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Review Article

Comparison of Indian clinical practice guidelines for the management of hypertension with the World Health Organization, International Society of Hypertension, American, and European guidelines

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ABSTRACT

Hypertension is the leading risk factor for preventable cardiovascular diseases and all-cause mortality globally, with majority of the hypertension-attributed deaths occurring in low- and middle-income countries like India. Several international and national clinical practice guidelines (CPGs) provide evidence-informed recommendations to achieve optimal control. CPGs produced by the World Health Organization, International Society for Hypertension, American (AHA/ACC-2017), and European (ESC/ESH-2018) are "major" as they are widely used and are highly cited. We compared the main recommendations for the pharmacological management of hypertension among the major CPGs and the two existing Indian CPGs for similarities and shortcomings. Several deviations from the major CPGs were observed among Indian CPGs. Important shortcomings pertain to Indian CPGs' low priority for initial combination therapy and the use of single pill combinations. Having multiple CPGs providing conflicting recommendations might discourage the adoption of evidence-based practices. There is a need for updating Indian CPGs based on up-to-date evidence.

1. Introduction

Hypertension is the leading preventable risk factor for cardiovascular disease (CVD), chronic kidney disease, and all-cause mortality globally.[1] In India, over a quarter of all deaths annually are due to CVDs, and hypertension is a leading cause for disability-adjusted life years.[1,2] Severe gaps persist in the treatment and control of hypertension, which are often attributed to poor adherence to clinical practice guidelines (CPGs). The National Academy of Medicine defines CPGs as "statements that include recommendations intended to optimise patient care that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options".[3]

Given the increasing burden, CPGs for the management of hypertension (henceforth, CPGs) have been produced, historically, by several organisations at global and country levels. However, the lack of consensus between international and national guidelines can be glaring, with disagreements even in the definition of hypertension.[4] In this paper, we compare the major recommendations for the pharmacological management of hypertension in international CPGs and Indian CPGs.

2. Methods

We included the CPGs published by the World Health Organization (WHO, 2021),[5] the International Society for Hypertension (ISH, 2020),[6] the American Heart Association/American Colleges of Cardiology (AHA/ACC, 2017)[7] and the European Society of Cardiology/European Society of Hypertension (ESC/ESH, 2018).[8] These four CPGs are collectively referred to as 'major CPGs' in this paper. To identify Indian CPGs, we conducted search on Google using appropriate search terms (hypertension, high blood pressure, guidelines), and we also reviewed previously published and relevant reviews on this topic and checked government websites related to healthcare. We excluded consensus and

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position statements and expert opinions. We identified two Indian CPGs: (i) Standard Treatment Guidelines: Hypertension—Screening, Diagnosis, Assessment, and Management of Primary Hypertension in Adults in India by the Ministry of Health & Family Welfare (MoHFW, 2016)[9]; (ii) Indian Guidelines on Hypertension–IV (IGH-IV, 2019).[10]

3. Results

3.1. Definition of hypertension

Hypertension is clinically defined as blood pressure (BP) ≥130/80 mm Hg by ACC/AHA and as ≥140/90 mm Hg by the other major CPGs (implicitly by WHO) and Indian CPGs (Table 1).

3.2. Blood pressure threshold for initiating pharmacological treatment

All CPGs recommend addition of pharmacological treatment to lifestyle interventions at BP ≥ 140/90 mm Hg (Table 2). For patients with CVD or high CVD risk, separate thresholds for initiation are provided by the ACC/AHA (≥130/80 mm Hg) and the WHO (≥130 mm Hg). The ESC/ESH only suggests "considering" addition at 130–139/80–89 mm Hg in very high risk because of CVD. Among Indian CPGs, only IGH-IV recommends addition at BP ≥ 130/80 mmHg for patients with CVD or CVD risk.

3.3. Drug classes recommended as first-line treatment

All CPGs recommend renin-angiotensin-system inhibitors (RASi), thiazide/-like diuretics, and calcium channel blockers (CCBs) as first line treatment. ESC/ESH also lists beta-blockers as first line treatment, while others recommend them as first-line only in patients with CVD. IGH-IV recommendations on beta-blockers appear contradictory: they are stated "no longer first-line"; however, "newer" beta-blockers are listed as first-line treatment for younger individuals.

There appears to be a lack of consensus among CPGs on the recommendations on thiazide and thiazide-like diuretics. ACC/AHA recommends using "thiazide" or "thiazide-type" diuretics interchangeably. ISH prefers thiazide-like diuretics over thiazide diuretics; the latter is only recommended as an alternative when the former is unavailable. ESC/ESH and WHO mention "thiazide/thiazide-like" without a preference. Among Indian CPGs, IGH-IV simply mentions "diuretics" without specifying sub-classes, while MoHFW mentions both "thiazide" and "thiazide-like" diuretics, giving precedence to the former.

Among CCBs, WHO and ISH specifically recommend dihydropyridines (DHPs). ISH only recommends non-DHPs as an alternative when DHPs are unavailable. AHA/ACC, ESC/ESH, and Indian CPGs make no specific recommendations on CCB sub-classes.

4. Treatment strategy/steps for uncomplicated hypertension

Except ACC/AHA, all CPGs present a stepwise treatment approach in a flowchart with four to seven steps. However, only WHO and MoHFW CPGs mention individual drugs and doses in their stepwise treatment approach. All major CPGs recommend initiating pharmacological treatment with a combination of drugs from the two first line classes for most patients, followed by dose intensification or addition of a third drug or both. ESC/ESH and ISH recommend monotherapy as initial treatment for patients with low-risk or age ≥80 years or frailty. Among the major CPGs, ISH explicitly mentions initiation with "low-dose" combination therapy, while ESC/ESH and WHO provides rationale supporting initiation with low–dose combinations. Among Indian CPGs, IGH-IV and MoHFW recommend initiation with combination therapy only for BP ≥ 160/100 mmHg and BP ≥ 180/110 mmHg, respectively.

5. Single pill combinations (SPCs)

All major CPGs recommend treatment initiation using SPCs unless unaffordable (ACC/AHA, WHO, ISH), unavailable (WHO), or contraindicated (ESC/ESH, WHO). Among Indian CPGs, while IGH-IV encourages using SPCs only for those patients who qualify for combination therapy, MoFHW recommends SPCs only "after stabilizing BP with two drugs given separately".

6. BP targets

ACC/AHA recommends target BP of <130/80 mmHg for all patients. ESC/ESH and ISH recommend age-based target BP (<140/90 if age ≥65 years, and ≤130/80 if age <65 years). WHO recommends <140/90 mmHg and SBP <130 mmHg in CVD or high CVD risk. Both Indian CPGs recommend age-based target BP; MoHFW recommends <140/90 mmHg if age <80 years, and <150/90 mmHg if age ≥80 years, and IGH-IV <130/80 mmHg if age <60 years, and 130–140/80–90 mmHg if age ≥60 years. Only three CPGs provide time targets to achieve the target BP: ESC/ESH (3–6 months), ISH (3 months), and MoHFW (6–8 weeks).

7. Frequency of follow up

ACC/AHA and WHO recommend monthly follow-up until target BP is achieved after initiating pharmacological treatment. ESC/ESH recommends a follow-up within 2 months of initiating treatment. IGH-IV recommend monthly follow-up until target BP is achieved. MoHFW recommend a follow-up within 2 weeks after initiation and within 4 weeks after treatment modification. Only WHO and IGH-IV specify follow-up recommendations (i.e., within 3–6 months) for those at target BP.

8. Out-of-office BP measurement for initial evaluation and monitoring BP control

All major CPGs acknowledge the superiority of out-of-office measurements, i.e., ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM), over office measurements for

Table 1
Classification of blood pressure based on clinic blood pressure thresholds or ranges.

	Major CPGs			Indian CPGs	
	2017 ACC/AHA	2018 ESC/ESH	2020 ISH	2016 MoHFW	2019 IGH-IV
Non-HTN	Normal: <120 & <80 Elevated: 120–129 & <80	Optimal: <120 & <80 Normal: 120–129 &/or 80–84 High normal: 130–139 &/or 85–89	Normal: <130 & <85 High normal: 130–139 &/or 85–89	Optimal: <120 & <80 Normal: 120–129 &/or 80–84 High normal: 130–139 &/or 85–89	Optimal: <120 & <80 Normal: <130 & <85 High normal: 130–139 or 85–89
HTN	≥130 or ≥80 Stage 1: 130–139 or 80–89 Stage 2: ≥140 or ≥90	≥140 or ≥90 Grade 1: 140–159 &/or 90–99 Grade 2: 160–179 &/or 100–109 Grade 3: ≥180 &/or ≥110	≥140 or ≥90 Grade 1: 140–159 &/or 90–99 Grade 2: ≥160 &/or ≥100	≥140 or ≥90 Grade 1: 140–159 &/or 90–99 Grade 2: 160–179 &/or 100–109 Grade 3: ≥180 &/or ≥110	≥140 or ≥90 Grade 1: 140–159 or 90–99 Grade 2: 160–179 or 100–109 Grade 3: ≥180 or ≥110

The 2021 WHO guideline did not report classification. CPG: Clinical practice guideline; HTN: hypertension.

Table 2
Summary of guidelines recommendations for pharmacological management of hypertension.

Current Practice Guidelines	*Major CPGs*				*Indian CPGs*	
	2017 ACC/AHA	2018 ESC/ESH	2020 ISH	2021 WHO	2016 MoHFW	2019 IGH-IV
BP threshold (mmHg) for adding pharmacological therapy	≥140/90 ≥130/80 if CVD/high CVD risk	≥140/90 ≥160/90 if age ≥80 years Consider in 130–139/85–89 if very high risk of CVD	≥140/90	SBP ≥140 or DBP ≥90 SBP ≥130 if CVD/high CVD risk/DM/CKD Should initiate in ≤4 weeks	≥140/90	>140/90 >130/80 if CVD
BP Target (mmHg)	<130/80	18–65 years: 120–129(130–139 if CKD)/70–79 ≥65 years: 130–139/70–79	<65 years: 120–130/70–80 ≥65 years: <140/90	<140/90 CVD/high CVD risk/DM/CKD: SBP <130	<80 years: <140/90 ≥80 years: <150/90	<60 years: 120–130/70–80 ≥60 years: 130–140/80–90
BP measurement for initial evaluation and monitoring control	ABPM or HBPM preferred.	ABPM/HBPM or repeated office measurements.	Office BP measurement is more common. Where possible, ABPM/HBPM should be used for confirmation.	No specifications.	Office measurement preferred.	ABPM or HBPM preferred. Alternative is repeated office measurements.
First-line BPLDs	Four classes: 1. Thiazide/thiazide-type 2. RASI 3. CCBs	Four classes: 1. RASI 2. CCB 3. Thiazide/thiazide-like 4. Beta-blockers	Three classes: 1. RASI 2. DHP CCB 3. Thiazide-like	Four classes: 1. Thiazide/thiazide-like 2. RASI 3. Long acting DHP CCBs	Three classes: 1. RASI 2. CCBs 3. Thiazide	Four classes 1. RASI 2. CCB 3. Diuretics 4. Newer Beta-blockers
Stepwise approach with specific classes/drugs, dose (mg)	NR	4 steps 1. [RASI + CCB/Diuretic] 2. [RASI + CCB + Diuretic] 3. [RASI + CCB + Diuretic (MRA/BB/α-B) 4. Refer to a specialist	4 steps: 1. Low dose [RASI + CCB] 2. Full dose [RASI + CCB] 3. [RASI + CCB + Diuretic] 4. [RASI + CCB + Diuretic] + Spironolactone 12.5–50	Example protocol 1 (initiation with SPC) 5 steps 1. [Telm 40 + Amlo 5] 2. [Telm 80 + Amlo 10) 3. [Telm 80 + Amlo 10] + Hctz 25/C 12.5 4. Telm 80 + Amlo 10 + Hctz 50/Chlo 25 5. Refer to a specialist Example protocols 2: 7 steps 1. Amlo 5 2. Amlo 10 3. Amlo 10 + Telm 40 4. Amlo 10 + Telm 80 5. Amlo 10 + Telm 80 + (Hctz 25/Chlo 12.5) 6. Telm 80 + Amlo 10 + (Hctz 50/Chlo 25) 7. Refer to a specialist	1. Enal 5/Los 50 or Amlo 5 or Hctz/Chlo 12.5 2. Add a second drug [Enal 5/Amlo 2.5–5/Hctz 12.5] 3. Enal 5 + Amlo 2.5 + Hctz 12.5 4. Enal 10 + Amlo 10 + Hctz 25 5. Refer to specialist	1. RASI or CCB or Diuretic 2. RASI + CCB/Diuretic 3. RASI + CCB + Diuretic 4. RASI + CCB + Diuretic + MRA 5. Add MRA or α-B; in special cases: centrally acting drugs or direct vasodilators 6. Refer to specialist
Combination therapy/SPC	First-line if BP ≥ 140/90 and if average BP > 20/10 above target. Either as SPCs or as separate agents.	First-line for all patients, except in low-risk grade I hypertension or age ≥80 or frail. SPC for most	First-line with an SPC, unless unavailable/unaffordable.	First-line preferably with a SPC.	Initiate with combination only if BP > 180/110. SPCs only after BP is stabilized with two drugs given separately	Initiate with combination if BP > 160/100, preferably a SPC.
Frequency of follow-up	Monthly: after initiation/change in BPLDs until target BP achieved 3-6 monthly: if BP < 140/90	At least once within the first 2 months of BPLD	For treated patients: 1–2 home BP measurements per week or month Hypertensive emergency: Monthly follow-up until target BP	Monthly: after initiation or change of BPLDs until target BP achieved Every 3–6 monthly: if BP at target	1–2 weeks: after initiation of therapy 2–4 weeks: after change of BPLDs	Monthly: after initiation or change of BPLDs until target BP achieved 3 monthly (high risk) or 5 monthly (low–moderate risk): if target BP achieved
Target time for BP control	NR	3–6 months: if BP 140–159/90–99 3 months: if BP ≥ 160/90	Within 3 months	NR	6–8 weeks	–

All single pill combinations are provided in parantheses [ ].
ACC/AHA: American College of Cardiology/American Heart Association; ESC/ESH: European Society of Cardiology/European Society of Hypertension; WHO: World Health Organization; ISH: International Society of Hypertension; MoHFW: Ministry of Health and Family Welfare; IGH-IV: Indian Guidelines on Hypertension-IV; CPG: Clinical practice guideline.
ACEI: Angiotensin-converting enzyme inhibitors; ARB: Angiotensin receptor blockers; RASi: Renin Angiotensin System Inhibitors (includes angiotensin-converting enzyme inhibitors and angiotensin receptor blockers); CCBs: Calcium Channel Blockers; MRA: Mineralocorticoid receptor antagonists. α-B: alpha blockers; Diuretics mainly include thiazide and thiazide-like diuretics.
Amlo = Amlodipine; Los: Losartan; Telm = Telmisartan; Hctz = Hydrochlorothiazide; Chlo = Chlorthalidone; Enal: Enalapril.

confirming diagnosis and monitoring BP control, except WHO, which states that ABPM is expensive and calls for more evidence for HBPM. ESC/ESH underlines that ABPM may have stronger prognosis, utility in nocturnal monitoring, and better representativeness of real-life settings than HBPM, while the latter is more accessible and comfortable for the patient. IGH-IV prefers ABPM and HBPM, but MoHFW does not recommend out-of-office BP measurements due to poor feasibility in India.

9. Tailoring of treatment for special patient groups

All CPGs provide recommendations on tailoring therapy for various patient groups and comorbidities (Supplementary Table 1), except IGH-IV, which only provides age-based recommendations. For elderly, ESC/ESH and ISH recommend monotherapy of first-line classes; ACC/AHA provide no specific recommendation, while WHO and Indian CPGs recommend CCB or diuretic. In pregnancy, major CPGs recommend similar drugs (DHPs/methyldopa/labetalol), and among Indian CPGs, only MoHFW provided a recommendation (CCB). For CKD, ESC/ESH recommends any first line class, other major CPGs recommend RASI, and MoHFW recommends RASI or CCB. For diabetes mellitus, except WHO (that recommends RASI), major CPGs recommend any first line class. MoHFW too recommends any first line class for diabetes. For stroke, major CPGs recommend RASI with or without thiazide diuretic (or CCB by ESC/ESH), and MoHFW recommends RASI.

10. Discussion

We assessed the alignment of main recommendations for pharmacological management of hypertension in major international CPGs and two Indian CPGs and found major discrepancies. Previous studies have compared national and international CPGs for the management of hypertension. A 2022 study by Philip et al compared CPGs of 48 different countries from various income groups, including India's 2016 MoHFW CPG and IGH-III (2013).[11] However, that study did not include the WHO (2021) CPG, and more importantly, it presents pooled results for countries by income-group, without specific results for Indian CPGs. WHO (2021) CPG was also omitted in the study by Chia et al, which compared Asian CPGs with the major CPGs.[12] Although the IGH-IV (2019) was included in this study, it does not provide India-specific comparisons except for BP definitions, target BP, and treatments in special groups. Therefore, our review is novel in presenting a simple, ready reference comparison of hypertension CPGs for Indian clinicians, with special emphasis on the pharmacological management.

Glaring shortcomings of the Indian CPGs include its low priority for initial combination therapy and the use of SPCs—a strategy that improves treatment adherence in hypertension which is now recommended by all major CPGs.[13] Although the MoHFW guideline is outdated, the IGH-IV (2019), published after ACC/AHA (2017) and ESC/ESH (2018), does not recommend combination therapy and presents several other deviations from the major CPGs. Recommending target BP based solely on age, without considering other factors such as the presence of CVDs and cardiovascular risks including comorbidities, is another shortcoming of the Indian CPGs. Further, compared with high-income countries, LMICs like India have a high burden of uncontrolled hypertension among the young adults. Indian CPGs should also consider adding recommendations specific to this population.

Summary

Several deviations from the major CPGs were observed among Indian CPGs. Having multiple guidelines within a country that deviate from one another may discourage the adoption of evidence-based practices. There is an urgent need for updating Indian CPGs based on up-to-date evidence.

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Contributorship statement

AS conceived the study idea. AS and GS searched and retrieved the relevant clinical practice guidelines. GS and RD conducted the data extraction and summarized the findings. GS and AS wrote the first draft of the manuscript, with inputs from JPB and PPM. All authors read and approved the final version of the manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ihj.2023.12.009.

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