

EARLIER STAGE OF HYPERTENSION

Prehypertension: What to Do?

Arvind K Pancholia

ABSTRACT

Prehypertension (PHTN) is a global health problem that carries the risk of being prone to developing hypertension in the future along with double the risk of cardiovascular disease (CVD). Its prevalence is 25 to 50% based on data from different countries, and it varies with age, sex, birth weight, and body mass index (BMI). Regarding its pathophysiology, several mechanisms have been proposed, but the most validated are Ras activation, oxidative stress, inflammatory cytokines, sympathetic overdrive, and central nervous system activation. Therapeutic lifestyle changes are the foundation for all therapies in prehypertensive patients, which are recommended by almost all guidelines. Drug therapy has also been tried in a couple of trials and is recommended in high-risk patients.

Keywords: Dietary approaches to stop hypertension diet, Hypertension, Sodium

How to cite this article: Pancholia AK. Prehypertension: What to Do? *Hypertens J* 2017;3(2):67-71.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

In 1939, Robinson and Brucer suggested the value of clinically overt hypertension when the levels are 120 to 139 mm Hg (systolic) and 80 to 89 mm Hg (diastolic).¹ Three decades later, it was termed as "borderline hypertension";² then in 1997, it was changed to "high-normal blood pressure (BP)."³ The term "PHTN" was coined in 2003 by the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7).¹ This report intended to identify those individuals in whom early intervention by healthy lifestyles could reduce BP and the rate of converting from PHTN to hypertension. The PHTN precedes clinical hypertension and is associated with increased incidence of CVD.²⁻⁴

DEFINITION

The PHTN is defined as a systolic BP (SBP) of 120 to 139 mmHg and/or a diastolic BP of 80 to 89 mmHg.

Head

Department of Medicine and Preventive Cardiology, Arihant Hospital & Research Centre, Indore, Madhya Pradesh, India

Corresponding Author: Arvind K Pancholia, Head, Department of Medicine and Preventive Cardiology, Arihant Hospital & Research Centre, Indore, Madhya Pradesh, India, Phone: +919827027920, e-mail: drpancholia@gmail.com

Later on, the European Society of Cardiology (ESC) and the European Society of Hypertension (ESH) bifurcated it into normal (120–129 systolic and 80–84 diastolic) and high-normal (130–139 systolic and 85–89 diastolic). The ESH–ESC committee decided against using the term "PHTN" for several reasons:

- There is no reason to combine the two different groups because the risk of developing hypertension was definitely higher in those with high-normal BP than in patients with normal BP.
- The term "PHTN" can create anxiety in many subjects along with unnecessary medical visits and tests.
- Although lifestyle changes are recommended by the JNC7 for all PHTNs, this category is a highly differentiated one, with the extremes consisting of subjects with no need of any intervention.

PREVALENCE

The National Health and Nutrition Examination Survey (NHANES), 1999–2000 reported that the overall prevalence of PHTN was 31% all over the world, which was higher in men than in women.⁵ A statistical analysis of disease-free adult NHANES participants, which was conducted from 1999 to 2006, found that the overall prevalence of PHTN in disease-free adults was 36.3%.⁶

Prevalence increases in people with⁷

- Diabetes,
- Microalbuminuria,
- Chronic kidney disease (CKD),
- Heavy alcohol consumption, and
- Overweight/obese.

Prevalence in India

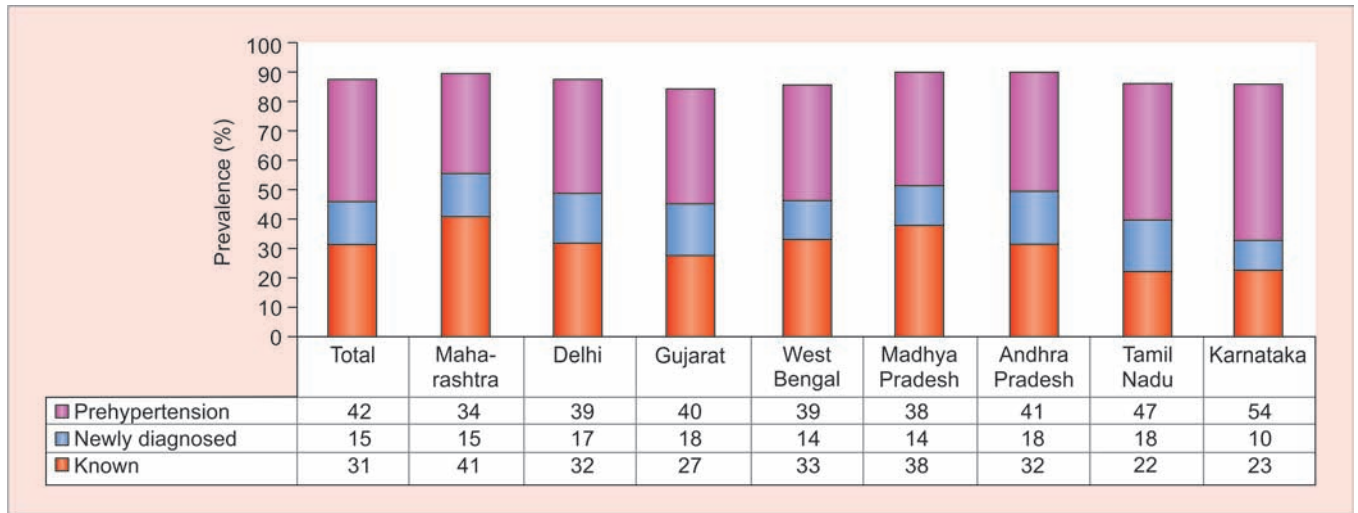
In a study from northern India, the reported prevalence of PHTN is 44%,⁸ whereas a study in urban Chennai indicated a 47% prevalence of PHTN in adults >18 years.⁹ In another study, the reported prevalence is 40% in males and 30% in females.¹⁰ The statewise prevalence in India is shown in Graph 1.

RISK FACTORS

The risk factors are indicated in Table 1.

WHY CARE FOR PHTN

Patients with PHTN are at twice the risk of developing hypertension.¹¹ The PHTN is also associated with



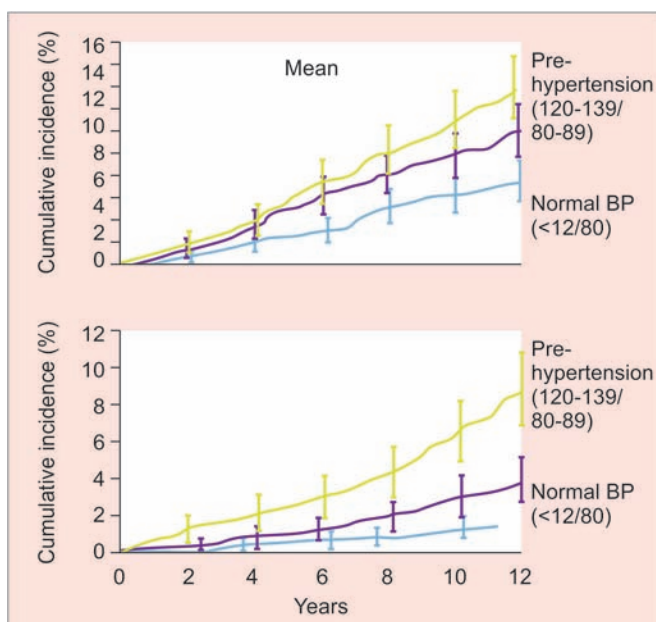
Graph 1: Statewise prevalence of PHTN in India

Table 1: Risk factors

Overweight or obese
Age: > More in young patients
Sex: M>F
Black race
Family history
Lack of exercise
Diet high in salt (sodium) or low in potassium
Tobacco use
Alcohol

increased CVD. According to the Framingham study, there is increased risk of myocardial infarction by 3.5 fold and an increased risk of coronary artery disease by 1.7 fold¹¹ (Graph 2).

Results from the Strong Heart Study¹² showed an increased risk of CV events when PHTN is associated with diabetes compared with diabetes or PHTN alone (Graph 3).

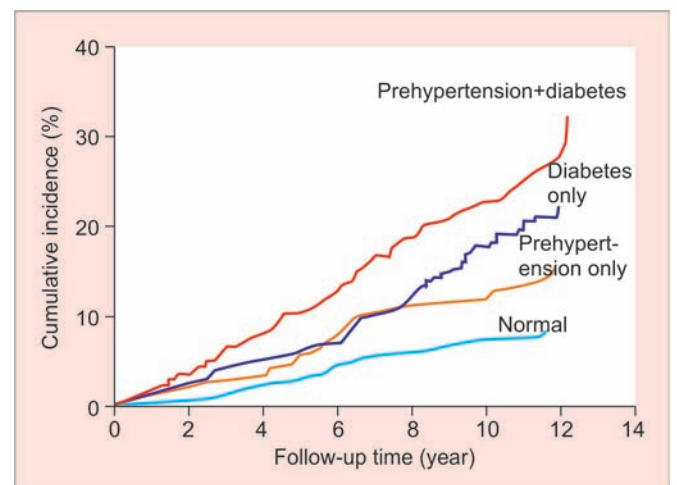


Graph 2: PHTN and CV risk (Source: Vasan et al¹¹)

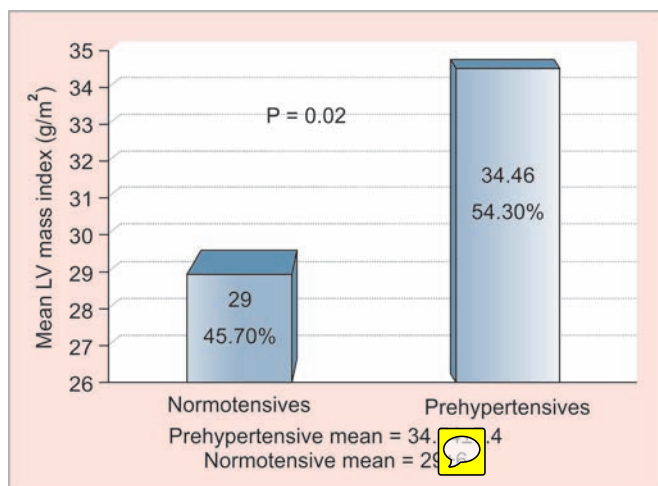
The study also showed that 37% of prehypertensives will progress to hypertension over the next 4 years. There is a 2-fold increased risk of diabetes also in PHTN. Compared with a normal BP, PHTN is associated with a 27% increase in all causes of death and a 66% increase in cardiovascular deaths.¹³

Analysis from the CARDIA study suggests that PHTN in early adulthood leads to increased coronary calcium later in life.¹⁴ The PHTN is also associated with increased carotid intima thickness.¹⁵ There is increase in left ventricular (LV) mass index also with PHTN¹⁶ (Graph 4).

It is also associated with increased risk of CKD.¹⁷ A study also showed the worsening of renal function by 11 to 91% in prehypertensive individuals. Preexisting diabetes showed a strong relationship of PHTN and CKD risk. The basic pathophysiology for the development of CKD is the greater degree of renal arteriosclerosis and mesangial proliferation in prehypertensives.¹⁷ High-normal BP is associated with poor cognitive performance also. The relationship between BP and cognitive



Graph 3: Strong heart study (Source: Segura and Ruilope¹²)



Graph 4: PHTN and LV mass index (Source: Mousa et al¹⁶)

Table 2: Joint national committee 7 recommendations: Prehypertension lifestyle changes

Items	Modifications	Effects on pressure
Sodium intake	Allowable maximum is 2.4 gm of sodium or 6 grams of sodium chloride	5.1/2.7 mm Hg for 1800 mg/day sodium reduction
Weight loss	Maintain normal body weight (body mass index 18.5 to 24.9), per kg lost	1.1/0.9 mm Hg for 1 kg weight loss
Alcohol	Limit to 2 drinks/day men (1 drink/day women & lightweight person)	2 to 4 mm Hg
Exercise	Do 30 minutes of aerobic exercise for 4 to 7 days a week	4.9/3.7 mm Hg for 120 to 150 minutes/week of exercise
Healthy diet	Take diet rich in fruits, vegetables	11.4/5.5 mm Hg

performance is linear, even in normotensive and prehypertensive ranges.¹⁸ The PHTN also predicts pregnancy-induced hypertension and its postpartum progression.¹⁹ The PHTN is also linked with metabolic syndrome and CVD (Flow Chart 1).

PATHOPHYSIOLOGY

Many hypotheses are proposed to explain the underlying pathophysiology of PHTN.

- Renin–angiotensin–aldosterone system activation
- Oxidative stress
- Inflammation
- Sympathetic nervous system activation
- Central mechanism

PHTN: WHAT TO DO ?

Therapeutic Lifestyle Changes

Practically all the guidelines, previous³ and recent guidelines,²⁰ recommend specific lifestyle modifications for

Flow Chart 1: Cardiometabolic syndrome and link with CVD (Source: Expert Rev Cardiovasc Ther 2013)

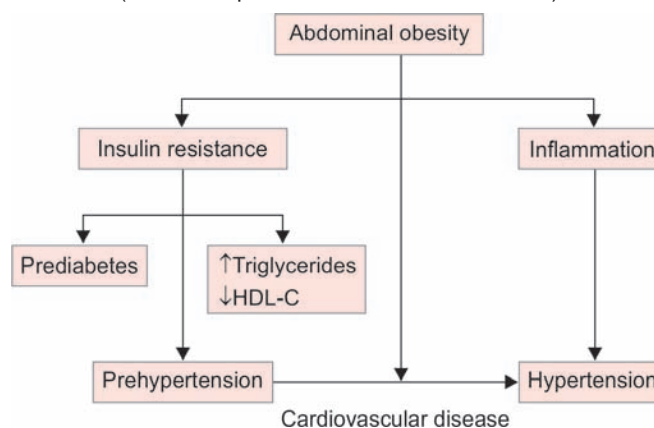


Table 3: DASH diet

The DASH eating plan

High in

- Fruits and vegetables (four or five servings each per day)
- Fiber (seven or eight servings per day)
- Low-fat dairy products (two or three servings per day)
- Lean meat (two servings per day)
- Calcium
- Magnesium
- Potassium

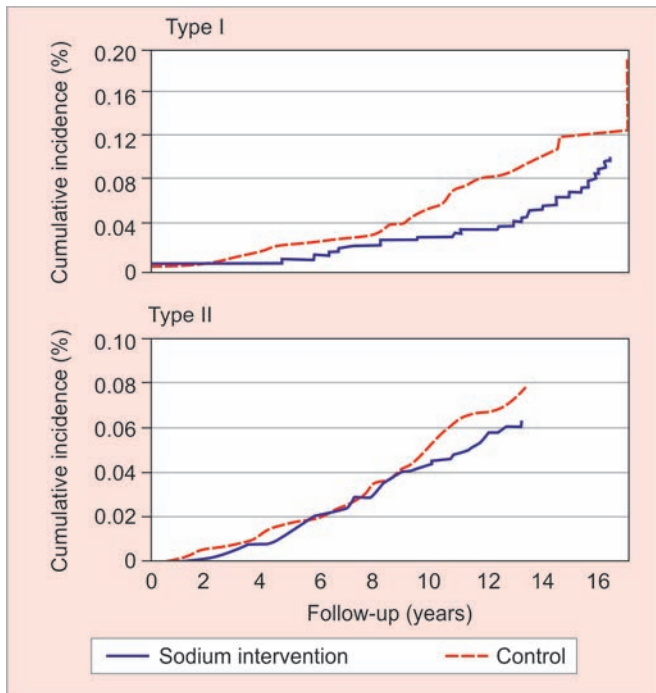
Low in

- Saturated fat
- Cholesterol
- Salt

PHTN. The most recent recommendations (JNC7 report)⁴ are as follows:

- Maintaining BMI between 18.5 and 24.9 kg/m²; this is expected to reduce SBP by 5 to 20 mm Hg for each 10-kg reduction in weight.
- Consuming more fruits and vegetables in diet; this is expected to reduce SBP by 8 to 14 mm Hg.
- Restricting sodium to no more than 6 gm of table salt per day; this is expected to reduce SBP by 2 to 8 mm Hg
- Brisk walking for at least 30 minutes per day or regular aerobic physical activity; this is expected to reduce SBP by 4 to 9 mm Hg.
- Reducing alcohol consumption; this reduces SBP by 2 to 4 mm Hg (Table 2).

Dietary Approaches to Stop Hypertension (DASH) diet plan²¹ (Table 3), which uses a diet rich in fruits, vegetables, legumes, nuts, and low-fat dietary products and low saturated fats, has a significant lowering of BP. The DASH diet can reduce BP by 8 to 14 mm Hg, an effect that was augmented even further when dietary sodium was restricted.



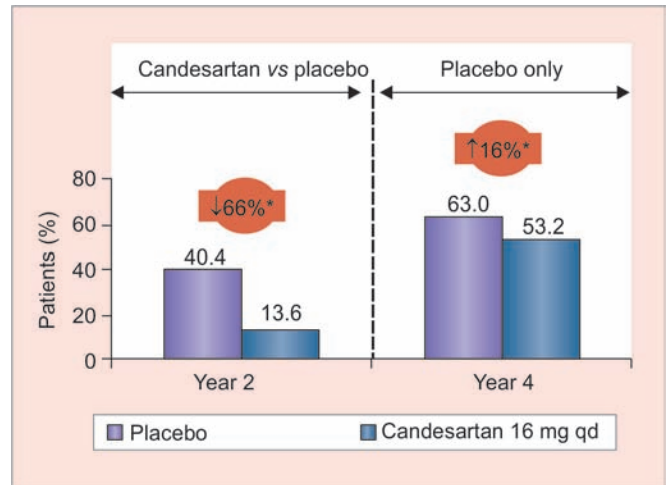
Graph 5: Cumulative incidence of CVD by sodium intervention group in TOHP I and II (Source: Cook NR et al.²³)

The OmniHeart Collaborative Research Group study²² in which the DASH diet was modified to provide more protein and unsaturated fat and less carbohydrate showed impressive reductions of BP. The Trials of Hypertension Prevention (TOHP) I and TOHP II trials²³ (Graph 5) showed that dietary sodium reduction for 18 months (TOHP I) or for 36 to 48 months (TOHP II) reduces the primary end points (myocardial infarction, stroke, coronary revascularization, or cardiovascular-related death) in middle-aged individuals with PHTN by 25% lower compared with placebo group. The PREMIER trial²⁴ demonstrated that multicomponent behavioral interventions with and without the DASH diet produced significant reductions in the 10-year risk of coronary heart disease in subjects with PHTN.

PHARMACOTHERAPY

The primary approach to treat PHTN is therapeutic lifestyle changes, which have been recommended by several guidelines. Pharmacotherapy is recommended mainly in high-risk groups with CVD and CKD. However, there is still no consensus. Few trials have been done with different pharmacological agents with mixed results.

The Trial of Preventing Hypertension (TROPHY) study evaluated the effect of angiotensin II receptor antagonist candesartan cilexetil on the prevention of PHTN progressing to stage 1 hypertension²⁵ (Graph 6). After 4 years, stage 1 hypertension developed in two-thirds of patients in the placebo group, while in the intervention group, there was 66% reduction in the risk of development of incident hypertension.



Graph 6: TROPHY: Reduction in new-onset hypertension (Source: Julius et al²⁵)

The PHARAO study is the prevention of hypertension with the angiotensin-converting enzyme inhibitor Ramipril in patients with high-normal BP—a prospective, randomized, controlled prevention trial of the German Hypertension League.²⁶ The study showed significant reduction in the risk of progression to manifest hypertension by 34.4%.

The PREVER prevention trial²⁷ is the combination of chlorthalidone and amiloride in prehypertensive patients that effectively reduces the risk of incident hypertension and beneficially affects LV mass. After 18 months, the incidence of hypertension was 11.7% in the diuretic arm vs 19.5% in the placebo arm.

Follow-up of Prehypertensive Patients

Subjects with PHTN need to be treated and evaluated every month or two, until the BP goal is reached and then every 3 to 6 months thereafter. Subjects with complications/end organ damage, such as heart or kidney disease may need to be evaluated more frequently at regular intervals.

CONCLUSION

- Prehypertension is a common problem in the community.
- Its prevalence is on the rise.
- It is associated with increased risk of hypertension, target organ damage, and CVD.
- Healthy lifestyle is the foundation for all therapies in persons with PHTN.
- Drug therapies have been tried, but there is no convincing evidence that antihypertensive therapy changes the course of PHTN.

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