



Hypertension in India leads to **1.1 million** deaths annually¹

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Hypertension: Epidemiology and identification

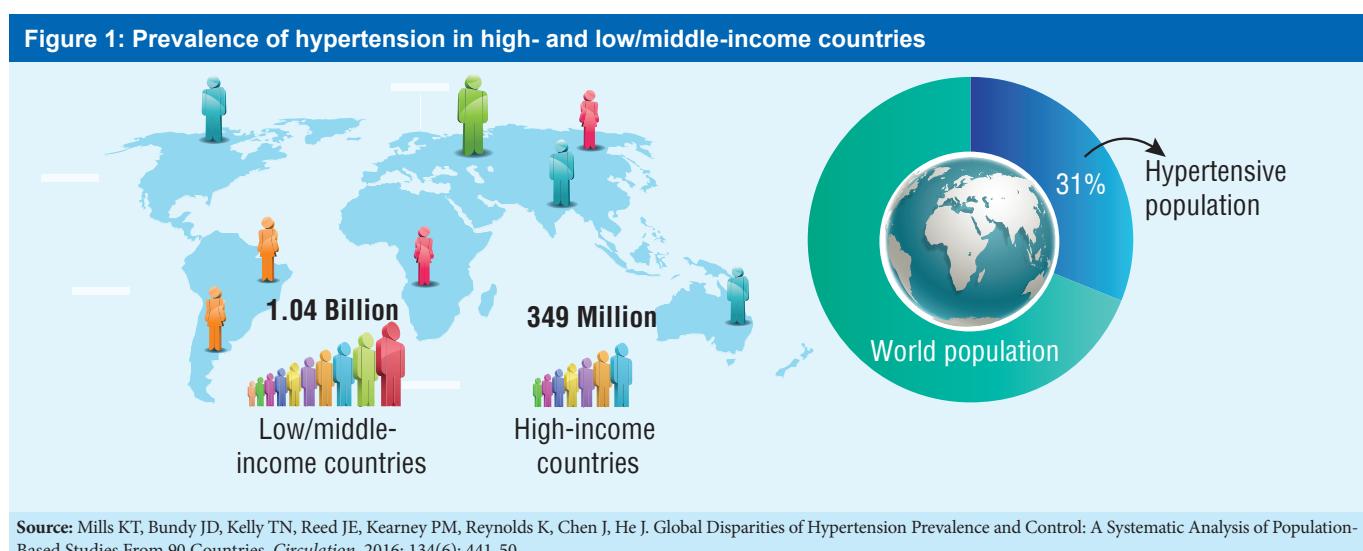
BURDEN OF HYPERTENSION

Hypertension is defined as chronic elevation of systemic arterial pressure wherein systolic blood pressure (SBP) is ≥ 140 mm Hg and/or diastolic blood pressure is ≥ 90 mm Hg. It is one of the most common chronic disorders worldwide.¹ A recently published systemic analysis² of population-based studies revealed that **1.39 billion adults worldwide had hypertension in 2010, representing 31% of the global adult population.** The report also highlighted clear regional disparity in prevalence of hypertension, citing three-times higher prevalence of hypertension in low/middle-income countries compared to high-income

countries (1.04 billion vs. 349 million respectively), as depicted in **Figure 1.**

In India, a region-specific systematic review³ and meta-analysis of the prevalence of hypertension among country's patients was conducted. **Overall prevalence for hypertension in India was 29.8%.** Significant differences in hypertension prevalence were noted between rural and urban parts (27.6% and 33.8%). Regional estimates for the prevalence of hypertension were as follows: 14.5%, 31.7%, 18.1%, and 21.1% for rural north, east, west, and south India; and 28.8%, 34.5%, 35.8%, and 31.8% for urban north, east, west, and south India, respectively.

Figure 1: Prevalence of hypertension in high- and low/middle-income countries



Source: Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global Disparities of Hypertension Prevalence and Control: A Systematic Analysis of Population-Based Studies From 90 Countries. *Circulation.* 2016; 134(6): 441-50.



Furthermore, hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease (CHD) deaths in India.³ Thus, it can be posited that hypertension exerts a substantial public health burden on cardiovascular health status and healthcare systems in India.

IDENTIFICATION OF HIGH RISK HYPERTENSIVE PATIENTS

Hypertension is one of the major risk factors and is correlated with a risk of stroke, coronary artery disease, peripheral vascular disease, heart failure, and renal disease. The risk of a cardiovascular event increases dramatically when a hypertensive patient has any of these aforementioned conditions.⁴ A summary of high-risk conditions is listed in **Table 1**. Clustering of risk factors also increases the risk of cardiovascular events. Identifying and treating risk factors in patients at high risk can significantly reduce the risk.⁴ **Recent ACC/AHA guidelines suggest that a lower BP target is generally better than a higher BP target and patients at high risk of cardiovascular disorders will benefit from SBP treatment goal <120 mm Hg.**⁵ Additionally, it has been reported that chronic antihypertensive treatment to maintain normal blood pressure decreases the relative risk of myocardial infarction and heart failure by 20% to 25% and of stroke by 30% to 40%.⁶ **RAS blockers (ARBs and ACE inhibitors) are widely used treatment options for hypertension management, particularly in high-risk patients.** Recent evidence also indicates that ARBs may provide superior protection against recurrence of cardiovascular events in high-risk patients compared to ACE inhibitors.⁷

CONCLUSION

It is thus promulgated that identification of high-risk patients by global risk evaluation is recommended for

Table 1: High risk conditions in hypertension

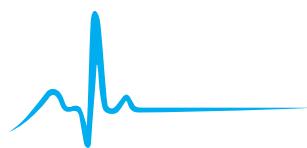
- Systolic blood pressure ≥ 180 mm Hg and/or diastolic blood pressure ≥ 110 mm Hg
- Diabetes mellitus
- Metabolic syndrome
- Three or more cardiovascular risk factors
- One or more manifestations of subclinical organ damage, e.g., left ventricular hypertrophy
- Established coronary artery disease
- Established cerebrovascular disease
- Established peripheral vascular disease
- Established chronic kidney disease

Source: Tsai W-C. Treatment options for hypertension in high-risk patients. *Vascular Health and Risk Management*. 2011; 7: 137-141.

every hypertensive patient. Successful prevention of cardiovascular events in high-risk patients requires identification of patients at risk and comprehensive risk factor management, including treatment of hypertension.⁴

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Screening of hypertension and managing its complications

RATIONALE FOR SCREENING OF HYPERTENSION

There are generally no signs or symptoms associated with high blood pressure, therefore, it is usually found through screening. The same measurement techniques used for screening and confirmation are also used for blood pressure monitoring after a diagnosis to monitor treatment effectiveness and BP control.¹ Office (clinical) blood pressure recording using mercury sphygmomanometer, for long, was recognized as the gold standard method for blood pressure measurement. Recent introduction of aneroid and digital blood pressure measuring devices have significantly improved blood pressure detection, additionally reducing risk of mercury spill and toxicity.² Additional 24-hour ambulatory blood pressure monitoring (ABPM) and Home blood pressure monitoring (HBPM) are now being recommended as adjuvant to office blood pressure measurement, particularly for ruling out white coat hypertension and masked hypertension.³

Secondary causes of hypertension are usually treatable and should be screened, particularly in selected indications. The ACC/AHA guidelines⁴ recommend looking for secondary causes of hypertension in:

- ❖ Those with early-onset hypertension (onset < 30 years of age)
- ❖ Those with abrupt-onset hypertension
- ❖ Those with drug-resistant or drug-induced hypertension
- ❖ Those with exacerbation of previously-controlled hypertension

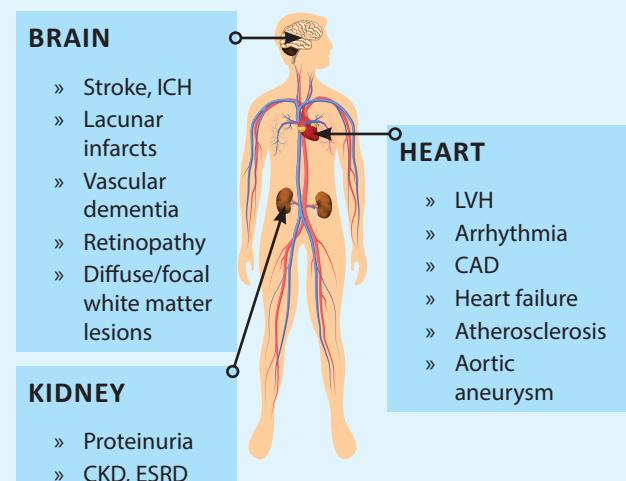
- ❖ Those with accelerated or malignant hypertension
- ❖ Those with hypertension and disproportionate end-organ damage
- ❖ Elderly (≥ 65 years) with onset of diastolic hypertension
- ❖ Those with unprovoked or excessive hypokalemia

COMPLICATIONS OF HYPERTENSION

Hypertensive cardiovascular disease

Cardiovascular (CV) end-organ damage is common in persistent hypertension (Figure 1). It is primarily a result of structural and functional changes in the heart

Figure 1: End-organ damage in hypertension



CAD-Coronary artery disease; CKD-Chronic kidney disease; ESRD-End-stage renal disease; ICH-Intracerebral hemorrhage; LVH-Left ventricular hypertrophy

Source: Schmieder RE. End Organ Damage In Hypertension. *Dtsch Arztebl Int.* 2010; 107(49): 866-873.



which eventually compromise myocardial function. Notable structural and functional CV complications in hypertensive patients include left ventricular hypertrophy (LVH) with concomitant decrease in left ventricle cavity size, reduced cardiac reserve, left ventricular diastolic dysfunction followed by decrease in left ventricular ejection fraction (LVEF), atrial and ventricular arrhythmias. In turn, LVH is a robust risk factor for acute myocardial infarction (AMI), heart failure, and sudden cardiac deaths (SCD). Furthermore, hypertension is an independent facilitator of atherosclerotic plaque formation. Atherosclerotic coronary artery disease (CAD) is a common form of CV end-organ damage in hypertension.^{5,6}

Hypertensive cerebrovascular damage

Elevated blood pressure also adversely affects both cerebral micro- and macrocirculation. Vascular (ischemic) and hemorrhagic strokes are recognized cerebrovascular complications of hypertension. Although ischemic strokes are the most common; cerebral bleeds, lacunar infarcts, focal and/or diffuse cerebral white matter lesions are also notable cerebrovascular complications in hypertensive patients. Vascular dementia is commonly seen in poorly controlled hypertension.⁵ A potential therapeutic strategy by controlling blood pressure has been studied so as to achieve optimal brain perfusion and thus, reduce the occurrence of cerebrovascular damage and cognitive dysfunction.⁷ A meta-analysis of longitudinal studies⁸ showed that anti-hypertensive treatment reduces the risk of the development of cognitive decline and vascular dementia but failed to reverse the already established hypertension-associated cognitive dysfunction.

Hypertensive renal damage

Sustained and poorly-controlled high blood pressure also adversely affects renal vasculature. Chronic kidney disease (CKD) with or without progression to end-stage renal disease (ESRD) is an end-organ manifestation of persistently elevated blood pressure (Figure 1). According to available data, up to 35% patients with hypertension and elevated CV risk have eGFR < 60 mL/min/1.73 m².⁹ Also, co-morbid CKD considerably worsens prognosis in hypertensive patients with pre-existing CV disease,

particularly in those with stable CAD, heart failure, peripheral arterial disease, and coronary interventions.⁹

Hypertension and diabetes comorbidity

Hypertension frequently co-exists with diabetes, significantly increasing complication rates and worsening outcomes in subjects with this comorbidity. More than 50% of patients with diabetes have coexisting hypertension. Comorbid hypertension incurs high risk of both micro and macrovascular complications in patients with diabetes, particularly aggravating their risk of CV diseases. Patients with diabetes with co-associated hypertension have four-times higher risk of CV diseases, including CAD and stroke, compared to their counterparts with normal blood pressure. Notably, hypertension is an independent predictor of both CV and renal diseases, and further augments risk of these complications in patients with diabetes-hypertension co-morbidity.¹⁰ Early and aggressive control of blood pressure in hypertensive patients with diabetes can reduce risk of potentially lethal CV events and renal disease progression, thereby significantly improving overall patient outcomes.^{11,12}

Managing complications of hypertension

General recommendation of blood pressure reduction is <140/90 mm Hg, irrespective of the hypertensive patient's age. If organ damage is present, a reduction to values of about 130/80 mm Hg should be the objective. This specifically is applicable to patients with diabetes mellitus, hypertensive nephropathy, and after a stroke or myocardial infarction. Furthermore, results of INVEST study (hypertensive patients after myocardial infarction) and ONTARGET study (high-risk patients of which 70% had hypertension) showed that there is a potentially increased risk due to a blood pressure reduction that is too low. However, this should not be a concern unless the blood pressure drops to <120/75 mm Hg.⁵

Large body of evidence on individual antihypertensive agents has found effects on hypertensive end organ damage that were independent of the blood pressure. Differential treatment considerations for the selection of antihypertensive agents is based on the understanding



Table 1: Differential treatment considerations for the selection of antihypertensive agents

Subclinical end organ damage	
Left-ventricular hypertrophy	ARB, ACEI, CA
Elevated albuminuria	ARB, ACEI
Renal dysfunction	ARB, ACEI
Irreversible hypertensive end organ damage	
Prior stroke	Any antihypertensive
Prior myocardial infarction	BB, ARB, ACEI
Angina pectoris, CHD	BB, CA
Heart failure	Diuretics, BB, ARB, ACEI, MR antagonists
Left-ventricular dysfunction	ARB, ACEI
Atrial Fibrillation	
• Prevention, recurrence	ARB, ACEI
• Permanent	BB, non-dihydropyridine calcium antagonists
Tachyarrhythmia	BB
Chronic renal insufficiency, proteinuria	ARB, ACEI, loop diuretics
Peripheral arterial occlusive disease	CA
ACEI, ACE inhibitor; ARB, angiotensin receptor blocker; CA, calcium antagonist; BB, beta blocker; MR-antagonist, mineralocorticoid antagonist; CHD, coronary heart disease; MI, myocardial infarction	
Source: Schmieder RE. End organ damage in hypertension. <i>Dtsch Arztebl Int.</i> 2010; 107(49): 866-73.	

that not only the blood pressure but also additional factors are of significance in the pathogenesis of organ damage (Table 1).⁵

CONCLUSION

Hypertension is a common cardiovascular disorder worldwide which if left untreated can predispose to

serious end-organ complications. Hypertension is a major risk factor for several cardiovascular diseases and also an independent predictor of renal injury. Risk of these complications is aggravated in patients with hypertension and diabetes comorbidity. Timely detection of hypertension in patients with or without diabetes and its early, aggressive control can significantly reduce cardiovascular events and renal disease progression.

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Guide to hypertension management: Treatment approach and when to refer?

WHEN TO INITIATE ANTIHYPERTENSIVE TREATMENT?

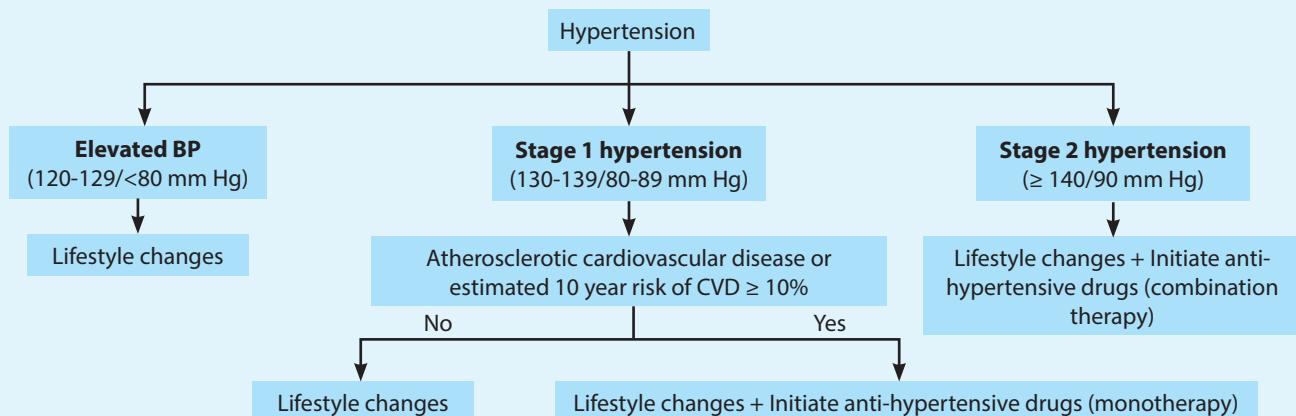
Evidence-based recommendations of the JNC 8 proposed initiation of antihypertensive drug therapy in all hypertensive adults \geq 60 years of age at blood pressure \geq 150/90 mm Hg. In hypertensive subjects $<$ 60 years of age, drug therapy is recommended at blood pressure \geq 140/90 mm Hg. Recommended target blood pressure goals are $<$ 150/90 mm Hg in adults \geq 60 years and $<$ 140/90 mm Hg in adults $<$ 60 years. In those with coexisting diabetes or CKD, antihypertensive drug therapy is recommended at blood pressure $>$ 140/90 mm Hg, with the goal of reducing SBP to $<$ 140 mm Hg and DBP to $<$ 90 mm Hg.¹

The recent ACC/AHA guidelines² have also specified blood pressure thresholds for treatment initiation

(Figure 1). Additionally, they recommended evaluation of risk of atherosclerotic cardiovascular disease (ASCVD) for guiding treatment decisions and improving its cost effectiveness. These guidelines recommended:

- ❖ Lifestyle modifications (non-pharmacological therapy; Table 1) in all adults with blood pressure between 120-129/ $<$ 80 mm Hg.
- ❖ Lifestyle modifications along with additional antihypertensive drug therapy are recommended in all adults with blood pressure between 130-139/80-89 mm Hg; in those with preexisting CV disease or high CV risk (10- year estimated risk \geq 10%).
- ❖ In all hypertensive adults with blood pressure \geq 140/90 mm Hg, antihypertensive drug therapy should be initiated along with lifestyle modifications, irrespective of CV risk status.

Figure 1: Specified blood pressure thresholds for antihypertensive treatment initiation according to 2017 ACC/AHA guidelines



Source: Whelton PK, Carey RM, et al. 2017. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018; 71(6): e13-e115.



Table 1: Lifestyle changes for prevention and treatment of hypertension: ACC/AHA recommendations

Non-pharmacologic Intervention		Dose	Approximate Impact on SBP	
			Hypertension	Normotension
Weight loss	Weight/body fat	Ideal body weight is the best goal but at least 1 kg reduction in body weight for most adults who are overweight. Expect about 1 mm Hg for every 1 kg reduction in body weight.	↓5 mm Hg	↓2/3 mm Hg
Healthy diet	Dietary Approaches to Stop Hypertension (DASH) dietary pattern	Diet rich in fruits, vegetables, whole grains, and low-fat dairy products with reduced content of saturated and total fat	↓11 mm Hg	↓3 mm Hg
Reduced intake of dietary sodium	Dietary sodium	Optimal goal is <1,500 mg/day, but at least 1,000 mg/day reduction in most adults	↓5/6 mm Hg	↓2/3 mm Hg
Enhanced intake of dietary potassium	Dietary potassium	3,500–5,000 mg/day, preferably by consumption of a diet rich in potassium	↓4/5 mm Hg	↓2 mm Hg
Physical activity	Aerobic	<ul style="list-style-type: none"> • 90–150 min/wk • 65%–75% heart rate reserve 	↓5/8 mm Hg	↓2/4 mm Hg
	Dynamic resistance	<ul style="list-style-type: none"> • 90–150 min/wk • 50%–80% 1 repetition maximum • 6 exercises, 3 sets/exercise, 10 repetitions/set 	↓4 mm Hg	↓2 mm Hg
	Isometric resistance	<ul style="list-style-type: none"> • 4 x 2 min (hand grip), 1 min rest between exercises, 30%–40% maximum voluntary contraction, 3 sessions/wk • 8–10 wk 	↓5 mm Hg	↓4 mm Hg
Moderation in alcohol intake	Alcohol consumption	<p>In individuals who drink alcohol, reduce alcohol to</p> <ul style="list-style-type: none"> • Men: ≤2 drinks daily • Women: ≤1 drink daily 	↓4 mm Hg	↓3 mm Hg

Source: Whelton PK, Carey RM, et al. 2017. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018; 71(6): e13-e115.

- ❖ Initiation of antihypertensive drug therapy in all hypertensive patients with coexisting diabetes or CKD at blood pressure > 130/80 mm Hg; recommended blood pressure target in them should be < 130/80 mm Hg.

PHARMACOLOGICAL TREATMENT

There is convincing evidence to show that optimizing blood pressure control using pharmacological antihypertensive therapy can reduce risk of coronary events, strokes, and heart failures. Several classes of antihypertensive drugs are currently available; including diuretics, RAS blockers (angiotensin converting enzyme inhibitors [ACE inhibitors] and angiotensin receptor blockers [ARBs]), calcium channel blockers (CCB), and beta-blockers.^{3,4} Results of the recent Systolic Pressure Intervention Trial

(SPRINT) trial⁴ showed that intensive blood pressure lowering (SBP < 120 mm Hg) in hypertensive patients ≥ 50 years with increased CV risk but without diabetes or prior stroke resulted in 25% greater reduction in risk of combined outcomes of myocardial infarction, stroke, heart failure, or CV deaths compared to standard blood pressure lowering (SBP < 140 mm Hg). Although intensive blood pressure control is still not unequivocally recommended strategy.

Different classes of antihypertensive drugs are currently available for blood pressure lowering. In uncomplicated hypertension, first-line antihypertensive therapy should include a diuretic, RAS blockers (ARBs or ACE inhibitors) or CCB. RAS blockers are widely used treatment options for hypertension management, particularly in high-risk patients.⁵ The CCB are another



class of commonly used antihypertensive agents. They are effective in blood pressure lowering, and additionally improve most CV outcomes, except heart failure.⁶ Moreover, CCB are deemed inferior to RAS blockers in patients with preexisting renal disease, and hence are not recommended as monotherapy in this category of patients.⁷

CHOICE OF ANTIHYPERTENSIVE THERAPY

Physicians can make their choice among the several antihypertensive treatment options. The recent ACC/AHA guidelines² recommended diuretics, ARB/ACE inhibitors, or CCB as front-line therapy in hypertension including those with diabetes; additionally suggested preferable use of either ARB or an ACE inhibitor in the presence of albuminuria. In patients with CKD with albuminuria ≥ 300 mg/day or ≥ 300 mg/g albumin-to-creatinine ratio, ACE inhibitor is initially recommended, while ARB should be used in ACE-intolerant patients.

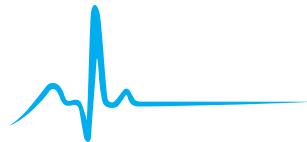
CONCLUSION

Hypertension is a major problem in India and the most prevalent chronic disease. Most of the subjects have mild to moderate hypertension and the initial strategies for management involve lifestyle changes focussing on reduction of dietary salt, fat and alcohol and increase

in potassium, fruits, and vegetables. Pharmacological treatment should be initiated after lifestyle interventions and choice of drug depends on age, the overall cardiovascular risk and co-morbidities. Management should focus on comprehensive risk reduction for better prognosis.

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