



INDIAN SOCIETY OF HYPERTENSION



CURRENT MEDICAL CONCEPTS



# Review Article

## Common but Underrated – Are we Neglecting these Hypertensive Subsets in India?

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### Abstract

Unusual subsets of hypertension need different strategies for detection, treatment and follow up. Isolated systolic hypertension of the young (ISH-Y), metabolic nocturnal hypertension (MNH) and white coat 'Alarm' are subsets which are found in India, but often go undetected. A detailed review of such unusual subsets.

**Key words:** Isolated Systolic hypertension, nocturnal hypertension, white coat hypertension

### Introduction

The detection, awareness, treatment, and control rates of hypertension are poor in Indian subcontinent; the huge 1.3 billion population posing a substantial challenge to health providers. The new data analysis in JAMA estimates that a systolic blood pressure (SBP) between 110 and 115 mmHg accounts for 212 million disability-adjusted life year worldwide; of which, 39 million (around 20%) are from India.<sup>[1]</sup> The scenario of hypertension detection management in India is challenging; as per the National Capital Region cross-sectional database, there is a progressive increase in prevalence – from 23% in urban areas and 11% rural areas in 1991–1994 period to 42.2% urban and 29.9% rural in 2012–2014. More concerning is the fact that these cross-sectional data show that there has been no substantial change in terms of awareness, treatment, and control rates of hypertension in the tested population between the two time periods.<sup>[2]</sup>

The data from Jaipur (Jaipur Heart watch), in contrast, show progressive rise in awareness (13–56%), treatment (95–36%), and control (2–21%) from 1991 to 1994 compared to 2012–2014 period, despite the point that the numbers fell short of the WHO global monitoring framework and UN sustainable development goal.<sup>[3]</sup>

### Why Bother about Subsets?

The availability of an array of drugs has made drug choice confusing among general practitioners (GPs), the group who tend to see the

hypertensives in the first place. Clear demarcation of some of these hypertensives into distinct subsets would give a distinct advantage in choosing out the target population, defining their outcome, and treating them with guideline-recommended therapy.

This review aims at looking at some of the subsets unique in the Indian population.

### Are they Common?

Despite the fact that epidemiological data are not available, most GPs and specialists tend to see such patients of hypertension off and on. A clear knowledge about such subset would enable them to better document such subsets making it possible to organize a database of such distinct subsets.

### Why are these Subsets Unusual?

Several subsets of hypertension are described depending on etiology, pathophysiology, and associated comorbidities. Classification depending on elevation of systolic, diastolic, or both parameters also helping subclassification. We describe three new subsets of hypertension which are seen in clinical practice which need to be defined as subsets since they need different diagnostic criteria, different outcome, as well as different modality of treatment. These subsets are unusual in that they differ in presentation, outcome, and treatment.

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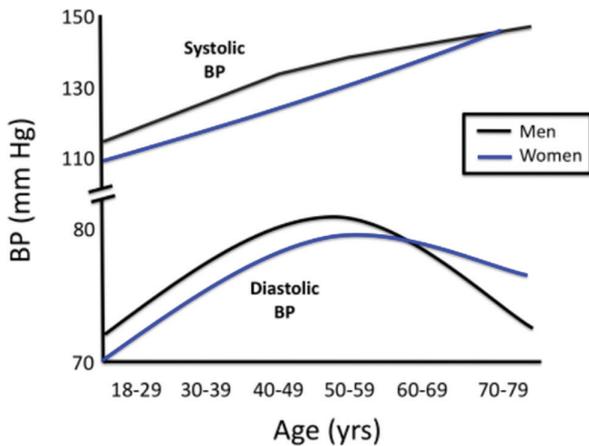


Unusual subsets  
 Isolated systolic hypertension in the young (ISH-Y)  
 Metabolic nocturnal hypertension (MNH)  
 White Coat "Alarm"

**Subset 1**

**ISH-Y**

With increase in age, SBP tends to increase, while diastolic blood pressure (DBP) tends to decrease.<sup>[4]</sup>



(Adapted from JNC 7 and Burt *et al.*, 1995, Hypertension 23: 305-313)

Isolated elevation of SBP Isolated systolic hypertension (ISH) is generally seen in elderly population with increased peripheral resistance and stiff arteries. The diastolic pressure is typically normal or low.

An almost similar blood pressure (BP) reading with isolated elevation of SBP may be seen in stress prone, young people who are generally anxious and exhibit features of sympathetic overdrive.

In ISH-Y, the BP elevation is driven entirely by sympathetic overstimulation. Clinical signs of sympathetic overdrive include sinus tachycardia, tremor, sweating, and features of anxiety [Box 1]. They are generally <40 years of age, working in high-stress jobs (IT sector) and handling time-bound projects with their corporate future at stake.

Salient features  
 ISH-Y  
 Age < 40  
 ISH  
 Sinus tachycardia  
 Fine tremor  
 Job stress  
 Absence of family history of hypertension  
 Good response to beta-blockers

Data from a large French cohort of 19,386 hypertensives were classified into three categories; those with heart rate (HR) between 60 and 80, 80 and 100, and >100. There was progressive increase in mortality (coronary heart disease, cardiovascular disease, and all-cause mortality) with increase in HR, proving the relationship between HR and outcome in hypertension.<sup>[5]</sup>

Julius *et al.* analyzed the data of 15,193 patients enrolled in the valsartan antihypertensive long-term use evaluation trial. It showed that, even those with well-controlled BP, a faster HR increases cardiovascular (CV) event rate, compared to those with controlled HR, indicating the important and pivotal role of sympathetic nervous system activity in determining the outcome of hypertensive patients.<sup>[6]</sup> The national health service (NHS) guideline also recommends the use of beta-blockers in this subgroup of patients with ISH and sinus tachycardia, driven by an excess of sympathetic outflow.

Among the array of beta-blockers available in the market, these young patients of ISH-Y tend to have better compliance with highly selective beta-blockers, in view of the absence of side effects such as fatigue, bronchospasm, and erectile dysfunction. This makes cardioselective  $\beta$ -blocker such as bisoprolol and nebivolol as preferred agent for the treatment of ISH-Y.

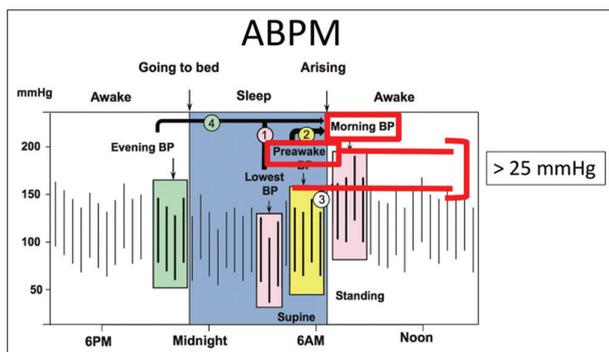
**Subset 2**

**Metabolic Nocturnal Hypertension (Metabolic Owl)**

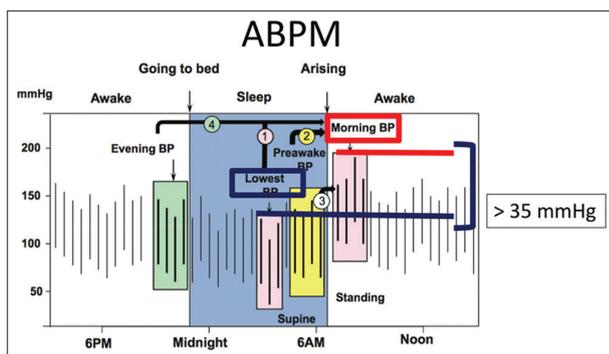
There are middle-aged patients with a typical clinical picture of obesity, impaired fasting glucose (IFG)/Frank diabetes, and metabolic syndrome with host of metabolic derangement including increase triglycerides and uric acid levels. They often have features of obstructive sleep apnea (OSA). Their echocardiogram and Echo tend to show evidence of the left ventricular hypertrophy (LVH), but more often, the office BP is not severely elevated. In fact, a dichotomy between office measures BP (mismatch) and LVH is given a clue to the diagnosis. Many patients can have classical Class 2 effort angina [Box 2].

Salient features  
 Metabolic nocturnal hypertension  
 Middle age  
 Mild "office" hypertension  
 Metabolic derangement (IFG, diabetes mellitus, hypertriglyceridemia, and uric acid elevation)  
 OSA  
 Ambulatory blood pressure monitoring (ABPM) – High nocturnal BP load  
 Good response to renin-angiotensin-aldosterone system inhibitors.

Ambulatory BP in these patients shows a typical pattern of mild daytime hypertension with severely elevated nocturnal BP. This pattern was previously confused with masked hypertension. Isolated nocturnal hypertension tends to increase total mortality and cardiovascular events for more than isolated daytime hypertension.



**Chart 1:** Difference between morning blood pressure (BP) and pre-awake BP in ABPM



**Chart 2:** Difference between morning blood pressure (BP) and lowest nocturnal BP

In a review of data on nocturnal hypertension, Li *et al.*<sup>[7]</sup> clearly showed that isolated nocturnal hypertension is seen more often in Chinese (10.9%) and Japanese (10.5%) population as well as South African people (10.2%) in comparison to lower rates among West European population (6%). This might account for the lack of data and clinical importance of nocturnal hypertension in literature and guidelines since majority of data and guideline emanate out of the western world.

Angina in these patients can result from decreased coronary blood flow as a result of decreased coronary flow reserve.

An increase in intake of high fructose corn syrup, which is used as a sweetening agent in packaged food and sweetened beverages (cola) can exacerbate the metabolic derangement by increasing uric acid and triglycerides in this subset.

### Subset 3

#### White Coat Alarm

White-coat hypertension (WCH) is a stress response of the patient resulting in elevation of BP during interaction with a medical personal. In general, this condition is thought to be benign. An ambulatory BP shows normal BP values as the patient goes outside the area of medical consultation (hospital). WCH is defined as an office BP >140/90 with 24-h ambulatory

BP average of < 130/80. It is estimated that 15–30% of people with elevated office BP has WCH. It is estimated that, generally, the BP of any patient tends to progressively drop by 15/7 mmHg during the third office visit compared to the first visit even in the absence of intervention of lifestyle or pharmacologic agents. Persistently, elevated office BP of > 140/90, measured out of office BP < 130/80, normal ABPM average BP < 130/80, and absence of target organ damage are thought to be clues to suspect the diagnosis of WCH.<sup>[8]</sup>

The long-term outcome of WCH is unclear. While most studies agree that patients of WCH have a higher chance of progression to sustained hypertension; and the risk of WCH is more than normotensive patients while less than those with sustained hypertension, the actual natural history is unclear since studies have looked into different groups of patients.

The analysis of IDACO database shows that International Database on ABPM in relation to CV Outcomes shows that compared to normotensives, WCH with low baseline risk has similar outcomes, while those with high baseline risk (ISH, age, and diabetes) have a higher CV risk with WCH in comparison to normotensives.<sup>[9]</sup>

The subgroup that we find a high risk is the one with WCH with an early morning rise of BP. Studies have shown that those with early morning BP rise have a higher chance of plaque rupture (connected to protein misfolding and the inappropriate activation of proteasome-ubiquitin pathway). Careful interpretation of the ABPM tends to give a clue to the warning signals of this subset.

In addition to the WCH in the ABPM, a difference of morning BP in comparison to pre-awake BP of more than 25 mmHg or a difference between morning BP and lowest nocturnal BP of more than 35 mmHg points to the possible presence of this subset. Since the BP rise tends to be triggered by sympathetic system and the overall nocturnal BP is normal, beta-blockers are likely to be more effective in this subset. The presence of sinus tachycardia also points to this diagnosis.

### Conclusion

The three subsets of hypertension discussed above are unique in nature pertaining to their diagnosis, prognosis, and treatment. Understanding their clinical presentation would help the clinician in targeting their therapy more precisely for a better outcome.

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