). In patients with Hypertension and CAD, majority (62%) preferred the combination of telmisartan with metoprolol (Table 3). Most clinicians (63%) favored the triple-drug combination of telmisartan, a CCB, and a beta blocker for managing Hypertension in young patients at risk of CVD (Table 4). Nearly 47% favored a triple-drug combination consisting of telmisartan, a CCB, and a diuretic, while 45% preferred telmisartan with a CCB and a beta blocker for managing uncontrolled Hypertension in elderly patients (Fig. 4).

Table 2: Distribution of response to preferred CCB combination with telmisartan

Combination	Response rate (n = 651)
Telmisartan + amlodipine	395 (60.68%)
Telmisartan + cilnidipine	248 (38.1%)
Telmisartan + benidipine	4 (0.61%)
Telmisartan + efonidipine	1 (0.15%)
Telmisartan + azelnidipine	3 (0.46%)

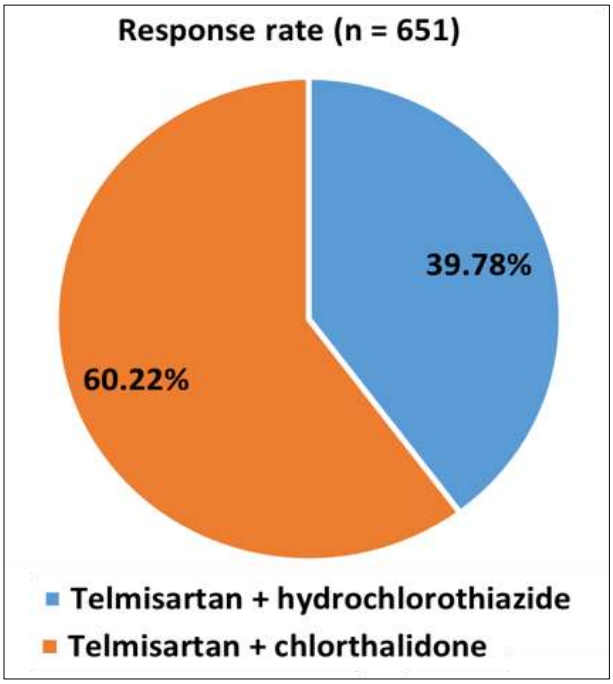

Fig 3: Distribution of response to preferred diuretic in combination with telmisartan

Table 3: Distribution of response to preferred beta-blocker in combination with telmisartan for Hypertension and CAD

Combination	Response rate (n = 651)
Telmisartan + metoprolol	403 (61.9%)
Telmisartan + bisoprolol	247 (37.94%)
Telmisartan + carvedilol	1 (0.15%)

Table 4: Distribution of response to preferred triple drug combination for uncontrolled young hypertensive patients with CVD risk

Triple drug combination	Response rate (n = 651)
Telmisartan + CCB + diuretic	203 (31.18%)
Telmisartan + CCB+ beta blocker	413 (63.44%)
CCB+ beta blocker+ diuretic	34 (5.22%)
ARB + beta blocker +diuretic	1 (0.15%)

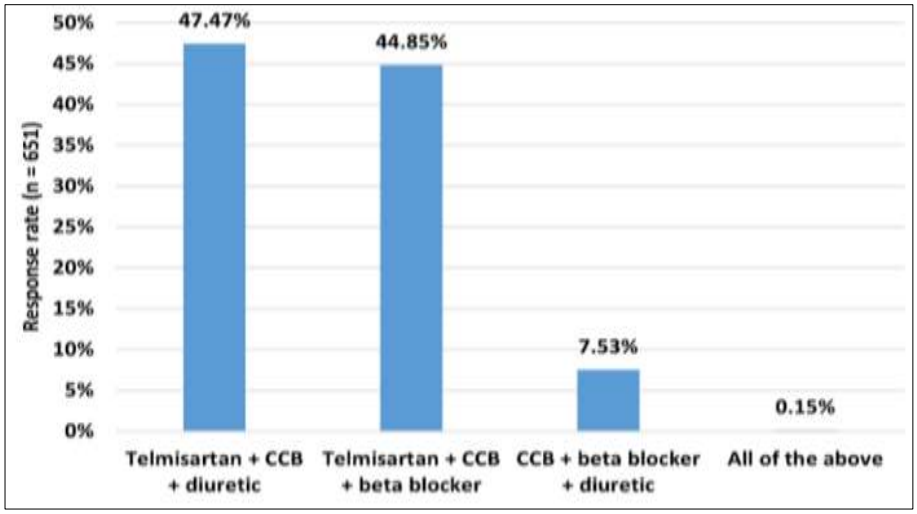

Fig 4: Distribution of response to preferred triple drug combinations for elderly patients with uncontrolled Hypertension

Discussion

The current survey, based on expert opinion regarding the prescription practice of telmisartan and its combinations, holds significant relevance in making informed clinical decisions regarding their use in Hypertension management. Majority of the clinicians favored ARBs as the first-line treatment for Hypertension, with telmisartan being the most commonly prescribed ARB in clinical practice, preferred by nearly all clinicians. All international guidelines highlight the central role of renin-angiotensin-aldosterone system inhibitors (RAASis) in antihypertensive treatment, recommending ARBs as one of a primary choice for Hypertension management [14]. Consistent with the current study results, a cross-sectional survey conducted in Indian healthcare settings revealed physicians' preference towards ARBs as the initial treatment for hypertensive patients, aligning closely with international guideline recommendations. Telmisartan notably emerges as the favored ARB among practitioners, particularly for hypertensive patients with concurrent comorbidities [15].

Several studies, including randomized controlled trials (RCTs) and real-world studies, have substantiated the effectiveness of telmisartan in reducing BP among Indian patients diagnosed with Hypertension [16-19]. Telmisartan is endorsed as the preferred ARB treatment option due to its diverse clinical advantages, including prolonged BP control and CV protection [20]. A systematic review by Suksomboon *et al*., encompassing eight clinical trials, revealed that telmisartan exhibited superiority in reducing fasting plasma glucose levels and increasing adiponectin levels compared to other ARBs [21]. In a meta-analysis by Wang *et al*., comprising 21 RCTs, telmisartan was found to outperform other ARBs in enhancing insulin resistance while also reducing levels of fasting blood glucose and insulin [22]. A meta-analysis comprising twenty-eight RCTs, involving 5157 patients, reported that telmisartan offers superior BP control compared to ACEIs (enalapril, ramipril, and perindopril), with fewer drug-related adverse events and improved tolerability among hypertensive patients [23].

In the current survey, clinicians widely favored FDC therapy for managing Hypertension, citing benefits such as reduced pill burden and improved patient adherence. Additionally, the majority preferred FDC therapy for patients with uncontrolled Hypertension. Studies indicated that the clinical utilization of FDCs presents numerous advantages and holds promise in addressing various challenges and barriers in effectively managing Hypertension. A notable advantage is the potential of FDCs to mitigate clinical inertia in Hypertension control, as they simultaneously introduce or escalate the dosage of two drugs. Furthermore, other significant benefits encompass improved efficacy, reduced pill burden, enhanced medication adherence, and the alleviation of side effects and adverse events associated with single-agent monotherapy [24-26] Bramlage *et al*. noted that patients with Hypertension on FDC exhibited enhanced persistence and adherence to treatment [27].

Majority of the current survey clinicians preferred combining telmisartan with amlodipine as the preferred CCB and chlorthalidone as the preferred diuretic along with telmisartan. A review, encompassing eight randomized, double-blind trials, revealed that a combination of telmisartan and amlodipine enables many individuals to reach their BP targets after unsuccessful attempts with monotherapy. Moreover, initiating therapy with this combination results in a more rapid achievement of BP targets compared to either monotherapy alone [28]. A prospective, open-label study by Sagarad *et al*. observed that the combination of telmisartan and chlorthalidone resulted in significant reductions in both systolic and diastolic blood pressure (BP) at the end of four-week therapy period. These reductions were sustained till the eighth week. No significant clinical adverse events were reported throughout the study duration [29]. In a nationwide survey conducted by Kathiresan *et al*. across India, it was noted that the FDC of telmisartan and metoprolol demonstrated effectiveness in enhancing BP control, reducing heart rate, and improving patient compliance and adherence to therapy. These findings align with the current study results, which revealed a predominant preference among clinicians for the combination of telmisartan with metoprolol in patients with Hypertension and CAD [30].

Majority of the present survey respondents preferred the triple-drug combination of telmisartan, a CCB, and a beta blocker for managing Hypertension in young patients at risk of CVD. Additionally, a significant majority favored a triple-drug combination comprising telmisartan, a CCB, and a diuretic. In a multicenter phase 3 trial conducted by Cho *et al*., it was concluded that the standard dose triple combination of telmisartan 80 mg, amlodipine 5 mg, and

chlorthalidone 25 mg is both efficacious and safe in treating primary Hypertension. The BP-lowering efficacy of this combination was found to be superior to that of the dual combination of telmisartan 80 mg and amlodipine 5 mg, with particularly pronounced effects observed in elderly patients and women [31]. Faruqui *et al*. identified the triple drug fixed-dose combination of telmisartan, amlodipine, and hydrochlorothiazide as an effective and safe option for the optimal management of Hypertension [32]. The triple drug combination of telmisartan, amlodipine, and hydrochlorothiazide may play a significant role in achieving the desired BP goals in patients with essential Hypertension who are otherwise inadequately managed by either monotherapy or dual drug therapy [33].

The present study offers valuable insights into clinicians' perspectives on the utilization of telmisartan and its combinations in the management of Hypertension in Indian settings. The findings, obtained from a meticulously designed and validated questionnaire-based survey, hold significant relevance in making informed decisions regarding optimal treatment options, thereby improving patient outcomes in Hypertension management. However, it is essential to acknowledge certain limitations of the study. Relying on expert judgments may introduce bias, as individual viewpoints and preferences could have influenced the reported conclusions. Therefore, it is imperative to interpret the results with these limitations in mind and consider further research to validate and expand upon the findings.

Conclusion

Telmisartan emerged as the favored first-line treatment among clinicians, widely preferred for its efficacy and widespread use. FDC therapy was favored for its benefits in reducing pill burden and enhancing patient adherence, particularly in cases of uncontrolled Hypertension. Clinicians showed preference for specific combinations, such as telmisartan with amlodipine or chlorthalidone, and favored combinations like telmisartan with metoprolol for patients with Hypertension and CAD. Additionally, the triple-drug combination of telmisartan, CCB, and a beta blocker was preferred for young patients at risk of CVD, with a significant majority favoring the inclusion of a diuretic in this combination.

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Author's Contribution

Not available.

Conflict of Interest

Not available.

Financial Support

Not available.

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