



ISSN Print: 2664-8881
ISSN Online: 2664-889X
Impact Factor: RJIF 8
IJMS 2023; 5(2): 06-11
www.medicinejournal.in
Received: 05-07-2023
Accepted: 17-07-2023

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International Journal of **Medicine Sciences**

Cardiovascular risk prevention in hypertensive patients: An Indian perspective

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DOI: <https://doi.org/10.33545/26648881.2023.v5.i2a.37>

Abstract

Hypertension is significantly connected to almost all acquired cardiovascular illnesses, making it one of the most significant risk factors. The management strategy for hypertension differs depending on various patient factors, such as age, gender and the presence of comorbid conditions such as diabetes and chronic kidney disease (CKD). Key strategies for effectively managing risk factors and preventing cardiovascular risk in hypertension may include diet control, exercise, reduced salt intake, home blood pressure monitoring and patient education, among others. Blood pressure objectives and control should be tailored to each individual depending on a variety of characteristics such as age, gender, comorbidities such as diabetes and CKD. This review contains Indian specialists' opinions and examines measures for cardiovascular risk prevention in hypertensive patients.

Keywords: Hypertension management, cardiovascular prevention, elderly, hypertension prevention, chronic kidney disease

Introduction

Elevated blood pressure is the primary cause of premature death worldwide, affecting over 1.13 billion people, two-thirds of whom live in low- and middle-income countries. Despite the availability of pharmacologic treatments for high blood pressure, less than one in every five people manages to achieve blood pressure control^[1]. In India, hypertension is the leading cause of mortality and disability. The 2019-2020 National Family Health Survey (NFHS-5) found that 24% of men and 21% of women in India had hypertension, up from 19% and 17%, respectively, in the year 2015-16^[2]. Hypertension among young persons is widespread, impacting one in every eight adults aged 20 to 40 years^[3].

Globally, hypertension is the major cause of preventable morbidity and mortality. The negative effects of high blood pressure on hypertension-mediated organ damage and cardiovascular outcomes, including damage to the heart, kidneys and brain, are undeniable^[4].

Meetings with Indian experts were scheduled to better understand the burden of hypertension in India, the impact of high blood pressure on cardiovascular damage, cardiovascular risk profile and risk stratification in hypertensive patients and prevention of cardiovascular risk in the population. This review summarizes literature and presents the perspectives of Indian experts on cardiovascular risk prevention in hypertensive patients in India.

Relationship between Blood Pressure and Cardiovascular Damage

Hypertension is a common and substantial cause of atherosclerotic cardiovascular disease. It hastens the formation of plaque in arteries, increasing the risk of a variety of adverse effects, including coronary heart disease (CHD), the most common and fatal complication of hypertension^[5]. Diabetes, cigarette smoking and dyslipidemia, in addition to high blood pressure, are major risk factors for atherosclerosis and hence CHD^[6]. Despite the use of cut-offs to classify blood pressure as optimal, normal, high-normal, or high (hypertension), there is a linear relationship between blood pressure and cardiovascular events^[7].

High-normal blood pressure and various stages of hypertension (stage 1, stage 2 and higher) were found to increase the risk of CHD in both men and women in the Framingham Heart Study^[8]. A recent study conducted by Wang *et al.* found that one-standard-deviation increase in cumulative systolic blood pressure (SBP) load was associated with a 14% increase in

significant cardiovascular incidents, a 13% increase in mortality from all causes and a 21% increase in death due to cardiovascular issues^[9]. Oort SV *et al.* employed the 2-sample Mendelian randomization approach to evaluate the causal relationships of 18 cardiovascular risk variables and lifestyle behaviours with hypertension to identify targets for the prevention of hypertension and its related disease burden^[10]. High-density lipoprotein cholesterol, triglycerides, body mass index, alcohol dependence, sleeplessness and education level were found as causal risk variables for hypertension in this Mendelian randomization study. This implies that these modifiable risk variables are important targets for hypertension prevention^[10].

Indian experts believe that obesity, dyslipidemia, smoking and diabetes are commonly observed as some of the common risk factors for hypertension. Physical inactivity, processed carbohydrates in the diet, obesity in children and excessive consumption of packaged food are risk factors for high blood pressure.

Blood Pressure Goal: How Aggressive Should It Be?

The American Heart Association/American College of Cardiology (AHA/ACC) and the European Society of Cardiology (ESC) have disagreed on how to define hypertension since 2017. The ESC maintained the previous criteria (SBP 140-149 mmHg and diastolic blood pressure [DBP] 90-99 mmHg), but the AHA/ACC established a lower threshold (SBP 130-139 mmHg and DBP 80-89 mmHg) to characterize hypertension. Despite the inconsistency of these criteria, both guidelines advise treating high blood pressure with non-pharmacological interventions first and using antihypertensive drugs only if the risk becomes severe^[11, 12, 13].

Treatment of hypertension has been proven in clinical trials to reduce the incidence of cardiovascular disease outcomes such as incident stroke (by 35% to 40%), myocardial infarction (by 15% to 25%), and heart failure (by up to 64%)^[14, 15, 16]. The optimal target for reducing SBP remains uncertain. Although observational studies have shown a gradual increase in cardiovascular risk as SBP exceeds 115 mm Hg^[17], evidence from randomized controlled trials in the general population of hypertensive patients only supports treatment aimed at achieving an SBP target of <150 mm Hg. There is limited data available regarding lower blood pressure targets^[18].

The Systolic Blood Pressure Intervention Trial (SPRINT) concluded that in patients at high cardiovascular risk, aiming for an SBP of <120 mm Hg resulted in lower rates of major adverse cardiovascular events and all-cause mortality than aiming for an SBP of <140 mm Hg, both during and after the trial. It is worth mentioning, however, that some side effects were more common in the intensive therapy group^[19].

Phillips *et al.* conducted research to assess the influence of baseline 10-year risk of cardiovascular disease (CVD) on primary endpoint events and all causes of adverse events in SPRINT. The study suggested that in adults with hypertension, intensive treatment would provide more benefits than harm for those with a 10-year risk for CVD \geq 18.2%. On the other hand, for individuals with a risk of <18.2%, a standard blood pressure goal would be a suitable management approach.

Indian specialists agreed that the blood pressure target should vary depending on the patient profile, with BP targets of 130/85 mmHg being recommended for all young

hypertensive patients and those with multiple cardiovascular risk factors or comorbidities. In older patients with few risk factors and comorbidities, blood pressure objectives can be modified up to 140/90 mm Hg. It is always recommended to modify the blood pressure targets based on risk factors, comorbidities and other considerations. Individualization is essential.

International guidelines for hypertension management have categorized cardiovascular risk based on blood pressure, cardiovascular risk factors, organ damage and the presence of diabetes or cardiovascular or kidney disease. The risk is classified as low, moderate, high or very high, based on the 10-year risk of cardiovascular mortality as defined by the 2012 ESC prevention guidelines^[20].

Cardiovascular risk assessment tools, according to all Indian experts, are not employed in ordinary clinical practice. Clinicians assess cardiovascular risk using clinical judgment. However, experts agreed that using a tool to assess cardiovascular risk can motivate patients to self-manage their blood pressure on a regular basis and to initiate and maintain lifestyle management strategies.

Cardiovascular Risk Profiles and Risk Stratification in Hypertensive Patients

Managing Hypertension in young adults

In one of the recent studies conducted in Korea, young individuals under the age of 40 years with stage 1 hypertension, according to the 2017 ACC/AHA BP guideline, have a greater risk of developing subsequent CVD events if they have had isolated systolic hypertension (ISH), isolated diastolic hypertension (IDH) or systolic and diastolic hypertension (SDH) compared to those individuals with normal blood pressure. Stage 1 SDH was associated with a greater incidence of CVD than stage 1 ISH and IDH. Categorizing patients based on stage 1 ISH, IDH and SDH may help identify high-risk people and enhance risk stratification^[21].

Expert recommendations

- It is necessary to properly assess blood pressure. It is recommended that office blood pressure be assessed three times.
- A thorough examination of the patient is essential. Echocardiogram, microalbuminuria, creatinine, serum calcium and potassium levels, lipid levels, liver enzymes, C-reactive protein and other parameters must all be evaluated and reported.
- Angiotensin receptor blockers (ARBs) are recommended. To maintain ARBs, serum calcium and potassium levels must be monitored and kept normal. Unless there is evidence of ischemia, beta-blockers should not be recommended. If blood pressure cannot be controlled with ARBs, calcium channel blockers (CCBs) are the next best option. Beta-blockers are a treatment option for patients suffering from obstructive sleep apnea.
- Lifestyle changes can undoubtedly be explored in young, concerned hypertensive patients. Avoiding junk food, improved sleep patterns, frequent physical activity and home blood pressure monitoring are all recommended. If the patient appears to be adhering to the lifestyle adjustments, therapy can be delayed by 1 to 3 months. Home blood pressure should be compared to office blood

pressure. Patients are reassured when both are under control.

- In young patients with hypertension, a 10-year cardiovascular risk assessment is critical. A blood pressure target of 130/80 mmHg is attempted and a target of 120/75 mmHg can be attempted for those with comorbidities.
- Young women with hypertension should rule out any hormonal therapy. A history of pregnancy-induced hypertension (PIH) should be obtained and checked out. Hypothyroidism should be suspected and ruled out. If necessary, an endocrinologist's advice and evaluation should be requested.

Management of hypertension patients with diabetes

Non-communicable diseases (NCDs) are on the rise around the world, with CVD (of which hypertension is a substantial risk factor) and diabetes mellitus being two of the most frequent. NCDs account for 62% of all deaths in India, while premature deaths account for 48% of total national mortality. As a result, hypertension and diabetes are major public health concerns [22].

Patients with diabetes mellitus face a similar risk of cardiovascular death as patients with a previous myocardial infarction. A study based on the Framingham cohort found that hypertension contributes to 30% of all-cause death and 25% of any cardiovascular event in patients with DM. In contrast, after adjusting for HTN, the population attributable risk from DM was only 7% for all-cause death and 9% for any cardiovascular event. The study concluded that hypertension is likely the main contributor to cardiovascular outcomes in patients with diabetes [23]. The experts also concurred that the twin epidemic of hypertension and diabetes is increasing in India, which is impacting adverse cardiovascular outcomes.

Due to the high prevalence and significant impact of both diabetes and hypertension on cardiovascular risk, managing hypertension in diabetic individuals is crucial. Consequently, several professional organizations and expert groups have proposed recommendations, including lifestyle modifications and medications, for the management of hypertension in adults with diabetes [24].

Expert recommendations

- Proteinuria estimation is particularly significant in these patients and chronic kidney disease (CKD) at an early stage should not be overlooked. At the time of diagnosis, 50% of hypertensive individuals with diabetes have stage 2 or 3 CKD, with an estimated glomerular filtration rate (eGFR) ranging from 60 to 90 mL/min/1.73 m².
- The type of therapy used depends on creatinine levels. The use of ARBs/angiotensin-converting enzyme inhibitors is preferred. It is critical to monitor serum potassium and calcium levels.
- Long-term damage to target organs is caused by the combination of diabetes and hypertension. The signs should be identified and managed ahead of time. Eye examination nephrologists' evaluations and other tests are to be performed.

Managing hypertension in the elderly

Hypertension rises with age and is linked to poor cardiovascular outcomes in the elderly, including heart failure, stroke, myocardial infarction and mortality. Studies

have often excluded older adults from hypertension management, but recent studies including UK Prospective Diabetes Study UKPDS), the Systolic HTN in the Elderly Program (SHEP), SPRINT, Systolic Hypertension in Europe (Syst-Eur), Medical Research Council Working Party and The Hypertension in the Very Elderly Trial (HYVET) demonstrate cardiovascular benefits in treating hypertension in older adults. Recognition and appropriate treatment of hypertension in older adults is important [25].

Expert recommendations

- The elderly have difficulty tolerating anti-hypertensives.
- Anti-hypertensive can be started at a low dose and can be escalated slowly to a higher dose if required.
- ARB/ACE inhibitors can cause orthostatic hypotension in this group. Alpha-blockers can be useful. However, alpha-blockers and diuretics should be used with caution due to the risk of syncope and orthostatic hypotension.
- Variability in blood pressure, particularly systolic blood pressure, is highly prevalent among the elderly. It frequently results in a stroke. It must be evaluated and regulated.

Managing hypertensive patients with CKD

The prevalence of CKD is increasing globally and is strongly linked to the development of CVD. Hypertension is both a cause and a consequence of CKD and affects most CKD patients. Proper management of hypertension is crucial in CKD patients, as it helps to slow the progression of the disease and reduces the risk of CVD [26].

Expert recommendations

- Morning vs. bedtime - both therapy modes have the same effect, as proved in studies and clinically in India.
- The early morning rise in blood pressure is critical. If patients are on multiple medications, it is best to take one in the morning and one in the evening.
- Nifedipine, alpha-blockers and cilnidipine are the most preferred medications. Serum potassium should be monitored when using ARBs,
- CKD patients are more likely to develop resistant hypertension rather than hypotension. Dialysis can cause hypotension and fluid depletion. Such patients must be closely followed and individualization is essential.
- Patients with hypertension and CKD are more prone to the rapid progression of CV events.
- Aggressive blood pressure control to <130/80 mmHg is needed in patients with hypertension and CKD

Management of hypertension in women

Worldwide, hypertension is regarded as the leading risk factor for CVD. High blood pressure is more common in men than in women at a younger age, although this gradually reverses beyond the age of 50 years [27].

Randomized controlled trials with CVD outcomes have shown that blood pressure lowering with medications benefits both hypertensive women and men, with no consistent differences in outcomes by sex. The INDANA intervention trials and the BP-Lowering Treatment Trialists' Collaboration overview showed no significant differences in treatment benefit between sexes, with comparable blood pressure reductions and no significant sex-related differences in CVD outcomes. No differences in the effects of specific

antihypertensive medications on blood pressure or CVD outcomes by sex were identified [27].

Expert recommendations

- Women are overlooked during the screening, diagnosis and treatment stages. Because they receive therapy late, complications can arise quickly and aggressively.
- Women in their twenties can present with atypical hypertension. They should be evaluated aggressively and thoroughly. Postmenopausal women with hypertension are treated in the same way as men.

Recommendations for Optimal Management of Risk Factors and Prevention of Cardiovascular Risk in Hypertension

Local hypertension societies in Asia are focusing on hypertension management and minimizing its cardiovascular consequences. Strategies tailored to the specific features of hypertension in Asia are likely to be effective in its management. The following seven strategies are recommended by HOPE Asia Network [28]:

- Home-based blood pressure monitoring-guided hypertension management
- Strict blood pressure control
- Reducing morning home blood pressure as the 1st target and night-time blood pressure as the 2nd target for high-risk patients
- Widespread screening to improve awareness
- Use of telemedicine strategies
- Choice of preferred antihypertensive agents
- Strict reduction of sodium intake

A key element of preventing CVD is improving one's lifestyle and diet is among the most effective ways to achieve reductions and control of blood pressure. The Dietary Approach to Stop Hypertension (DASH) diet is a dietary approach that encourages the consumption of fruits, vegetables, low-fat dairy products, whole grains, poultry, fish and nuts, while minimizing the intake of red meat, sweets, sugar-containing beverages, total fat, saturated fat and cholesterol [29].

In addition to diet, it is well established that regular exercise provides numerous health benefits and increasing physical activity levels should be a priority in healthcare. Studies have shown that individuals with hypertension are typically less physically active than those without, and there is strong evidence indicating that regular exercise can help lower blood pressure, particularly in individuals with hypertension [30]. Patient education and awareness also play a crucial role in the management and control of hypertension.

Expert recommendations

- Diet is crucial in Indian patients with hypertension. Salt restriction is critical and patients should be warned and emphasized about it. Intake of high carbohydrate diet, alcohol and caffeine is harmful. Dietary advice may be recommended for patients who can afford it.
- Regular blood pressure monitoring is critical, especially with home blood pressure monitoring.
- Involving family members and relatives in patient care can be beneficial.

- Another important aspect that can improve clinical outcomes in individuals with hypertension is smoking cessation.
- Patient education is essential. As previously noted, lifestyle changes and adherence to therapy are critical.

Personalized cardiovascular disease prevention

The increasing availability of lipid-lowering, anticoagulant and antidiabetic medications, along with ever-evolving treatment goals outlined in guidelines, has added complexity to cardiovascular disease prevention [31]. Unfortunately, there is a substantial gap between optimal treatment goals and what most patients can practically achieve. The new European guidelines for cardiovascular disease prevention have been framed taking this concern into account. [31]

The recommendations employ a new two-step methodology. Step 1 includes all patients and establishes basic therapy goals. Step 2 comprises heightened treatment goals and is only indicated when an individual assessment of residual risk has been completed. This evaluation considers the patient's progress towards accomplishing Step 1 objectives. Furthermore, considerations such as frailty, comorbidities, risk factors and the patient's preferences and requirements are considered during the assessment process [31].

Step 1 [31]

Step 1 guidelines are universally applicable

- Lifestyle changes including quitting smoking, physical activity, maintaining a healthy weight and adopting a nutritious diet
- Drug-assisted smoking cessation, prioritizing complete smoking cessation regardless of potential weight gain.
- Physical activity involves 300 minutes of moderate-intensity or 150 minutes of vigorous-intensity exercise per week, along with regular resistance training.
- Reducing sedentary behaviour.
- Dietary advice aligned with other guidelines, emphasizing limitations on salt, saturated fat, sugar, processed food and meat consumption.
- Regular intake of fish, Mediterranean foods, fibre, pulses, nuts, fruits and vegetables
- Maximum recommended alcohol consumption of 100 grams per week (equivalent to one unit of alcohol daily).
- Maintaining normal weight or losing weight if overweight, in accordance with dietary recommendations.
- Medication treatment for individuals with systolic blood pressure >160 mmHg, with a target of 140/80 mmHg, regardless of other concerns.
- Assessment of lifetime risk and expected treatment benefits even for seemingly healthy persons with low or moderate risk.
- Determination of treatment targets for blood pressure, glycated haemoglobin (HbA1c) and low-density lipoprotein (LDL) cholesterol depending on individual patient risk level.
- High-intensity statins, possibly in combination with ezetimibe, for patients at high and very high risk and proprotein convertase subtilisin/kexin type 9 inhibitors for patients not meeting LDL cholesterol targets.
- Combination treatment for patients with hypertension, while monotherapy for patients at risk of hypotension.

- Assessment of medication adherence before escalating treatment.
- HbA1c target of 53 mmol/mol (7%) for patients with diabetes and lower targets for younger patients or those with shorter disease duration.
- Metformin as the first-line treatment for type 2 diabetes and sodium-glucose cotransporter-2 inhibitors or glucagon-like peptide-1 analogues for patients with cardiovascular disease or target organ damage.
- Single or dual antiplatelet therapy, with individualized selection and duration based on coronary anatomy, bleeding risk and potential need for anticoagulation for individuals with established cardiovascular disease
- Consulting healthcare professionals for antiplatelet therapy decisions

Step 2 ^[31]

Once the Step 1 treatment goals for blood pressure and LDL cholesterol are met, it is necessary to conduct an individual assessment to determine whether treatment should be escalated to Step 2:

- Consideration of factors such as risk modifiers, age, frailty and patient preferences, similar to the original risk assessment.
- Systolic blood pressure target of 130 mmHg for all groups if tolerated.
- Blood pressure target of 140 mmHg for patients over 70 years, as well as those with chronic kidney disease.
- LDL cholesterol treatment goals for high-risk and very high-risk patients of 1.8 mmol/L and 1.4 mmol/L, respectively.

However, the guidelines emphasize the need for greater research into the effects of decreasing LDL cholesterol to 1.4 mmol/l and its practicality, particularly in primary care settings

Summary

Almost all acquired CVDs, cerebral stroke and renal failure are strongly linked to hypertension, making it one of the most significant risk factors. The classification of high-normal blood pressure versus hypertension is based on arbitrary cut-off values, with hypertension being the level that warrants intervention to lower blood pressure due to documented preventive benefits. Individualization is the key. Management strategy varies as per patients' age, gender and comorbid conditions like diabetes and CKD. Diet, exercise, low salt intake, home blood pressure monitoring and patient education are key strategies for the optimal management of risk factors and prevention of cardiovascular risk in hypertension.

Author Contributions

The author made significant contributions to the inception of the advisory board meetings, documented the conversations, and substantively evaluated and approved the final version for submission.

Source of Funding

The expert panel discussion was organized in collaboration with Abbott Healthcare Pvt. Ltd. This article is based on the expert group discussion's viewpoints. The views expressed and discussed in the meetings, as well as those presented in

this paper, are the authors' independent views, not those of Abbott Healthcare Pvt. Ltd.

Conflict of Interest

For their involvement in the focused group discussion, both authors received speaker's honoraria from Abbott Healthcare Pvt. Ltd. VT Shah is a member of Cardiology Society of India, Chembur Indian Medical Association, Association of Physicians of India, Mahim Dharavi Medical Association, American College of Cardiology, and European Society of Cardiology. Samir Kubba is a member of Cardiology Society of India, Association of Physicians of India, East Delhi Physician Association, American College of Cardiology, and European Society of Cardiology.

Acknowledgement

The authors acknowledge Indyte medical communication (C2C) for medical writing support and editorial assistance.

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