Prehypertension

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ABSTRACT
The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and treatment of High Blood Pressure suggested a new classification for high-normal BP levels—the Pre-Hypertension. Normal blood pressure systolic <120 mmHg and diastolic <80 mmHg Prehypertension—systolic 120 to 139 mmHg or diastolic 80 to 89 mmHg. Prehypertension is often associated with multiple additional cardiovascular risk factors, such as obesity, diabetes mellitus, dyslipidemia, and inflammatory markers, and evidence of organ damage for example, microalbuminuria, retinal arteriolar narrowing, increased carotid arterial intima-media thickness, left ventricular hypertrophy and coronary artery disease. Nonpharmacological treatment with lifestyle modifications such as weight loss, dietary modification and increased physical activity is recommended for all patients with prehypertension. Where as pharmacological therapy is indicated for some patients with prehypertension who have specific co-morbidities, including diabetes mellitus, chronic kidney disease and coronary artery disease. Because of its high prevalence and long-term complications, prehypertension has been estimated to decrease the average life expectancy by as much as five years. Unfortunately, current preventive strategies, although admirable from both individual and societal perspectives, are weak.

INTRODUCTION
The term ‘prehypertension’ was coined in 1939 in the context of early studies that linked high blood pressure recorded for life insurance purposes to subsequent morbidity and mortality. Long-term follow-up of patients destined to develop essential (primary) hypertension demonstrates that blood pressure (BP) readings gradually increase over time.

DEFINITION
Prehypertension, defined as the blood-pressure range of 120 to 139 mm Hg systolic or 80 to 89 mm Hg diastolic, the condition heralds arterial hypertension and thus may be considered a starting point in the cardiovascular disease continuum. The seventh report of the Joint National Committee (JNC 7) published in 2003 proposed the following classification based upon the average of two or more properly measured readings at each of two or more visits after an initial screen (Table 1).

The European Society of Hypertension and the European Society of Cardiology (ESH_ESC) guidelines for the hypertension consider prehypertensive to be categorized into, Normal blood pressure* (systolic blood pressure SBP, 120 to 129 mmHg or diastolic blood pressure DBP, 80 to 84 mmHg) and High

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SB-P mmHg*</th>
<th>DBP mmHg LS</th>
<th>Drug Therapy**</th>
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<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>&lt; 80</td>
<td>Encourage</td>
</tr>
<tr>
<td>Pre hypertension</td>
<td>120-139</td>
<td>Or 80 – 89</td>
<td>Yes</td>
</tr>
<tr>
<td>Stage 1 Hypertension</td>
<td>140-159</td>
<td>Or 90-99</td>
<td>Yes</td>
</tr>
<tr>
<td>Stage 2 Hypertension</td>
<td>&gt; 160</td>
<td>Or &gt;100</td>
<td>Yes</td>
</tr>
</tbody>
</table>

*Treatment determined by highest BP category: ** Consider treatment for compelling indications Regardless of BP Normal. JNC 7 Express. JAMA 2003 Sep 10; 290 (10); 114.
PREHYPERTENSION: REASON FOR CREATING A CLASSIFICATION

In 2007, the ESC Committee decided not to use the term 'prehypertension'. The term pre hypertension is more likely to create anxiety in a large subset of population and Hence IHG (International hypertension Guidelines) does not recommend the use of the term “pre hypertension”.

Despite the fierce opposition the new terminology was adopted at the strength of scientific research showing that previously considered normal and high normal blood pressure levels still contained a significant risk of cardiovascular disease (CVD). Experts noted that by introducing this new categorization of hypertension there was progress in bringing prehypertension to the attention of doctors and the general public for better hypertension prevention. When we use of the term high hypertension is clearly higher than that of high blood pressure actually people with pre-hypertension. The prevalence of pre-hypertension in the range of 40-60%. Ongoing nutrition transition with progressive shift indicates the prevalence of prehypertension in rural States of India by the National Nutrition Monitoring Bureau is rapidly increasing in India. A survey conducted in nine men to be about 45 %. A few studies from different regions of India(e.g. Dr. Mohan cures study at Chennai) have also indicated the prevalence of prehypertension in the range of 40-60%. Ongoing nutrition transition with progressive shift to a westernized diet may further accentuate the risk. It turns out that a huge number of people in any given population are actually people with pre-hypertension. The prevalence of prehypertension is clearly higher than that of high blood pressure itself. Individuals who are overweight or obese are at risk of

RESONS FOR CREATING A CLASSIFICATION OF PREHYPERTENSION:

- Increase awareness of lifetime risk of hypertension.
- Increased awareness of reduced risk of cardiovascular complications.
- Identify individuals in whom early intervention by lifestyle modifications could lower blood pressure.

EPIDEMIOLOGY

Data from the 1999 and 2000 National Health and Nutrition Examination Survey (NHANES III) suggested that the prevalence of prehypertension among adults in the United States was approximately 31%. The prevalence was markedly higher among men than women (39 and 23 percent, respectively). The prevalence of hypertension and cardiovascular disease is rapidly increasing in India. A survey conducted in nine States of India by the National Nutrition Monitoring Bureau reported the pooled estimate of prehypertension in rural men to be about 45 %. A few studies from different regions of India(e.g. Dr. Mohan cures study at Chennai) have also indicated the prevalence of prehypertension in the range of 40-60%. Ongoing nutrition transition with progressive shift to a westernized diet may further accentuate the risk. It turns out that a huge number of people in any given population are actually people with pre-hypertension. The prevalence of prehypertension is clearly higher than that of high blood pressure itself. Individuals who are overweight or obese are at risk of
Prehypertension

Prehypertension is one step towards hypertension, hence the same factors are involved in both.

RISK FACTORS

Elevated concentrations of creative protein, Tumor necrosis factor – (α) alpha homocysteine, oxidized low – density lipoprotein, gamma-glutamyl transferase, micoalbuminuria, and other inflammatory markers are associated with higher blood pressure. Prehypertension also accelerates the development of left ventricular (LV) hypertrophy and diastolic dysfunction.

ATTICA STUDY

Toika et al illustrated evidence of sub clinical atherosclerosis, by measuring intima-media thickness of the carotid and brachial arteries in healthy men with borderline hypertension. prehypertension males and females had 31% higher CRP , 32% higher TNF α 15% higher oxidized LDL 9% higher amyloidal, 6% higher homocysteine levels and10% higher WBC counts compared to normotensives. Thus inflammation plays a significant role in prehypertension also.

Subject with prehypertension have clinical characteristics of the insulin resistance. An autonomic imbalance shifting with
augmented sympathetic tone and a significantly impaired parasympathetic activity is seen in prehypertension. The increased CV risk with prehypertension is smaller than the risk associated with having diabetes but is greater than that associated with smoking.

In the cohort of 60,785 women enrolled in the Women’s Health Initiative (WHI), important cardiovascular risk factors—including age, BMI, and prevalence of diabetes mellitus and Hypercholesterolemia- increased- across rising categories of blood pressure.

A study of 36,424 Israelis, of whom 51% of men and 36% of women had prehypertension, demonstrated that, compared with normotensive individuals, those with prehypertension had higher levels of blood glucose, total cholesterol, LDL cholesterol and triglycerides, higher BMI, and lower levels of HDL cholesterol. BMI was the strongest predictor of prehypertension. Prehypertension is also more prevalent in individuals with diabetes mellitus than in those without. In a 12 year follow-up study of 2,629 American Indians who were free from hypertension at baseline examination, the prevalence of prehypertension was significantly higher in those who subsequently developed diabetes mellitus than in those who did not.

**SUBCLINICAL DISEASE AND CARDIOVASCULAR MAKERS**

Accordingly, the Rotterdam Study, a prospective, population-based study with 1,900 participants (≥55 years of age, including 739 with normal blood pressure and 1,161 with prehypertension), found that individuals with prehypertension had significantly smaller arteriolar and venular diameters and arteriolar-venular ratios than normotensive individuals, indicating the presence of microvascular damage.

**MICROALBUMINURIA**

An organ- specific manifestation of generalized endothelial dysfunction that is associated with increased risk of cardiovascular disease- is more common in individuals with prehypertension than in those with normal blood pressure. There is also an association of serum uric acid levels in prehypertension as in establish that hypertension.

**PSYCHOSOCIAL FACTORS**

A study of 2334 middle aged men, in the US with prehypertension showed that men with high trait anger scores, revealed a modest association with progression to hypertension and CHD. The study also showed that long term psychological stress in persons with prehypertension, is associated with development of combined CHD and CHD related deaths.

**SYMPTOMS**

No symptoms at all until high blood pressure advances even to hypertension stage 2. This is precisely the reason why there are more people with pre-hypertension than hypertension itself in many societies. The only way to detect pre-hypertension is to frequently take blood pressure measurements even at home using a home blood pressure monitor.

Some reports present headache and blurred vision amongst others as symptoms of pre-hypertension. However, these symptoms and signs may be caused by other things which are not necessarily high blood pressure. Therefore they are not reliable signs and symptoms of pre-hypertension.

**NON PHARMACOLOGICAL TREATMENT**

**Lifestyle modification**

There is much evidence pointing to the benefits of treating the condition using lifestyle changes such as dietary modifications, weight loss and reduction in sodium intake. The effects of these modifications when put together produce substantial results. The Dietary Approaches to Stop Hypertension (DASH) eating plan, which uses a diet rich in fruits, vegetables, legumes, nuts, and low – fat dietary products and low saturated fats, induced a significant lowering of BP, which was reduced even further when dietary sodium was restricted. It is well recognized that higher salt intake is associated with higher blood pressure and reduction in salt intake lowers blood pressure (Table 2).

A follow-up study of the PREMIER trial demonstrated that multicomponent behavioral interventions with and without the DASH diet - produced significant reductions in the 10 year risk of coronary heart disease.

The Optimal Macro Nutrient intake trial to prevent Heart disease (Omni Heart) tested the effects of diets rich in carbohydrate, protein (half from plant sources) or unsaturated fat (predominantly monounsaturated fat) for 6 weeks. This study demonstrates that a variety of healthy diets can effectively lower cardiovascular risk factors and overall risk of cardiovascular disease.

In a study by Engelhard et al consumption of tomato extracts, which contain carotenoids such as lycopene, beta carotene and vit E led to significant reduction in the levels of systolic and diastolic BP. Thus natural antioxidants could reduce BP levels in patient with mild hypertension or prehypertension.

A 10-15 year follow-up of the Trials of Hypertension Prevention 1 and 2 studies (TOHP 1 and 2) assessed the remote effects of dietary sodium reduction for 18 months (THOP 1) or for 36-48 months (TOHP 2) on risk of cardiovascular disease (myocardial infarction, stroke, coronary revascularization, or cardiovascular-related death) in middle-aged individuals with prehypertension. Risk of a cardiovascular event was 25% lower the intervention group than in the placebo group (Figure 5).

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PHARMACOLOGICAL TREATMENT

Good strategy is to manage the condition with the main aim of lowering blood pressure to within normal range, preventing a rise in blood pressure with age, careful monitoring for signs of end-organ damage and also to prevent blood pressure related cardiovascular diseases.

TROPHY

In this trial Participants with prehypertension were randomly assigned to receive candesartan cilexetil or placebo for 2 years, followed by 2 years of placebo for all participants. In addition, all participants received instructions for lifestyle modification. During the first 2 years, the risk of developing hypertension was reduced by 66.3% in the participants who received candesartan cilexetil compared with placebo group; the magnitude of risk of risk reduction decreased to 16% by year 4, but was still statistically different from placebo.

PHARAO TRIAL

Participants with prehypertension were randomly assigned to receive ramipril or placebo and were followed for 3 years. The study showed statistically significant 34% reduction in risk for the ramipril group.

CAMELOT TRIAL

Patients underwent coronary intravascular ultrasound examination at baseline and after 2 years of amlodipine, enalapril maleate, or placebo therapy. Patients who received active treatment and who achieved blood pressure values within the prehypertensive range had no major change (0.9 mm³) in atheroma volume, where as those who became or remained hypertensive had a 12.0 mm³ increase, and who achieved normal blood pressure values had a decrease in atheroma volume of 4.6 mm³.

Further study is required to determine the role, if any, of pharmacotherapy in prehypertension among individuals without other indications for such therapy (e.g., chronic kidney disease, heart failure).

CONCLUSION

Individuals with prehypertension have an increased risk of full-blown hypertension, target organ damage and cardiovascular-related morbidity and mortality. If there is a future for drug treatment of prehypertension, we need to learn who should be treated for how many years, and with which drug and at what dose. There is no convincing evidence that transient antihypertensive therapy changes the course of prehypertension or hypertension for now, a healthy lifestyle is the foundation for all therapies in persons with prehypertension.

REFERENCES

2. Pharmacotherapy for Prehypertension- Mission Ac-


