INDIAN SOCIETY OF HYPERTENSION

Indian Society of Hypertension (InSH) Consensus Guideline for the Management of Hypertension, 2023

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List of Abbreviations

ABI - Ankle-Brachial Index
ABPM - Ambulatory Blood Pressure Monitoring
ACE: Angiotensin-Converting Enzyme
ACEi - Angiotensin-Converting Enzyme Inhibitors
ACS: Acute Coronary Syndrome
AF - Atrial Fibrillation
AI: Artificial Intelligence
AO: Abdominal Obesity
ARBs: Angiotensin Receptor Blockers/Angiotensin II Receptor Antagonists
ART: Antiretroviral Therapy
AT-1: Angiotensin AT-1 Receptor
BBs: Beta-Blockers
BMI: Body Mass Index
BP: Blood Pressure
CAD: Coronary Artery Disease
CCBs: Calcium Channel Blockers
CKD: Chronic Kidney Disease
CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration
CO: Combined Obesity
COPD: Chronic Obstructive Pulmonary Disease
COVID-19: Coronavirus Disease 2019
cSBP: Central Systolic Blood Pressure
CVD: Cardiovascular Disease
DASH: Dietary Approach to Stop Hypertension
DBP: Diastolic Blood Pressure
DM: Diabetes Mellitus
ECG: Electrocardiogram
eGFR: Estimated Glomerular Filtration Rate
EHRs: Electronic Health Records
GO: Generalized Obesity
GLP-1: Glucagon-Like Peptide-1
GLP1RA: Glucagon-Like Peptide 1 Receptor Agonists
HBPM - Home Blood Pressure Monitoring
HF - Heart Failure
HFpEF - Heart Failure with Preserved Ejection Fraction
HMOD: Hypertension Mediated Organ Damage
ICMR-INDIAB: Indian Council of Medical Research - India Diabetes (ICMR-INDIAB)
ICT: Information/Communication Technology
IHD - Ischemic Heart Disease
INOCA - Myocardial Ischemia and No Obstructive Coronary Artery Disease
InSH - Indian Society of Hypertension
LASI: Longitudinal Ageing Study of India
LCD: Liquid Crystal Display
LDH: Lactate Dehydrogenase
LDL-C: Low-Density Lipoprotein Cholesterol
LED: Light Emitting Diode
LV - Left Ventricular
LVH: Left Ventricular Hypertrophy
MAP: Mean Arterial Pressure
MH: Masked Hypertension
MINOCA - Myocardial Infarction with No Obstructive Coronary Artery Disease
ML: Machine Learning
MRAs: Mineralocorticoid Receptor Antagonists
MRI: Magnetic Resonance Imaging
NFHS: National Family Health Survey
NICU: Neonatal Intensive Care Unit
NO: Nitric Oxide
NSAIDs: Nonsteroidal Anti-Inflammatory Drugs
OBPM - Office Blood Pressure Measurement
OH: Orthostatic Hypotension
PAD - Peripheral Artery Disease
PLGF: Placental Growth Factor
PLHIV: Patients Living with HIV
PsA - Psoriatic Arthritis
PWA: Pulse Wave Analysis
PWV: Pulse Wave Velocity
RA: Rheumatoid Arthritis
RAS - Renin-Angiotensin System
RAAS: Renin-Angiotensin-Aldosterone System
RHD - Rheumatic Heart Disease
SBP: Systolic Blood Pressure
SCD: Sickle Cell Disease
SGLT2: Sodium-Glucose Co-Transporter-2
SGLT2is - Sodium-Glucose Cotransporter-2 Inhibitors
SLE: Systemic Lupus Erythematosus
SPCs: Single Pill Combinations
SRC: Scleroderma Renal Crisis
SRIs: Serotonin Reuptake Inhibitors
s-UA: Serum Uric Acid
TTE: Transthoracic Echocardiography
UACR - Urine Albumin-to-Creatinine Ratio
UTPI: Uterine Artery Pulsatility Index
VHD - Valvular Heart Disease
WC: Waist Circumference
WCH - White Coat Hypertension
WHO: World Health Organization
WHR: Waist Hip Ratio

Section 1 - INTRODUCTION

Hypertension is a global health concern, responsible for 10 to 12% all-cause mortality worldwide. In India, hypertension affects 32.6% of women and 38.7% of men over the age of 20 years. Its prevalence varies across wealth quintiles and states. Its multifaceted etiology includes genetic, lifestyle, and secondary factors, while intertwined risk factors like obesity,[1] diabetes,[2] pregnancy-related disorders,[3] and more, leading to a need for comprehensive management.[4] Lifestyle factors like physical inactivity, a high salt diet, and tobacco and alcohol use contribute to its occurrence. Undiagnosed hypertension also poses a significant challenge, particularly in rural areas, underscoring the importance of accurate measurement and awareness initiatives.[5–8] This trend underscores the urgent need for effective hypertension management strategies in India and similar contexts.

With a mission of taking the forefront in the campaign to control elevated blood pressure and its associated complications across the Indian subcontinent, the Indian Society of Hypertension (InSH) took the responsibility of creating a clinical guideline inspired by the International Society of Hypertension framework (ISH) to better adapt the knowledge, best practices and recommendations to the Indian context. The unique challenges in the Indian context necessitate dedicated guidelines tailored for the country. The silent yet pervasive issues of high prevalence substantial undiagnosed cases of hypertension are compounded by limited patient awareness of hypertension's often symptomless nature and the absence of standardized nationwide guidelines.[9] The country observes an alarming rise in mean systolic blood pressure and hypertension rates, particularly in rural areas, accompanied by geographical disparities favoring the more developed regions. Premature hypertension onset among the young and increasing mortality from hypertension-related conditions are sources of major concern. Patient awareness, treatment compliance, and control of hypertension remain suboptimal, with insufficient focus on strategies to minimize hypertension-mediated organ damage. The unequal allocation of resources at a country and state level further compounds the challenge. India's distinct socio-economic, geographical, and cultural diversity requires tailored strategies to avert the impending NCD pandemic, with hypertension and obesity at the forefront, particularly among the youth.

Section 2 - METHODOLOGY

The 2023 InSH guidelines aim to summarize the best available evidence for all aspects of hypertension management for people living in India. The guidelines were developed by a Special Committee of 56 experts from India, representing the areas of internal medicine, cardiology, nephrology, endocrinology, pediatrics, obstetrics and gynecology, general medicine, geriatrics, pharmacology and epidemiology. The core committee encompassed 5 clinical experts, 2 advisors, and section-specific committees of 3 to 6 experts each for a total of 13 sections. Each topic was assigned to a group of members responsible for reviewing and summarizing the available evidence within that topic. All recommendations were first raised by the respective section-level group and subsequently reviewed by members of other sections. All panel members reviewed the recommendations, and a Delphi Consensus was conducted to finalize the recommendations across all the sections.

Section 3 - HYPERTENSION DEFINITION

3.1 Definition of Hypertension

Hypertension (HTN), also known as high blood pressure, is characterized by an unusually elevated arterial blood pressure. International Society of Hypertension guidelines recommend that hypertension may be diagnosed when a person's systolic blood pressure (SBP) in the office is ≥ 140 mmHg and/ or their diastolic blood pressure (DBP) is ≥ 90 mmHg following repeated examinations.[10]

3.2 Classification of Hypertension

- Optimal Blood Pressure: <130 (systolic) / <85 (diastolic) mmHg
- High-Normal Blood Pressure: 130–139 (systolic) / 85–89 (diastolic) mmHg
- Grade 1 Hypertension: 140–159 (systolic) / 90–99 (diastolic) mmHg
- Grade 2 Hypertension: 160 and above (systolic) / >100 (diastolic) mmHg

According to the classification approaches developed by the International Society of Hypertension (ISH),[11] non-hypertensive subjects with a systolic pressure of 130 to 139 mm Hg or a diastolic pressure of 85 to 89 mmHg are categorized as having high-normal blood pressure (Table 1). Evidence shows that high-normal BP is associated with a mildly increased risk of cardiovascular diseases,[12] including atrial fibrillation.[13] A report provided evidence of impairment of autonomic regulation even in subjects with high-normal SBP.[14] Prospective data from the Women's Health Study also suggest that BP in the high normal range confers a moderately higher risk of major cardiovascular events and incident hypertension than normal BP.[15] This risk reduction is steeper in younger subjects than in the older subjects and is more when baseline blood pressure levels are high.[16] In a meta-analysis of 61 studies involving more than a million patients with hypertension and 12.7 million years of follow-up, it was observed that reducing systolic and diastolic BP reduced cardiovascular events.[17]

Recommendations

- Adults above the age of 18 years should be **screened for hypertension** at every point of contact with health professionals or allied health staff.
- Persons with high normal blood pressure or Grade 1 in the first office visit should be advised 7 days out of Office Blood Pressure Measurement OBPM (HBPM or ABPM)

Table 1: Classification of hypertension

	SYSTOLIC mmHg	DIASTOLIC mmHg
OPTIMAL BLOOD PRESSURE	<130	<85
HIGH NORMAL BLOOD PRESSURE	130 - 139	85 - 89
GRADE 1 HYPERTENSION	140 - 159	90 - 99
GRADE 2 HYPERTENSION	160 and above	>100

and **rechecked at the office within 1–2 weeks** and then continued on lifestyle modifications and recalled after 3 to 6 months depending upon personal risk factors.

- Patients with high normal blood pressure may be advised to **monitor their blood pressure at least twice daily (average of 2 values)**. Ambulatory blood pressure may be advised based on the resources available.
- Persons with Grade 1 or Grade 2 Hypertension should be referred to a qualified physician or should be started with pharmacological and/ or non-pharmacological interventions based on individual risk factors.
- Persons with systolic blood pressure greater than 180 mmHg and or diastolic blood pressure greater than 110 mmHg should be **immediately referred to a qualified physician** for further investigation to exclude any target organ damage and for initiation of treatment, which is required on an immediate basis for gradual reduction of blood pressure over hours, or days according to target organ damage (Figure 1).

Section 4 - BLOOD PRESSURE MEASUREMENT AND MONITORING OF BLOOD PRESSURE

4.1 Mercury Devices

Measuring accurate blood pressure in patients is critical for therapeutic decisions.[18] There are mainly two types of sphygmomanometers – manual and digital. Mercury-based manual sphygmomanometers have been responsible for ensuring uniformity of blood pressure measurement in the initial studies conducted to identify the cardiovascular risks associated with elevated blood pressure.[19] It remained the standard of care in blood pressure measurement for clinical practice until recently. In 2013–2014, international hypertension societies ultimately concluded that the risk of toxicity superseded any potential benefit of using mercury-based blood pressure devices. Electronic, non-mercury blood pressure monitoring devices have replaced the use of traditional mercury instruments in many settings.

4.2 Automated Electronic Devices

Instead of mercury-based devices, mercury-free electronic devices are now widely available. More recently, automated electronic devices have been introduced that do not require additional monitoring with a stethoscope. The upper-arm cuff automated blood pressure measurement has been used and recommended for office, home, and other ambulatory settings.[20] The cuff-blood pressure method, however, has two major limitations. First, it provides only intermittent blood pressure measurements in static conditions and cannot detect rapid and dynamic blood pressure fluctuations. Secondly, using a cuff introduces errors related to its size, shape, and positioning, and the compression of the limb during inflation may alert the user and induce anxiety and discomfort during daily activities and sleep (ambulatory electronic devices with a cuff).[21] Several approaches have recently been developed that use cuffless technologies to estimate blood pressure based on sensors, signal processing, and algorithms embedded in wearable devices, smartphones, pocket devices, or other types of devices.[22] While promising cuffless devices are yet to prove their accuracy in real-world settings and amongst Indian patients.

4.3 Office Blood Pressure Measurement (OBPM)

Office blood pressure measurement is often the first step in initiating a properly calibrated treatment plan. Office blood pressure measurement should commence at least 5 minutes after the time of the office visit, with the patient comfortably seated in a chair with back support, arms bared without constricting clothing, and supported at a heart level with their feet flat on the floor. Patients should not engage in conversations during the measurement process. The measurement arm should be supported on a flat surface with an appropriate-size cuff at the mid-sternal level.[23]Preferably, blood pressure should be measured in both arms simultaneously. A validated electronic device should be used to measure blood pressure for at least 3 readings 1-2 minutes apart. The first reading may be ignored, and an average of the last 2 readings should be charted and used for considering classification and treatment strategization. Such an exercise should be repeated on 3 separate occasions in the office to confirm the diagnosis (Figure 2).[24]

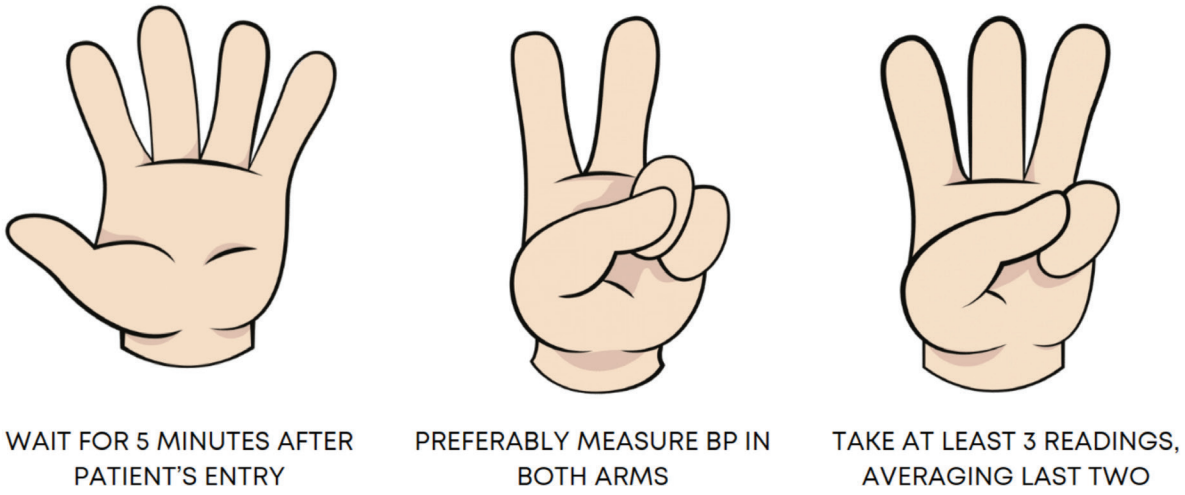


Figure 1: Blood pressure measurement

Assessment for the postural drop can be performed by measuring blood pressure in both supine and standing positions, as described in more detail in the recommendations. Additionally, blood pressure measurements between both arms may be used to assess the presence of coarctation. If blood pressure is found to be elevated, 4-extremity readings should be obtained to evaluate for vascular anomalies, in particular, aortic coarctation, which the presence of a heart murmur might further suggest. Lower-extremity blood pressure is typically equal to or higher than upper-extremity blood pressure. A right upper-extremity blood pressure greater than 10 mm Hg above that of lower-extremity blood pressure is a suggestive indication of aortic coarctation.[25]

4.4 Home Blood Pressure Monitoring (HBPM)

An alternative approach that has been adopted as a widely used method of monitoring blood pressure outside the office setting is the use of home blood pressure monitoring. Patients are responsible for performing their own blood pressure measurements, maintaining a log, and reporting data back to their physician's office.[26] Despite various concerns related to operator error, measurement techniques, health literacy, and routine compliance,[27] home blood pressure reading exercises have shown an association with fewer antihypertensive medications over time.[28] Patients should be educated about the various types of home-based blood pressure monitoring devices available and must receive a small training on the best practices and routines to follow. Patients must be encouraged not to respond to daily fluctuations in their blood pressure values by dose adjustments; rather, they should note all the blood pressure readings in the logbook and share them with their physicians (Figure 3).

4.5 Ambulatory Blood Pressure Monitoring (ABPM)

Current guidelines for the diagnosis and management of hypertension unanimously recommend using (where possible) 24-hours ambulatory blood pressure monitoring for assessing blood pressure variations over the whole day, including sleeping hours. ABPM has also been recommended as a prerequisite for individualizing hypertension management, especially in patients with additional risk factors and erratic office measurements in many countries.[29] ABPM also allows for assessing the responsiveness of blood pressure to physical and mental stressors. In clinical practice, ABPM is used to determine the presence of white-coat hypertension (high office BP without high out-of-office BP among those not taking antihypertensive medication) and masked hypertension (high out-of-office BP without high office BP among those not taking antihypertensive medication), white-coat effect (high office BP without high out-of-office BP among those taking antihypertensive medication), masked uncontrolled hypertension (high out-of-office BP without high office BP among those taking antihypertensive medication), nocturnal hypertension (high nighttime BP), and BP dipping patterns (i.e., dipping, non-dipping, extreme dipping, and reverse dipping) (Figure 3).[30,31]

4.6. Special Situations

4.6.1 White Coat Hypertension (WCH)

White coat hypertension (WCH) describes a blood pressure phenotype present in untreated individuals with elevated clinic blood pressure but normal out-of-office values. There has been a growing recognition of this phenomenon since it was first noted

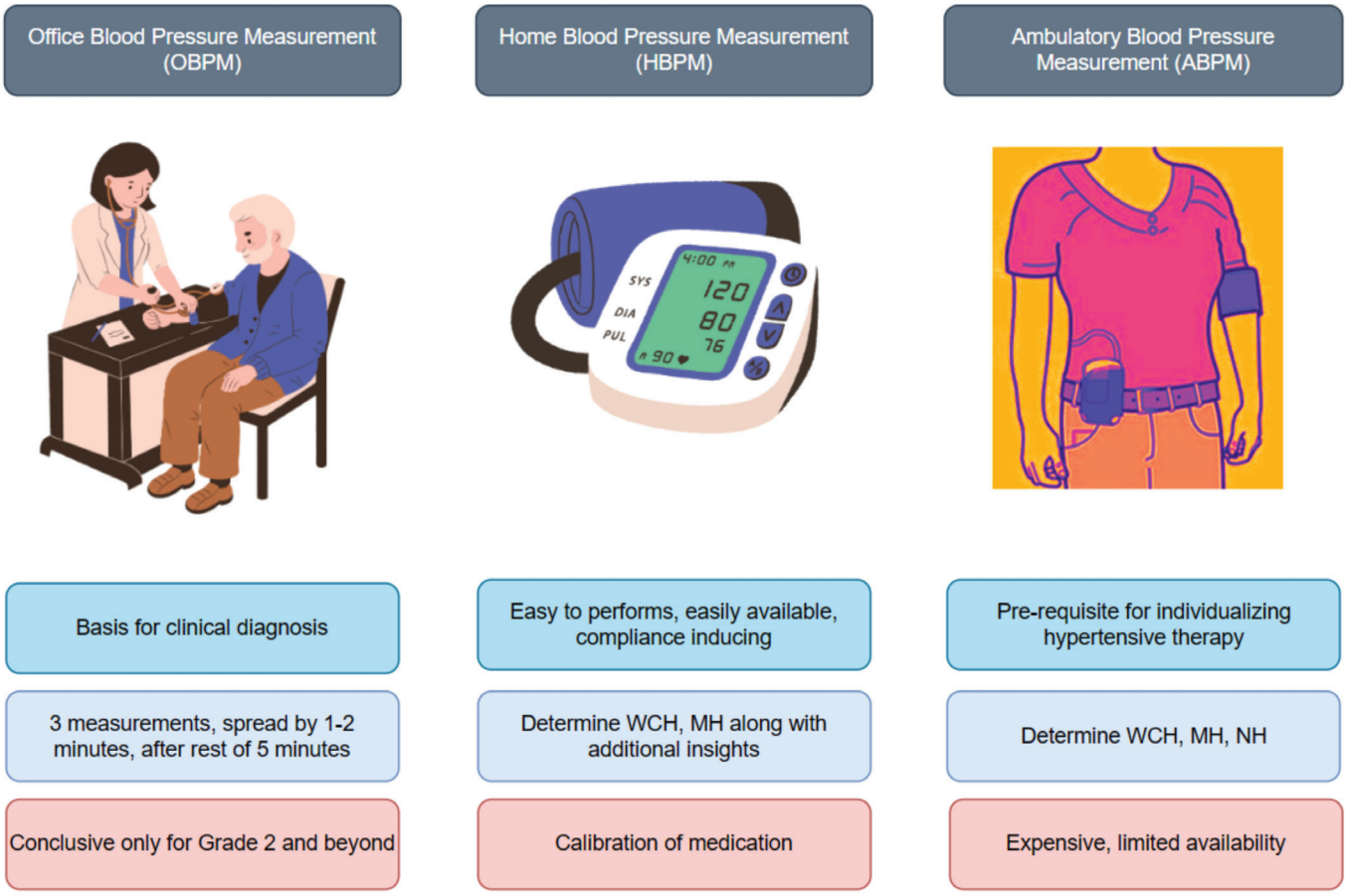


Figure 2: Office, home, and ambulatory blood pressure measurement

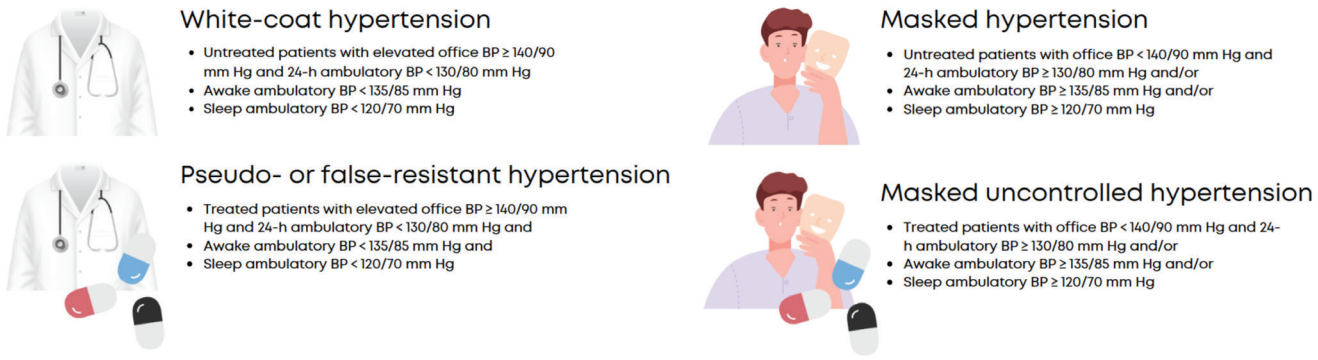


Figure 3: Criteria for the diagnosis of WCH and MH in clinical practice[38]

many decades ago, and it now features in both national and international hypertension guidelines.[32] WCH is an important phenomenon to understand because it is a proposed risk factor for the development of sustained hypertension, target organ damage, and possibly the occurrence of cardiovascular events.[33] Recently, WCH has been found to increase the relative risk of sustained hypertension by almost three-fold compared to patients with normal blood pressure. Furthermore, WCH can impair myocardial function; compared with normotensive patients, there is an increased risk of carotid atherosclerosis.[34] The diagnosis is confirmed when the office blood pressure presents a clinically significant elevation (>20 mmHg for systolic blood pressure and >10 mmHg for diastolic blood pressure) compared to out-of-office ABPM measurements or HBPM measurements. This condition should be well evaluated as it may give the false impression of uncontrolled hypertension (Figure 4).[35]

4.6.2 Masked Hypertension

Masked hypertension might be suspected in persons with an increased office blood pressure at some time, in young persons with normal or high normal office blood pressure who have left ventricular hypertrophy, in persons who have a family history of hypertension in both parents, in diabetics, in persons with multiple cardiovascular risk factors, and in obese individuals. Masked hypertension is estimated to occur in 10 to 30% of persons.[36] Masked hypertension was diagnosed by ambulatory blood pressure monitoring in 14% of persons and by home blood pressure monitoring in 11% of persons. It may be reasonable to screen for masked hypertension with ambulatory blood pressure monitoring or with home blood pressure monitoring if the office systolic blood pressure is 120 to 129 mmHg or if the office diastolic blood pressure is 75 to 79 mmHg (Figure 4).[37]

Recommendations

- Office BP is required for making a diagnosis of hypertension with at least 2 separate office BP measurements a few (3-4) weeks apart. The diagnosis of hypertension should be **based on an office blood pressure reading of >140/90.**
- Office BP measurements should be performed in **standardized conditions**, with an average of two of the triplicates.
- **Screening** for hypertension should be done by a physician or trained non-physician staff using an automated electronic BP instrument following a standardized BP measurement procedure.
- Blood pressure should be measured a **few (5) minutes after** the patient enters the office.
- Patient should be in a **relaxed state**, seated with the arm at the level of the heart, legs uncrossed, flat on the floor. The cuff should have a bladder whose length is about 80% and whose breadth is about **40% of the arm circumference.**
- BP should be measured in **both arms** at the first office visit. If there is a consistent difference between arms >10 mm Hg in repeated measurements, **use the arm with the higher BP**. If the difference is >20 mm Hg, consider further investigation.
- Mercury sphygmomanometers, aneroid, or cuffless automated BP devices **should not be used** to evaluate or manage hypertension in clinical practice.
- Automatic electronic upper-arm cuff devices are **recommended for office** and out-of-office BP measurements (home and ambulatory).
- Hybrid manual auscultatory devices with LCD or LED display, or digital countdown, or shock-resistant aneroid devices **can be used for office BP measurement** if automated devices are not available.
- Standing blood pressure: Measure in treated hypertensives after 1 min and again after 3 min when there are symptoms suggesting **postural hypotension** and at the first visit in the elderly and people with diabetes.
- **Home BP should be monitored for 7** (not fewer than 3) days with **duplicate** morning (with a 1-minute difference between them) and evening measurements before office visits. Average home BP should be calculated after discarding readings of the first day.
- **HBPM is recommended** for long-term follow-up of treated hypertension because it improves BP control, especially when combined with education and counseling.
- **ABPM** is recommended to identify **white-coat hypertension**, **masked hypertension,** and **nocturnal BP** phenotypes. Repeated ABPM may be necessary because these phenotypes have a limited reproducibility.

Section 5 - DIAGNOSIS OF HYPERTENSION, INVESTIGATIONS & ADDITIONAL EXAMINATION

5.1 Medical History

Medical history can reveal relevant chronic illnesses and other prior disease states that may affect the patient's health. The knowledge of patient's ongoing treatment for other disorders may impact the management of hypertension. Most people with hypertension don't feel any symptoms. Very high blood pressure can cause headaches, blurred vision, chest pain, and other symptoms. The medical history encompasses the documented hypertension duration, past blood pressure readings, and any coronary artery disease, heart failure, stroke, renal issues, peripheral arterial disease, dyslipidemia, diabetes, gout, sleep apnea, or pronounced snoring records.[39] The social history entails the extent of physical activity and consumption of tobacco, alcohol, and both prescribed and illicit stimulant substances. The dietary aspect of the history zeroes in on salt and stimulant intake, covering substances like tea, coffee, caffeine-containing soft drinks, and energy beverages.[39]

5.2 Physical Examination

A comprehensive physical examination is recommended for all patients with suspected or confirmed hypertension.[40,41] Physical examination and history also provide important clues about secondary hypertension, cardiovascular risk, and target organ damage (Figure 5).[42]

5.3. Endocrinological Examination

Screening for endocrine disorders that may contribute to elevated blood pressure is important during the physical examination for hypertension. The following additional details can be included in the endocrinological examination.[43–45] It is important to note that the screening for endocrine disorders should be performed in

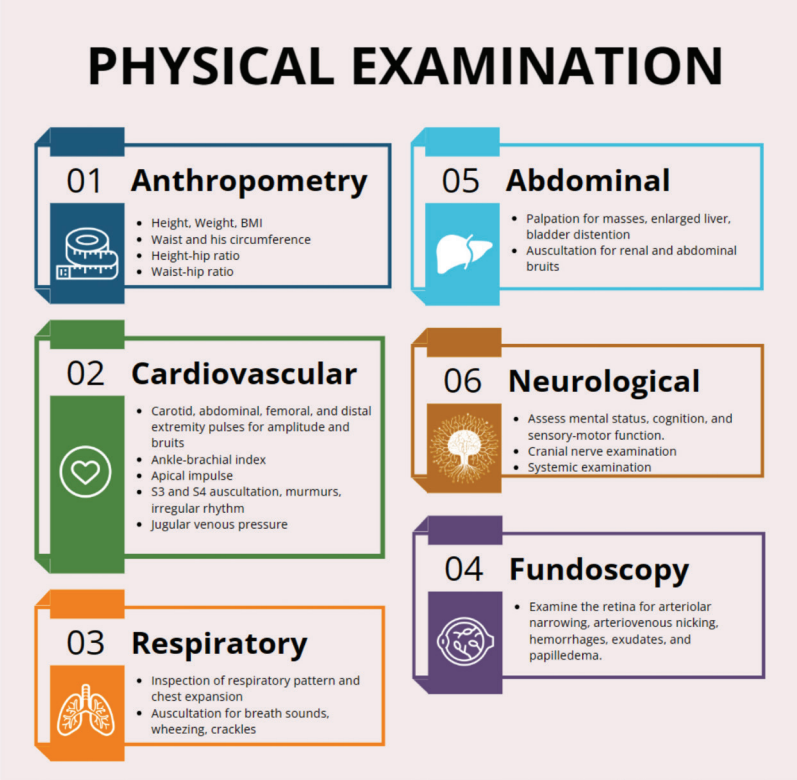


Figure 4: Physical examination.

conjunction with other components of the physical examination, medical history, and laboratory testing to obtain a comprehensive assessment of the patient's health and identify any underlying conditions contributing to hypertension.[43-48] Additional details have been discussed in Section 11.2.

5.4 Routine Clinical Chemistry Investigation

It is important to note that laboratory testing should be performed in conjunction with other components of the physical examination, medical history, and imaging studies to obtain a comprehensive assessment of the patient's health and identify any underlying conditions contributing to hypertension.[49–52] The principal goals of laboratory testing for hypertension are-

- to assist in global cardiovascular risk assessment (e.g., detection of end-organ damage and other cardiovascular risk factors),
- to identify remediable forms of hypertension (e.g., consideration of hyperaldosteronism with hypokalemia),
- to help guide drug selection and monitoring (e.g., avoidance of thiazide diuretics in a patient with hyponatremia).[53]

Essential investigations:

1. Complete Blood Count with hemoglobin
2. Electrocardiogram (ECG)
3. Urinalysis with microscopy, UACR
4. Kidney Function Tests, serum creatinine, BUN
5. Glycated hemoglobin
6. Lipid profile
7. *Echocardiogram (ECHO) - discuss benefits with patients, and if locally available

Additional investigations:

1. 24-hour urinary free cortisol or low dose dexamethasone suppression test to rule out Cushing's syndrome.
2. Complement levels and autoimmune profile in suspected cases of autoimmune diseases affecting the renal vasculature. Other specialized tests, including High sensitivity C-reactive protein (hsCRP), Lipoprotein a (Lp(a)), homocysteine, and uric acid,[49,50] transaminases, and alkaline phosphatase.[51]
3. Plasma-free metanephrines or 24-hours urinary fractionated metanephrines and normetanephrine to rule out pheochromocytoma.
4. Plasma renin-aldosterone ratio to rule out hyperaldosteronism.
5. Patients with renovascular hypertension should undergo an extensive evaluation to find the cause of uncontrolled hypertension; renal arteriography remains the gold standard for this assessment.[54]

5.5. Electrocardiogram

In a review of ECG parameters in the context of hypertension and arrhythmia risk, P wave duration and QT dispersion were noted to have decreased after BP was controlled with medication. In addition, T wave amplitudes have been noted to differ between hypertensive patients and normotensive individuals. ECG can detect signs of LVH, a common consequence of long-standing high blood pressure.[55] LVH is associated with an increased risk of cardiovascular events and can be identified by specific changes in the ECG pattern. Additionally, an ECG can identify arrhythmias, such as atrial fibrillation, which can be linked to hypertension and increase the risk of stroke.[56] However, some studies have shown that LVH diagnosis by ECHO is a better predictor of cardiovascular events compared to LVH diagnosis by ECG [57,58] as the sensitivity of ECG for LVH is low (only detects advanced hypertrophy). So, a normal ECG does not exclude LVH. Limitations of ECG include low sensitivity for LVH, difficulty detecting left atrial enlargement, operator-dependent interpretation, and the effect of posture/respiration/meals on ECG findings. Consider adding echocardiography to evaluate LV structure and function in more detail. Challenges with limited ECG availability or technical expertise to perform/interpret ECGs, especially in rural primary care settings in India.

5.6. Kidney Ultrasound

Renal ultrasound is an invaluable diagnostic instrument, capable of furnishing immediate insights at the bedside concerning potential underlying factors and subsequent implications linked to hypertension.[59]Doppler ultrasound can evaluate blood flow in renal arteries/veins and can detect renal artery stenosis contributing to hypertension.[60] In hypertensive subjects, it contributes to diagnosing early renal damage, acute or chronic nephropathies, and nephro-vascular disease.[61] Simple renal cysts, poor CMD, and stenosis of renal arteries may be the most common sonographic findings in hypertension. In cases where ultrasound is inconclusive or if complex cysts/masses are suspected, CT or MRI scanning may be considered for more definitive structural evaluation.[61,62]

Recommendations

- We recommend an ongoing initiative to **increase awareness of hypertension,** a widely prevalent but asymptomatic disease associated with many adverse outcomes like heart attacks, strokes, and kidney failure.
- All adults above 18 should undergo **opportunistic screening by healthcare providers** at all points of care in India.
- **Targeted screening** at the community level is suggested for high-risk groups like the **elderly** (>60 years), **obese, current smokers**, those with **diabetes** and existing **cardiovasculardisease** or their family history.
- **History and physical examination** for risk factors (smoking, obesity-diet, and exercise patterns, family history of premature CVD, angina, heart failure, stroke) should be done in all patients.
- The presence of **proteinuria doubles the risk of morbidity and mortality** for a certain BP and is an independent predictor of all-cause mortality in hypertension.

Section 6 - CARDIOVASCULAR RISK FACTORS

The identification and understanding of risk factors play a pivotal role in preventing and managing cardiovascular diseases.[63] In India, more than 10.5 million deaths occur annually, and CVD is the leading cause of death amongst men (20.3%) and women (16.9%). National Health Policy 2017 of India aims to reduce 25% of premature deaths from cardiovascular diseases besides screening and treatment of 80% of hypertensive patients by 2025.[64] Within India, the rates of CVD vary markedly, with the highest in the states of Kerala, Punjab, and Tamil Nadu. Moreover, these states also have the highest prevalence of raised cholesterol levels and blood pressure.

6.1 Diagnostic Approach

Cardiovascular risk assessment is necessary for effective CVD prevention, especially in high-risk individuals.[67] Conventional methods used for diagnosing heart disease are based on the medical history, physical examination, laboratory investigations, and detailed evaluation of related symptoms.[68] Angiography is considered as a gold standard for the identification of Coronary Artery Disease. Doppler and echocardiography can be combined for assistance in diagnosing valvular stenosis and/or regurgitation by measuring blood flow across valves. Priority may be given to transthoracic echocardiography (TTE), with a focus on the assessment of ventricular function and the presence of regional wall motion anomalies, to diagnose acute coronary syndrome (ACS) and rule out other etiologies.[69]

6.2 Cardiovascular Risk Factors

In developed countries, predominantly, there are five existing modifiable risk factors (high blood pressure, high blood cholesterol, tobacco use (chewing/smoking), diabetes mellitus, and obesity) which constitute approximately one-third of all CVD cases. In developing countries, in addition to these five existing modifiable risk factors, low vegetable and fruit intake and alcohol abuse rank first on the list of risk factors.[70] Nationwide representative data on the prevalence of CVD risk factors are available, and the India State-Level Disease Burden Initiative (part of the GBD study) has recently reported age-standardized prevalence data and trends for diabetes, hypertension, and obesity according to the economic transition levels of different Indian states and provides useful information on the disease burden.[71]Additionally, a study conducted in India demonstrated that hypertension nearly doubled the risk of fatal cardiovascular events in an urban community.[72]According to the World Health Organisation, the

Table 2: Investigative modalities.

	CHARACTERISTIC	DEFINITION
1	**Electrocardiography (ECG)** LV hypertrophy by ECG	Sum of the R-wave in aVL and the S-wave in lead V3 exceeding 2.8 mm in men and 2.0 mm in women (Cornell voltage criteria). R wave in aVL≥11 mm; Rv5 + S v1 >35 mm (Sokolow-Lyon criteria)
2	**Echocardiography** Increased LV mass	Increased LV mass by ASE criteria: LV mass index to body surface area (BSA), i.e., LV mass/BSA g/m2 >115 (men) and >95 (women)] E/e > 14 AND LA Index volume> 34 - suggestive of high end filling pressure A height indexed LV mass exceeds 47 in women or 50 in men
3	**Carotid ultrasound** Increased carotid artery IMT	Composite measure averaging standardized measures of the maximal common carotid artery IMT and maximal internal carotid artery IMT; a standardized carotid IMT that met or exceeded the sex-specific Common carotid IMT ≥1.0 mm.20
4	**Peripheral arterial disease** Reduced Ankle-brachial index	ABI is the ratio of the average systolic blood pressure at the ankle of each leg divided by the average systolic blood pressure in the arm with the highest blood pressure. An ankle-brachial index <0.9 in either leg is abnormal.
5	**Reduced Kidney function and glomerular endothelial dysfunction**	Microalbuminuria - A urine albumin to urine creatinine ratio ≥30 µg/mg. Reduced kidney function - Estimated glomerular filtration rate (eGFR) <60 mL/min per 1.73 m2
6	**Arterial stiffness** High pulse wave velocity	A carotid-femoral pulse wave velocity (CFPWV) >10 m/sec
7	**Brain Imaging** Subclinical brain injury on magnetic resonance imaging	Lacunar infarcts, white matter hyperintensities, microbleeds

prevalence of undiagnosed hypertension is generally high (WHO 2013), and it is evident from the previous studies that nearly 4/5th of the total burden of hypertension in India remains undetected.[75]

An increase in cardiovascular risk must be considered in patients with hypertension and chronic inflammatory diseases, chronic obstructive pulmonary disease (COPD), psychiatric disorders, and psychosocial stressors where an effective BP control is warranted.[76]Moreover, many epidemiological studies of cardiovascular risk factors in the mid and late twentieth century found that the risk factors are higher in upper socio-economic sections persons than in lower sections. However, some studies have reported that risk factors could be related to illiteracy in lower socio-economic sections.[77] A 2017 meta-analysis of 1.7 million individuals demonstrated an inverse association between socioeconomic position and premature mortality, highlighting social determinants as a key target for improving population health (Table 2).[78]

6.3 Cardiovascular Risk Scores

A complementary goal is to improve prediction to identify individuals who are more likely to develop CVD and who, therefore, should be receiving more intensive interventions where possible. To this effect, the risk assessment defined by the Framingham Study researchers was a great leap forward. There are also multiple predictive CVD risk score calculators, such as the Munster Heart Study (PROCAM) Risk Score, Sheffield Coronary Risk Tables, National Heart Foundation of New Zealand Guidelines, Dundee Coronary Risk Disc, and the SCORE project, among others. Most risk scores consider the patient's age, gender, family history of CAD, smoking history, history of diabetes, elevated Body mass index (BMI), systolic blood pressure, triglycerides, and High-density lipoprotein (HDL) levels.

Bansal *et al.* studied 194 patients attending a CV disease prevention clinic at a tertiary care center in North India. Four risk assessment models (Framingham Risk score, ACC/AHA risk score, JBS3 risk score, and the WHO risk score) were applied. The estimated risk scores were correlated with carotid intima-media thickness (cIMT) and coronary calcium score (CCS). Overall, the ACC/AHA risk score calculator and WHO risk score calculator significantly underestimated the CV risk as compared to JBS and FRS, with JBS being the least likely to underestimate the risk. JBS and FRS risk scores demonstrated a consistent relationship with cIMT and CCS.[79]

Table 3: Comparison of risk scores.

Birhanu MM, *et al. BMJ Open* 2022;**12**:e054617. doi:10.1136/bmjopen-2021-054617

Table 2 Concordance between categories* of absolute risk in cardiovascular risk prediction tools among adults without self-reported history of cardiovascular disease at baseline and aged 35–74 years

Comparison of cardiovascular risk prediction tools	Men (n=1466)			Women (n=1978)			Total (n=3444)		
	Agreement (%)	Quadratic weighted kappa	Spearman's r= (r_s)	Agreement (%)	Quadratic weighted kappa	Spearman's r (r_s)	Agreement (%)	Quadratic weighted kappa	Spearman's r (r_s)
FRS versus ARS	91.81	0.94	0.95	84.13	0.76	0.77	87.40	0.89	0.89
FRS versus WHO-RS	52.93	0.48	0.66	86.70	0.70	0.70	72.33	0.58	0.65
ARS versus WHO-RS	49.59	0.44	0.64	76.29	0.60	0.59	64.92	0.52	0.63
SCORE-low versus SCORE-high	74.28	0.80	0.85	90.09	0.86	0.85	83.36	0.84	0.86

Agreement was measured by using risk bands generated by the various risk tools.
*The category of risk bands are: <10%, 10% to <20%, or ≥20% risk for FRS, ARS and WHO-RS and <1%, 1% to <5%, or ≥5% risk for SCORE-high and SCORE-low.
ARS, Australian Risk Score; FRS, Framingham Risk Score; high, regions of high cardiovascular risk; low, regions of low cardiovascular risk; r_s, Spearman's r; SCORE, Systematic COronary Risk Evaluation; WHO-RS, WHO Risk Score.

Early identification and initiation of intensive primary prevention among individuals with a high risk of CVDs is important in reducing the CVD burden in India. Although almost all the major recent international guidelines, including the National Institute for Health and Care Excellence (NICE) 2014 guidelines, World Health Organization (WHO) 2007 guidelines, European Society of Cardiology (ESC) 2016 guidelines, and the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines and national guideline unanimously recommend assessment of cardiovascular risk, their adoption in India is suboptimal.[80–82] A fewcommon barriers to its decreased use are lack of national guidelines, too many choices for CVD risk score, the uncertainty of validity of these risk score models in the local context, time-consuming and lack of adjustment for the treatment.[83] Recalibrated models based on local populations can improve the validity of the risk score model,reduce the perceived barriers of physicians related to the local validity, and enhance the use of the CVD prediction model in the clinical setting for primary prevention.[84]

Recommendations

- The diagnostic workup for hypertensive individuals **should include an assessment of additional risk factors,** especially if there is a family history of CVD.
- Patients should be evaluated for **cardiovascular risk factors** like smoking, obesity, and diabetes by doctors and other medical professionals.
- In everyday practice, **a reasonable estimation of cardiovascular riskcan be established** by taking different risk factors into account: age (>65 years), sex (male > female), heart rate (>80 beats/min), increased body weight, diabetes, high LDL-C/triglyceride, family history of hypertension, early onset of menopause, smoking habits, and psychosocial or other socioeconomic factors.
- To lower the remaining cardiovascular risk, the therapeutic approach must **emphasize blood pressure control, lifestyle adjustments,** and the efficient treatment of the other risk factors.
- **Elevated serum uric acid (s-UA)** should be addressed with diet, urate-inducing medications (losartan, fibrates, atorvastatin), or urate-lowering medications in symptomatic patients (gout with s-UA >6 mg/dL [0.357 mmol/L]).
- **Hypertension and Coronary artery disease:** BP to belowered if ≥140/90 mmHg and treated to a target <130/80 mmHg (<140/80 in elderly patients).
- **Hypertension and previous stroke:** BP should be lowered if ≥140/90 mmHg and treated toa target <130/80 mmHg (<140/80 in elderly patients).
- **Hypertension and Heart failure:** BP to be lowered if ≥140/90 mmHg and treated to a target <130/80 mmHg but >120/70 mmHg.
- **Hypertension and chronic kidney disease:** BP should be lowered if ≥140/90 mmHg and treated to a target <130/80 mmHg (<140/80 in elderly patients).
- **Hypertension and chronic obstructive pulmonary disease:** BP should be lowered if ≥140/90 mm Hg and treated to a target <130/80 mm Hg (<140/80 in elderly patients).

Section 7 - HYPERTENSION-MEDIATED ORGAN DAMAGE (HMOD)

7.1 Definition and Role of HMOD in Hypertension Management

Sustained elevated blood pressure leads to detrimental effects on various organs because of the structural and functional

changes in arteries or end organs. Hypertension-Mediated Organ Damage(HMOD) may be present in people with less severe hypertension, including asymptomatic patients with increased BP, as well as patients with severe or long-term hypertension.[86] Moreover, subclinical HMOD can already be present at the time of hypertension diagnosis. By proactively identifying and addressing HMOD through comprehensive assessment and tailored interventions, healthcare professionals can substantially mitigate the detrimental impacts of hypertension on the heart, kidneys, brain, and other organs. Recognizing HMOD as a pivotal target for intervention is pivotal, fostering a paradigm shift in hypertension management towards more holistic, patient-centered care.

7.2 Specific Aspects of HMOD

7.3 Assessment to Detect HMOD

There are various methods used to assess and diagnose HMOD such as estimation of left ventricular mass index (LVMi) in ECHO, ECG, eye fundus examination; evaluation of kidney function and microalbuminuria. The recommended, but not obligatory HMOD assessment methods include measurement of cIMT by ultrasonography and measurement of pulse wave velocity (PWV). Another recently established metric utilized in the evaluation of hypertension patients is pulse wave analysis (PWA). It allows the central systolic blood pressure (cSBP) to be assessed. Even though cSBP is not a direct indicator of HMOD, it nonetheless has a considerably greater association with cardiovascular risk than standard arm BP readings.

7.4 Treatment Optimization and Prevention of HMOD

Proteinuria is a potent risk factor for adverse outcomes, including death. Increased levels of proteinuria have been directly correlated with a higher risk of mortality.[87] Compared to either diabetes or hypertension alone, the presence of both conditions significantly increases the risk of macrovascular and microvascular complications, such as coronary heart disease, peripheral artery disease, stroke, retinopathy, and nephropathy, as well as left ventricular hypertrophy and congestive heart failure. Undiagnosed hypertension in patients with diabetes is a significant risk factor for HMOD.

Renin-angiotensin-aldosterone receptor blockade is an essential part of the treatment of early end-organ damage.[88] Recent evidence highlights new approaches to manage HMOD. These include mineralocorticoid receptor antagonists (MRAs), glucose-lowering agents, endothelin receptor antagonists, and statins/fibrates. The novel MRA finerenone shows promise in reducing albuminuria and organ damage, despite potential hyperkalemia. Spironolactone is recommended as a fourth-line therapy for resistant hypertension. Sodium-glucose co-transporter-2 (SGLT2) inhibitors like canagliflozin and dapagliflozin demonstrate benefits in reducing nephropathy and albuminuria. GLP-1 agonists such as liraglutide offer cardiovascular improvements and decreased albuminuria. Endothelin receptor antagonists have mixed effects on albuminuria and blood pressure. Atrasentan shows promise in reducing albuminuria without significant fluid retention. A recent

Table 4: Hypertension-Mediated Organ Damage(HMOD).

HEART	Increased workload on the heart, hypertrophy Can lead to heart failure, development of Coronary Artery Disease
BRAIN	Damage to blood vessels in brain, increasing risk of strokes - both ischemic as well as hemorrhagic strokes
KIDNEY	Damage to blood vessels in kidneys, leading to Kidney dysfunction or even failure
EYES	Damage to retinal blood vessels causing vision problems, can lead to blindness in severe cases Advanced bilateral retinopathy is a complication of malignant hypertension Referral and consultation with an opthalmologist is necessary
BLOOD VESSELS	Sustained hypertension accelerates atherosclerosis - leading to peripheral artery disease. Reduces elasticity and makes vessels more prone to inflammation and ruptures. Increases chances of aneurysms and contribute to other vascular disorders

SONAR(Study of Diabetic Nephropathy with Atrasentan) study affirmed renal event reduction with no major heart failure or mortality differences against placebo.[89]

Recommendations

- In order to optimize the cardiovascular risk and kidney risk stratification, **evaluation of HMOD should be done as soon as the diagnosis of hypertension has been verified.** The information could have an impact on whether drug treatment is initiated or increased.
- It is advised that a basic screening for HMOD be undertaken in all hypertensive patients and that a more thorough assessment be carried out when the presence of HMOD is crucial for treatment decisions, despite the fact that poor technological provision and expense may restrict the search for HMOD in some countries. the tests that can be performed to determine HMOD.
- The following assessments to detect HMOD should be performed routinely in all patients with hypertension:
  - Serum creatinine and eGFR (CKD-EPI formula/ calculation): eGFR Calculator | National Kidney Foundation
  - 12-lead ECG
  - Preferably Urine Albumin Creatinine Ratio, else Urine protein-creatinine ratio, else Urine albumin
  - If available, Cystatin C may be used for early detection of suspected nephropathy

Routine Clinical Examination

- For all patients
  - A. Peripheral Vascular Examination
  - B. Carotid Artery and Femoral Pulse Palpation
  - C. Fundus Examination

- Screen all patients (with hypertension and those at risk for hypertension) for substances that may increase BP or interfere with the BP-lowering effect of antihypertensive medications.
- Consider lowering or eliminating things that elevate blood pressure when appropriate. Treat BP to target whether these medicines are necessary or preferred.
- All of the additional methods described above can improve how hypertension is managed in those who are affected by it, therefore they should all be taken into account when they are clinically appropriate and practical. To determine the effectiveness of treatment for specific individuals, serial measurement of HMOD (LVH and albuminuria) to track regression with antihypertensive treatment may be helpful, however, this has not been satisfactorily validated for the majority of HMOD markers.

Section 8 - EXACERBATORS AND INDUCERS OF HYPERTENSION

While a variety of factors contribute to Hypertension's development and progression, understanding its exacerbators is of utmost importance. Exacerbators are the underlying medical conditions, use of certain medications, and habits that can significantly worsen BP control.

8.1 Drug/Substance Exacerbators and Inducers of Hypertension

8.1.1 Sodium Intake

Long-term high sodium intake increases the risk for hypertension. Several health organizations advocate reduced salt intake, suggesting limits[90] below 2 grams/day of sodium or 5 grams/day of salt[91] on the premise that modest reductions in sodium intake will significantly decrease the incidence of cardiovascular disease in many hypertensive subjects[92] and in resistant hypertension.[93] According to leading Indian nutritionist Aman Puri, one teaspoon of table salt provides 2.3 grams, while that of rock salt provides 1.9 grams of sodium. BP sensitivity varies greatly among subgroups, with some showing greater salt tolerance.[94] Women and overweight individuals are additional subgroups considered salt-sensitive, however, the supporting evidence is relatively limited.[95]

8.1.2 Alcohol and Other Substances (caffeine, nicotine, and recreational drugs)

Alcohol consumption[96] is known to be associated with elevating blood pressure. Coffee-related acute hypertension[97] is also well documented. Recreational drugs such as cocaine[98] cause a severe increase in blood pressure, especially if the person is taking a beta-blocker.[99]Other recreational substances such as opioids,[100] amphetamine[101] and have led to the occurrence of cardiac arrhythmias in patients with hypertension.

8.1.3 Smoking

Smoking plays a role in the pathogenesis of coronary artery disease and can lead to sudden death. For individuals with severe heart conditions, discontinuing smoking provides substantial benefits and should be viewed as a therapeutic strategy rather than just a preventive measure.[102,103]

8.1.4 NSAIDS

Nonsteroidal anti-inflammatory drugs (NSAIDs) decrease the blood pressure-lowering effects of antihypertensive medications such as diuretics, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and beta-adrenergic blockers.[104,105] Traditional NSAIDs and selective COX 2 inhibitors[106] increase BP. Long-term NSAIDS use has also been associated with raised systemic vascular resistance.[106] Studies have indicated that their usage raises the likelihood of initiating antihypertensive medication therapy in patients aged 65 and over to a ratio of 1.55

for low daily dosages, 1.64 for medium daily doses, and 1.82 for high daily doses.[98]

8.1.5 Acetaminophen

Daily consumption of acetaminophen, an atypical NSAID devoid of any anti-inflammatory action, can raise the relative risk of hypertension by 1.34 times more.[105] Additionally, in people with hypertension, regular paracetamol usage elevates both SBP and DBP.[107]This rise in BP may lead to an increase in cardiovascular morbidity and mortality.[107]

8.1.6 Corticosteroids

Although the mechanism is not fully understood, corticosteroid use affects over 20% of the patients with hypertension.[108] Patients taking chronic medium doses of glucocorticoids (7.5 to 30 mg/day) experienced 3-28 hypertension episodes per 100 patient-years in placebo-controlled trials.[109] Findings reported in some observational studies have suggested that medium to high-dose glucocorticoids are linked to hypertension, while other studies have found no link.[110]

8.1.7 Calcineurin Inhibitors

Calcineurin inhibitors (CNI) are known to cause hypertension, with 50–80% of patients reported to have hypertension with chronic use.[111] Cyclosporine A (CsA) is associated with a higher incidence than tacrolimus. CNI are implicated in afferent arteriole vasoconstriction and activation of the renin-angiotensin system, promoting sodium retention and volume expansion. Furthermore, CsA and tacrolimus promote direct vasoconstriction by one or more of the following mechanisms: increased tone of vascular smooth muscle, reduced nitric oxide production, and activation of endothelin-1 receptor.[112] Apart from endothelial dysfunction, CsA treatment leads to increased production of the vasoconstrictive peptide endothelin-1, reduced glomerular filtration rates, and increased sodium reabsorption, thereby causing greater pressure loads. There is also evidence for CsA to influence blood pressure control through the renin-angiotensin-aldosterone system (RAAS).[113] Importantly, CsA-induced hypertension has been the subject of several meta-analyses.[114] When corticosteroids are added, blood pressure may further increase to levels requiring antihypertensive therapy within the first weeks or months.[115]

8.1.8 Menopausal Hormone Therapy and Oral Contraceptive Pills

Studies investigating the relationship between Menopausal hormone therapy (MHT) and blood pressure have been largely inconsistent; however, baseline data from the observational arm of the Women's Health Initiative (WHI) study found current MHT use was associated with an increased likelihood of hypertension.[116]Various clinical trials in normotensive women have either reported no difference in blood pressure with MHT, a decrease in blood pressure with MHT use, or a slight increase in blood pressure with MHT use, compared with placebo.[109] High doses of progestin (1-4 mcg) and estrogen (greater than 50 mcg) can increase the BP of an individual by up to 6/3 mmHg.[105] Similarly, studies in hypertensive postmenopausal women have either shown a slight decrease in blood pressure with MHT use, or no effect on blood pressure with MHT use.[117]

OCP-induced hypertension (OCPIH), which affects 1–8.5% of users of the combination oral contraceptive pill (OCP), is one of the main side effects of OCP use.[118] Numerous research on OCPIH has been conducted with older formulations with high estrogen levels. However, more recent research on low-dose estrogen formulations has also indicated a risk of hypertension.[118]

8.1.9. Anti-cancer Therapy

Hypertension and blood pressure (BP) may begin at the time of initiation of anticancer therapy and continue lifelong, which can result in interruptions in treatment and place patients at increased risk of cardiovascular disease (CVD) and mortality. Many contemporary cancer therapies are associated with cardiovascular toxicity, leading to heart disease, thromboembolic disease, and hypertension.[119] Management of hypertension in patients on anticancer therapy is largely empirical, with no current trial data supporting specific agents or treatment goals in this distinctive population.[120]

VEGF signaling pathway inhibitors (VSPIs) exert their anticancer effects by inhibiting VEGF-mediated tumor angiogenesis, depriving tumor cells of oxygen and nutrient supply.[121] VSPIs are associated with adverse cardiovascular effects, of which hypertension is the most frequent. They cause an acute increase in BP sustained during treatment in most patients.[122]

Human monoclonal antibodies (mAb) that neutralize VEGF are used to treat many solid tumors, including renal cell carcinoma, colorectal, lung, and breast cancer. Bevacizumab is a VEGF-targeted mAb. Bevacizumab therapy can lead to the development of hypertension and proteinuria as VEGF blockade induces endothelial dysfunction, with reduced production of nitric oxide and prostacyclin and overproduction of endothelin-1.[123]

Aromatase inhibitors may increase the risk of hypertension, hyperlipidemia, and cardiovascular (CV) disease. The major clinical trials that examined the safety of AIs include the Arimidex Tamoxifen alone or in combination (ATAC) study, the Breast International Group (BIG), and the Intergroup Exemestane Study (IES). In the ATAC trial, anastrozole was associated with higher rates of hypercholesterolemia and hypertension.[124]

Anti-vascular endothelial growth factor tyrosine kinase inhibitors (TKI) result in increased vasoconstrictor levels, decreased vasodilator levels, vascular rarefaction, and renal damage, which are possible mechanisms behind antiangiogenic-induced hypertension.[125] High blood pressure is considered a class effect of TKI treatment, although the mechanisms have not been fully described.[126,127]

8.1.10 Other Drugs

Approved drugs known as hypertensives can unexpectedly cause high blood pressure as a side effect. For instance, the antidepressant venlafaxine hydrochloride increases blood pressure by inhibiting serotonin and norepinephrine reuptake. Multikinase inhibitor therapy for thyroid cancer and tyrosine kinase inhibitor therapy are linked to hypertension.[128] Some antidepressants like selective norepinephrine and serotonin reuptake inhibitors (SNRI) can increase the BP of an individual up to 2/1 mmHg. Tricyclic antidepressants can increase hypertension in a ratio of 3.19.[105] In general, selective serotonin reuptake inhibitors (SSRIs) are safe for both patients with and without a history of cardiovascular disease because they have little effect on blood pressure levels..[129]

Sympathomimetic drugs mimic or stimulate the adrenergic nervous system, and they can raise blood pressure to alarming heights, particularly in hypertensive patients.[132] Many hypertensive patients are sensitive to all pressors, probably because they have hypertrophied vascular smooth muscles.[132] Sympathomimetics include common nasal decongestants, appetite suppressants with amphetamine-like actions, stimulants prescribed for attention-deficit/hyperactivity disorder, and bronchodilators.[132] While acute hypertension is part of the sympathomimetic toxidrome, it has multiple other pharmacologic causes. [133]

Ritodrine for premature labor induces severe hypertension via sympathetic neuroeffector junction activation.[134] The drug has proved to be efficient and relatively safe, yet a few cases of severe side effects, all related to its effect on the cardiovascular system, have already been reported.[134]

The use of bronchodilators of the β-2 agonist class can cause adverse effects on the cardiovascular, elevated blood pressure, tremor, palpitations, tachycardia, and headache, especially in the elderly and patients with preexisting cardiac disease.[135]

Physicians should be aware of the possibility that people with migraines develop hypertension when treating them with anti-CGRP (receptor) antibodies.[136] Caution for raised BP regarding anti-CGRP (receptor) antibodies should be added to clinical treatment guidelines for migraine.[136]

Liquorice mediates its effect on blood pressure via the action of glycyrrhizin on the kidney. Chronic liquorice consumption may cause ongoing, though ultimately transient, suppression of the renin–aldosterone axis following discontinuation of ingestion: this may continue for up to four months. Liquorice consumption should be considered in the evaluation of hypertension and hypokalemia.[137] [138]Carbenoxolone is a hemisuccinate derivative of glycyrrhetinic acid. It was originally developed as an antiulcer drug but was found to cause sodium retention, hypertension, hypokalemia, and suppression of the renin-angiotensin-aldosterone system.[139] Carbenoxolone may foster hypertension by multiple mechanisms.[140] It is possible that carbenoxolone, over a wide range of concentrations, inhibits 11β-hydroxysteroid dehydrogenase in vascular smooth muscle, increases intracellular glucocorticoid concentrations, and accentuates vasoconstrictor action.[140] These corticosteroids may be formed locally in the blood vessel or may reach the vascular smooth muscle after synthesis in the adrenal cortex.[140]

Partial or total non-adherence to antihypertensive therapy is associated with an increased risk of cardiovascular events and death at all ages. However, the risk is proportionally higher in old patients because they often suffer from multiple comorbidities and have intrinsically a higher cardiovascular risk. Studies have demonstrated that poor adherence increases the incidence of hospitalization in the elderly and the risk of death.[141]

Recommendations

- **Nonsteroidal anti-inflammatory drugs** (including selective inhibitors of the second isoform of cyclooxygenase) and steroids are the two most significant prescription medications that impact blood pressure.
- It is significant to highlight that each person's response to these chemicals will differ greatly, with greater increases seen in **older people**, those **whose baseline blood pressure is higher,** people **who are on antihypertensive medication,** and those with kidney disease.
- We must be **careful about which medications cause or worsen hypertension** when they are taken for other conditions. Therefore, it is imperative to test all patients (both those with hypertension and those at risk for developing it) for substances that could raise their blood pressure or interfere with the BP-lowering effects of antihypertensive drugs.

Section 9 - TREATMENT OF HYPERTENSION

9.1 Lifestyle Modification

9.1.1 Yoga and Mindfulness

The age-old Indian practice of yoga is known to help reduce stress and likely to reduce blood pressure.[142] The integrated response of Yoga Nidra on the hypothalamus results in decreased sympathetic nervous system activity and simultaneously increases the parasympathetic activity as well, by possible activation of the HPA axis.[143] EEG studies showed an initial increase in the beta wave activity during the practice, indicating a calm state of mind being induced in the practitioners.[144] There are many traditional schools of yoga, including Jnana Yoga, Bhakti Yoga, Karma Yoga, Patanjali Yoga, Kundalini Yoga, Hatha Yoga, Dhyana Yoga, Raja Yoga, etc., Hatha yoga which includes physical postures (asana), controlled breathing (pranayama), and meditation (dhyana) can be recommended as a relevant lifestyle modification.

Meditation practices can be classified into two broad categories - mindfulness meditation and concentrative meditation. Regardless of the nuances between these types of modalities, typical outcomes for most meditative practices are mental calmness and focus.[145]

Although there is limited evidence on the direct impact of mindfulness on hypertension control, these practices can be recommended to patients to ensure a comprehensive lifestyle modification strategy.

9.1.2 Dietary Modification

The DASH diet is a specially proposed dietary pattern promoted by the US-based National Heart, Lung, and Blood Institute to prevent or control hypertension.[146] This diet consists of fruits and vegetables combined with low-fat dairy products (with diminished saturated and total fat content), low levels of cholesterol, and whole grains, nuts, poultry, and fish. Usually, red meat, sweets, and sugar-containing beverages are exempted from the DASH diet and are enriched with potassium, magnesium, calcium, and fiber with excess antioxidants.[147] Additionally,a healthy gut flora can reduce inflammation and hence is expected to have a blood pressure-lowering effect.[148]

9.1.3 Additional lifestyle modifications

The American College of Cardiology and American Heart Association recommend six types of additional non-pharmacological interventions - alcohol intake reduction, salt intake reduction, increased potassium intake, physical activity, weight loss, and heart-healthy diets.[149] The International Society of Hypertension guidelines also highlighted the importance of non-pharmacological interventions and recommended them to be used along with the antihypertensive medications for optimum control of hypertension.[150] Growing evidence suggests that some of the non-pharmacological interventions could help reduce the needed dosage of antihypertensive medication or result in a greater reduction in blood pressure if used in combinationwith medications.[151] The body of evidence on other non-pharmacological interventions, such as yoga, healthy drinks, and stress reduction, is also growing.[142]

9.2. Pharmacological Management of Hypertension

- For decades, the blood pressure threshold of ≥140/90 mmHg is considered an indication for drug therapy in hypertensive individuals. However, in 2017, the American College of Cardiology (ACC) and the American Heart Association (AHA) guidelines recommended a BP of ≥130/80 mmHg as the cut-off for undergoing treatment in patients with high cardiovascular risks.[149] Recently, an analysis from the Blood Pressure Lowering Treatment Trialists' Collaboration (BPLTTC) suggests that pharmacological treatment should be provided to high-risk subjects with cardiovascular diseases, irrespective of their baseline BP and cardiovascular health status.[152] In August 2021, the World Health Organization (WHO) recommended that 140/90 mmHg BP could still be the threshold for initiating antihypertensive medications, but with a reduction in the treatment threshold to 130–139 mmHg for individuals with existing cardiovascular diseases.[153]
- Five major drug classes - ACE, ARBs, BBs, CCBs, and Thiazide/Thiazide-like diuretics form the basis of antihypertensive treatment strategies where ACE and ARBs belong to RAS blockers.[154]
- Patients with Grade 1 can be initiated with monotherapy (CCBs, ACE inhibitors, thiazide-like diuretics) in combination with lifestyle modifications. Average initial doses can be 5 mg of amlodipine, 5 mg of enalapril and 12.5 mg of hydrochlorothiazide.[155]
- Patients with Grade 2 hypertension should be initiated, preferably with dual therapy as the first treatment using a combination that is calibrated according to the patient's individual risk factors. Lifestyle modifications must equally support any combination therapy.
- According to ESH 2023, initiation of therapy with a two-drug combination is recommended for most hypertensive patients, where an RAS blocker with a CCB or Thiazide is a preferred combination.[156] Other combinations of the five major drug classes can be used.[157]
- Most combinations of antihypertensive agents, whether at fixed doses or free combinations, include a diuretic. These combinations have been shown to produce greater blood pressure reductions than those seen with monotherapies.
- It may be better to use a combination of medications rather than increasing the dosage of a single drug to prevent side effects.
- Combinations of a calcium antagonist with a renin–angiotensin system inhibitor (RASI), whether an angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB), have also been shown to be effective and safe in the management of the hypertensive patient.[158]

To avoid complications, it is important to start treatment as soon as possible, achieve the goals in the shortest time possible, and ensure treatment adherence.[159] Combination therapy, including Single Pill Combination (SPC), is recommended for high-risk groups with BP ≥ 160/100 mmHg and 20/10 mmHg higher than the target BP or those where monotherapy is inadequate. Low-dose SPC can be initiated in those with BP ≥ 140/90 mmHg.[160,161] Dual therapy may also be started in patients with high cardiovascular risk.

The use of SPCs is left to the discretion of the physician, its potential usefulness to improve drug adherence compared to free-drug equivalents is acknowledged.[162] Combining two medicines in a single pill can be cost-effective and has important benefits for patients and for health systems, including improved patient adherence to daily medication regimens, which may improve clinical outcomes; improved blood pressure control rates and shortened time to blood pressure control; and more efficient hypertension management for health systems by simplifying drug supply and procurement logistics.[163] On July 9, 2019, the WHO added fixed-dose combination antihypertensive medications to the WHO Essential Medicines List.

A 2021 Indian study by Kumar *et al*. mentions the success and tolerability of Telmisartan in Indians as mono or combination therapy, irrespective of the patient's age, duration, and stages of hypertension.[164] Patients more likely to have HMOD are recommended an initial treatment with a combination of two drugs, usually an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) in combination with a calcium channel blocker (CCB) or thiazide-type diuretic, which would be the optimal treatment for all manifestations of HMOD.[165]

9.2.1 Adherence to Anti-hypertensive Treatment

Poor adherence to hypertension treatment increases the risk of CV events and mortality, and higher adherence lowers the risk of CV events; thus, improving medication adherence should be the priority in any patient with HTN.[166] Multiple factors such as type of treatment, comorbidities, cost, and physician-patient relationship affect adherence.[167] Various methods, such as drug prescription records, pill count, digital tools, increased physician-patient collaboration, and involvement of other healthcare professionals, can help improve adherence.[168,169] Besides medication adherence, there is a wide variation in adherence to lifestyle therapy (diet, physical activity, salt, alcohol restriction, etc.). Ensuring compliance with such measures is also necessary. As adherence is one of the critical determinants of HTN control, we must adopt measures to enhance adherence. Given general unawareness and lack of HTN control, improving adherence is crucial in the Indian context.[170] Burnier and Egan, in their review, highlighted five major categories of such factors. These include sociodemographic, health-care team/system, therapy-related, condition-related, and patient-related factors. More than one factor may be the reason for suboptimal adherence.[171]

Recommendations

- To maximize treatment benefits, **BP lowering should take precedence over choosing specific antihypertensive medication groups.**
- **Key medication classes** in managing hypertension are ACEis, ARBs, BBs, CCBs, and Thiazide/Thiazide-like diuretics, and the foundation of hypertension treatment plans should consist of these medications and their combinations.
- For most hypertension patients, **a two-drug combination is advised for therapy initiation**. A CCB or Thiazide/Thiazide-like diuretic should be used with an RAS blocker (either an ACE inhibitor or an ARB).
- Patients with grade 1 hypertension and low-risk conditions whose blood pressure is only mildly increased (less than 150 mmHg SBP and 95 mmHg DBP) may be started with monotherapy.
- Apart from very high CV risk, fragility, and/or old age, those with high-normal BP can also be candidates for monotherapy unless indicated otherwise.
- **Treatment should be escalated to a three-drug combination**, often a RAS blocker, CCB, or a Thiazide/Thiazide-like diuretic, if blood pressure is not controlled with the initial two-drug combination after taking the maximum suggested and tolerable dose of each component.
- It is advised to **continue treatment in accordance with the guidelines for resistant hypertension if blood pressure** is not controlled with a three-drug combination when the maximum indicated and tolerated dose of each component is used.
- **Single pill combinations (SPCs)** should be used wherever possible, including when starting treatment with a two-drug combination and at all other times.
- BBs can be considered if multiple other circumstances exist where doing so would be beneficial.
- It is **not advised to combine two RAS blockers** because doing so increases the risk of side effects, including AKI.
- Blood pressure can be effectively controlled with little adverse effects when multiple medication classes with various mechanisms of action are used in combination therapy. Therapy can be started with two medications or as a fixed-dose combination for stage 2 hypertension.
- **Older people** have mild renin hypertension, so diuretics or CCBs are favored as first-line medicines; younger people have high renin hypertension thus ACEIs/ARBs or newer -blockers are preferable. The second stage involves combining one of the drugs from groups A [ACE inhibitor/ARB] or B [-blocker] with either C [calcium channel blocker] or D [thiazide diuretic] (step 1).
- After the blood pressure has been stabilized with a dose of two antihypertensive medications given separately in the same proportion, the prescription of an antihypertensive drug combination in a **single pill may be considered if it is available.**
- The recommended office threshold for starting pharmacological treatment in patients aged 18 to 79 is 140 mmHg for SBP and/or 90 mmHg for DBP.
- In patients ≥80 years, the recommended office SBP **threshold for initiation of drug treatment is 160 mmHg.**
- The office SBP and DBP thresholds for initiation of drug treatment in **frail patients** should be individualized.
- In adult patients with a **history** of **CVD**, predominantly CAD, drug treatment should be initiated in the high-normal BP range **(SBP ≥130 or DBP ≥80 mmHg).**
- Blood pressure **should be declined gradually**. To begin treatment, **start with low doses** of antihypertensive medication.

- Age, concurrent risk factors, the presence of HMOD, other coexisting conditions, socioeconomic variables, the drug's availability, and clinician acumen all play a role in the decision to use an antihypertensive medication.
- The main challenge in treating hypertension is lowering the risk of cardiovascular disease through appropriate blood pressure management. Overall, blood pressure reduction rather than therapy selection is what makes antihypertensive medication effective. Many people will need more than one medication to treat hypertension.
- **Evaluate adherence to antihypertensive treatment** as appropriate at each visit and prior to escalation of antihypertensive treatment.
- Consider the following strategies to improve medication adherence
    - reducing polypharmacy – use of single pill combinations
    - once-daily dosing over multiple times per day dosing
    - linking adherence behavior with daily habits
    - providing adherence feed
    - home BP monitoring
    - reminder packaging of medications
    - empowerment-based counseling for self-management
    - electronic adherence aids such as mobile phones or short messages services
    - multidisciplinary healthcare team approach (i.e., pharmacists) to improve monitoring for adherence

In adults with elevated BP who are overweight or obese, **weight reduction is strongly recommended** to reduce BP and improve CV outcomes.

- Vegetables, fruits, beans, nuts, seeds, vegetable oils, and fish and poultry, among animal products, are preferred dietary items. Limit your intake of fatty meats, full-fat dairy, sugar, sweetened beverages, and sweets. Overall, it is advised to follow a diet that is high in plant- and low in animal-based foods.
- To lower blood pressure and the risk of CVD in persons with hypertension who consume a high sodium diet, **salt alternatives rich in potassium are advised.**
- For people with increased BP, dietary salt (NaCl) limitation is advised to lower BP. It is advised to **limit salt intake to no more than 5 g** (less than 2 g sodium) per day.
- Adults with increased BP are advised to consume more potassium, ideally through dietary changes, **except those with severe CKD.**
- Adults with excessive blood pressure are advised to engage in **daily physical activity** and structured exercise to lower blood pressure and lower their cardiovascular risk profile. Aiming for **75–150 minutes of strenuous aerobic exercise each week,** or a comparable combination, or at least 150–300 minutes of aerobic exercise per week, is advised. Additionally, less time should be spent sedentary, and dynamic weight training should be included (2–3 times a week).
- Adult men and women who now drink alcohol and have high blood pressure or hypertension should be informed that **cutting back on alcohol consumption almost to the point of abstinence** will drop their blood pressure.
- **Alcohol shouldn't be advised** for CVD prevention because prior research that linked moderate drinking to lower CV risk is not well supported in subsequent studies.
- All smokers are advised to **quit smoking** to prevent ambulatory blood pressure rise, lower their risk of developing masked hypertension, and improve their CV health results.
- Controlled breathing techniques, mindfulness-based exercise, and meditation can all help to reduce stress.
- Saturated fat consumption should **not be more than 7%** of daily calorie intake, and it can be further decreased if there is hyperlipidemia.
- **Whole grains, fruits, vegetables, low-fat dairy products, and whole grains** should all be a part of a diet that is low in saturated fat and cholesterol.

Section 10 - COMORBIDITIES AND COMPLICATIONS OF HYPERTENSION AND THEIR MANAGEMENT

Hypertension is aprimary contributor to both mortality and morbidity of cardiovascular diseases (CVDs) like heart attacks and strokes. Uncontrolled blood pressure is a key risk factor for CVD, attributing to over 10 million annual deaths, surpassing the combined toll of all infectious diseases. Hypertension's impact leads to approximately 1.6 million yearly deaths in India, primarily attributed to ischemic heart disease and stroke.[172] Logistic regression models showed hypertension associated with a six- to eight-fold increase in odds of ischemic heart disease (IHD) and stroke mortality, while diabetes was linked to double the odds of IHD and elevated odds of stroke mortality.

10.1. Cardiovascular Disorders

10.1.1 Coronary Artery Disease (CAD)

Blood pressure distribution analysis revealed higher rates of pre-hypertension and hypertension in patients with CAD and diabetes. ACE inhibitors, like enalapril, lisinopril, and ramipril, induce blood vessel relaxation, reducing blood pressure and conferring cardioprotective benefits. ARBs such as losartan, valsartan, and telmisartan counteract angiotensin II's effects,

fostering vasodilation and blood pressure reduction. Beta-blockers, exemplified by metoprolol, carvedilol, and bisoprolol, ameliorate blood pressure and heart rate, which is particularly advantageous for CAD patients. CCBs like amlodipine and verapamil alleviate vessel tension and cardiac strain, contributing to blood pressure management. Diuretics, encompassing thiazide like diuretics and loop diuretics (e.g., furosemide), mitigate fluid and sodium retention, lowering blood volume and pressure.

Low-dose aspirin is crucial for preventing blood clot formation in CAD cases. Statins (e.g., atorvastatin, simvastatin, rosuvastatin) reduce cholesterol levels and lower cardiovascular risks. Beta-blockers manage hypertension and help with angina by reducing the heart's oxygen demands. Nitroglycerin dilates vessels, improving cardiac blood flow and relieving angina symptoms. Lifestyle changes are essential for managing hypertension and CAD, including a heart-healthy diet, regular exercise, weight management, smoking cessation, and stress reduction. Combining medication with these lifestyle adjustments is vital for a comprehensive approach to addressing hypertension and coronary artery disease.[173]

10.1.2 Heart Failure (HF)

The projected prevalence of HF in India is approximately 1% of the total population, affecting around 8-10 million individuals. Estimated HF-related mortality ranges from 0.1 to 0.16 million individuals annually.[174]A community-based study was conducted where HF was identified in 9% of the cases, out of which 67% exhibited preserved left ventricular (LV) systolic function, while 33% had LV systolic dysfunction. In the outpatient setting, HF prevalence was 22.5% among those below 30 years and 14.9% above 50 years, revealing a youthful HF demographic.

Policy-level measures such as salt and tobacco consumption restrictions have the potential for effective primordial prevention with broader impacts on heart failure prevention. Lifestyle modifications, including adopting a heart-healthy diet, engaging in regular physical activity, maintaining a healthy weight, quitting smoking, and managing stress, are pivotal in reducing the risk of heart failure among hypertensive individuals. Pharmacological interventions play a key role, with antihypertensive medications like ACE inhibitors, ARBs, beta-blockers, calcium channel blockers, and diuretics serving to control blood pressure and mitigate the risk of heart failure.The PARADIGM-HF trial reported that sacubitril/valsartan reduced cardiovascular deaths by 20% and HF-related hospitalizations by 21% compared to enalapril, albeit at a higher cost. The EMPEROR-Preserved trial shows promising results with SGLT2 inhibitors like empagliflozin in Heart failure with preserved ejection fraction (HFpEF) treatment, reducing hospitalizations regardless of diabetes status.[175]

10.1.3 Atrial Fibrillation

Atrial fibrillation (AF) is a common heart rhythm disorder andcontributes to a third of cardiac rhythm disorder-related hospital admissions. Although its effects on quality of life and survival are well-known in Western populations, information about AF in the Indian population is limited. Hypertension is a common risk factor for nonvalvular AF. Studies show that hypertension is prevalent among Indian AF patients but lower than other regions. Detecting and managing AF early could prevent strokes, but conventional screening methods are challenging and expensive in resource-limited settings. A study conducted in rural western India revealed a higher AF prevalence (5.1%) in this region compared to previous reports in India and is similar to estimates in North America and Europe. The historically low reported AF burden in low and middle-income countries might stem from limited screening.[176] The SMART-India (Smart Monitoring of Atrial Fibrillation in Real Time India) study introduced an innovative approach to identify undiagnosed chronic diseases among individuals in resource-limited settings.[177] Adherence to established management guidelines is crucial to prevent these complications.[178]

10.1.4 Valvular Heart Disease

Heart valve diseases contribute significantly to global cardiovascular morbidity and mortality, particularly in developing countries where rheumatic heart disease (RHD) prevails. Occurrence and patterns of valvular heart disease (VHD) can be studied using Echocardiography. RHD has been known to primarily affect the mitral valve, followed by the aortic, tricuspid, and pulmonary valves.[179] Advancements in surgical and percutaneous procedures and improved insights into optimal intervention timing contribute to the current heightened survival rates. Echocardiography remains the established standard for diagnosing and periodically evaluating individuals with valvular heart disease.

10.2 Hypertension and Cognitive Impairment

Hypertension is a risk factor for both vascular cognitive impairment and Alzheimer's disease, the two most common causes of dementia, collectively accounting for 85% of cases. Hypertension causes acute and chronic injury to the brain, accelerates brain atrophy, and engages neuroinflammatory processes, each of which contributes to cognitive impairment and major neurocognitive syndromes (dementia).[180] In addition to a "direct effect" of hypertension on brain structure and microvasculature, hypertension is a risk factor for other syndromes related to end-organ damage, most notably chronic kidney disease and heart failure.[181] Identification and treatment of hypertension is considered an important target for population-level reduction in the global burden of dementia.[182]

10.3 Vascular Disease

10.3.1 Lower Extremity Arterial Disease

A study amongst the elderly population of North Kerala, India, with 1148 respondents, reported an age-adjusted PAD prevalence of 26.7%, with no distinction between urban and rural areas. Although symptomatic PAD was infrequent, risk factors like diabetes, hypertension, high cholesterol, low high-density

lipoprotein cholesterol levels, sedentary lifestyle, and smoking were observed in varying proportions. Multivariate analysis indicated that age, smoking, and physical inactivity were significant predictors of PAD, and an independent association between PAD and CAD was found.[183]

PAD in the lower limbs is often overlooked despite being more prevalent than commonly reported. Routine assessment of the ankle-brachial index (ABI) is not commonly performed, especially in high-risk individuals with modifiable factors like smoking, diabetes, hypertension, and dyslipidemia. This lack of attention primarily stems from both primary care physicians and cardiologists, in stark contrast to the vigilance given to CAD.[184]

10.3.2 Aortic Dilatation, Aneurysm, and Dissection

Aortic root and ascending aorta aneurysms are typically linked to degenerative changes in the medial layer. In regions like India, where tuberculosis is widespread, it can emerge as an infrequent yet significant cause of aortic root dilation. Tubercular-related aortic dilation leading to dissection and subsequent aortic regurgitation is an unusual but noteworthy complication of tuberculosis, especially considering the global resurgence of drug-resistant tuberculosis and its association with conditions like acquired immunodeficiency syndrome. Although tubercular inflammation of the aorta is relatively frequent, the occurrence of tuberculous mycotic aneurysms in this vessel is rare, and involvement of the aortic root is even scarcer.[185]

Aortic dissection is rare in childhood and demands a high level of suspicion for prompt treatment. It should be considered in children with Marfan syndrome who experience chest pain. Medications like beta-blockers, calcium channel blockers, and angiotensin inhibitors can slow aortic dilation and reduce the risk of dissection.[186]

10.4 Other Comorbidities and their Management

10.4.1 Psoriatic Arthritis

Psoriatic arthritis (PsA) is linked to elevated rates of cardiometabolic conditions like hypertension, dyslipidemia, diabetes, obesity, and cardiovascular disease (CVD). These comorbidities, intertwined with disease severity, hinder treatment outcomes and necessitate increased medical attention and medication use. CVD is a leading cause of death in PsA, underscoring the need for a holistic management strategy encompassing skin, joint, and comorbidity treatment. Understanding the intricate interactions and mechanisms of these cardiometabolic comorbidities within psoriatic disease is crucial and requires further research. Approaches to enhancing CVD screening and management include education for healthcare professionals, seamless communication between specialists and primary care providers, and innovative models like interdisciplinary cardio-rheumatology clinics.[187]

10.4.2 Glaucoma in Hypertension

Glaucoma and arterial hypertension are age-related conditions, and their prevalence is expected to rise in the coming years. Glaucoma and hypertension share common physiological features, making their coexistence likely. High blood pressure contributes to glaucoma progression due to spikes in intraocular pressure. A prospective multidisciplinary study conducted in 2020 in India showed that women exhibited a higher glaucoma risk in hypertension. Diastolic blood pressure played a more crucial role in intraocular pressure elevation than systolic BP. Patients on calcium channel blockers had the most reduced intraocular pressure.[188]

10.4.3 Hypertension Oncology

Excluding renal cell carcinoma, the relationship between hypertension and various other cancers has yielded inconsistent results in different studies. A meta-analysis revealed positive associations between hypertension and kidney, colorectal, and breast cancers. While there were also positive associations with oesophageal adenocarcinoma, squamous cell carcinoma, liver, and endometrial cancer, many studies lacked comprehensive adjustments for various factors. Systolic and diastolic blood pressure demonstrated a positive link with kidney cancer risk but not with other types of cancer.[189] In the context of cancer treatment, combination therapies have become an essential strategy due to the limitations of single treatments. A common issue arising from cancer treatments is cancer treatment-induced hypertension, often seen as a result of combination therapies. A meta-analysis reported that cancer patients undergoing combination therapy had a higher risk of hypertension, particularly for more severe cases (grades 3-4). This comprehensive analysis provides valuable insights into the increased risk of hypertension in cancer patients undergoing multiple combination therapies, offering guidance for clinical practice and strategies to mitigate hypertension during cancer combination treatment.[190] There exists a significant overlap between the prevalence of hypertension and cancer due to shared risk factors like sedentary lifestyle, obesity, smoking, unhealthy diet, and alcohol consumption. The use of chemotherapy, along with adjuvant drugs effective in cancer treatment, has improved patient survival rates, subsequently increasing the occurrence of hypertension.[191] Managing hypertension in patients should adhere to general population guidelines, with special attention to potential hypotension rebound after cessation of cancer therapy. The optimal management of these complex cases necessitates collaborative care among oncologists, cardiologists, hypertension specialists, primary care providers, and pharmacists, aiming to maximize cancer treatment benefits while minimizing adverse cardiovascular effects.[192]

10.5 Hypertension Management during Follow-up

There is a direct correlation between quality of life and medication adherence, indicating that better adherence is associated with improved quality of life.[193] Poor knowledge of complications and

being asymptomatic at diagnosis were identified as risk factors for poor adherence. The study highlighted the need for comprehensive strategies to enhance medication adherence among hypertensive individuals in the rural population.[194] Studies reported varying adherence rates to antihypertensive drugs, influenced by factors like socioeconomic status, health literacy, disease awareness, forgetfulness, medication costs, and disease duration. Establishing a strong physician-patient relationship, incorporating counseling, and employing various strategies can identify and address poor adherence.

Recommendations

- **Calcium channel blockers and diuretics may be added to RAAS blockers** as a secondary form of therapy. Glucose intolerance has been seen with thiazide diuretics.
- If a patient has **proteinuria (or microalbuminuria)**, ACE inhibitors and ARBs, which suppress the renin-angiotensin systems, should be utilized.
- A SBP of less than 130 mmHg should be considered for people **with overt proteinuria**, but an SBP of less than 140 mmHg should be the objective for lowering blood pressure.
- Patients with hypertension with overt proteinuria (or microalbuminuria) should take **ACE inhibitors or ARBs since they efficiently lower albuminuria.** Following the start of therapy or any increase in the dosage of ACE inhibitors, it is advised to monitor serum creatinine and potassium throughout the first week of treatment.
- Other antihypertensive medications include **ACE inhibitors, Thiazide or thiazide-type diuretics,** and in cases of volume overload, loop diuretics such as furosemide.

Cardiovascular Disorders

- Antihypertensive treatment of hypertension is recommended to effectively prevent CAD.
- Drug therapy should begin in Grade 1 hypertension (SBP > 140 or DBP > 90 mmHg) in adult patients with or without CAD and lifestyle modifications. But it can be started in a high normal BP range if it does not come down to the optimal range on a lifestyle modification trial for 3-6 months.
- Patients with CAD have the same therapeutic goals as the general hypertensive population.
- It is advised to utilize medications like ACE inhibitors/ ARBs or BBs in people with hypertension and CAD.
- BBs and CCBs - both DHP and non-DHP- are particularly beneficial in individuals with hypertension and CAD who also have angina pectoris.
- In hypertensive patients with CAD, lowering heart rate to a range of 60 to 80 beats per minute is an additional therapy objective that can be achieved with BB or non-DHP CCBs.
- In general, BBs and non-DHP CCBs like diltiazem or verapamil should not be taken together.
- Patients with very low heart rates (50 beats per minute) shouldn't start BB or non-DHP.
- It is advised to treat hypertension to prevent heart failure successfully.
- Heart failure can be avoided by treating hypertension with any of the main antihypertensive medication groups, such as ACE inhibitors, ARBs, BBs, CCBs, and Thiazide/Thiazide-like diuretics.
- To prevent heart failure in hypertension, alpha-1 blockers (such as doxazosin) can be used, ideally in conjunction with BBs and Thiazide/Thiazide-like diuretics to prevent fluid retention and tachycardia.
- Patients with type-2 diabetes are highly recommended SGLT2is to prevent heart failure.
- In patients with hypertension and heart failure with reduced ejection fraction (HFrEF), it is recommended to combine drugs with documented outcome benefits, including ACE inhibitors/ ARBs, which could be substituted by ARNI (sacubitril/valsartan), BBs, Mineralocorticoid Receptor Antagonists (MRA)s, and SGLTis, if not contraindicated and well tolerated.
- A DHP-CCB can be introduced for blood pressure control if patients still have uncontrolled hypertension after up-titrating medications from the four main pharmacological classes (RAS-inhibitors, BBs, MRAs, and SGLTis) and using supplemental treatment with a diuretic to regulate fluid balance.
- Non-DHP-CCB should not be used in HFrEF because of their strong negative inotropic effect.
- As with HFrEF, patients with good blood pressure control benefit significantly, and a target of 130/80 should be met.
- Statins should be administered in hypertensive people with dyslipidemia.
- In individuals with HFpEF, it is advised to treat hypertension with all major antihypertensive medication classes (ACEIs or ARBs, BBs, CCBs, and Thiazide/Thiazide-like diuretics).
- Particularly in the lower HFpEF range, treatment with an MRA (spironolactone) can be recommended regardless of documented resistant hypertension.
- Patients at risk for AF, such as those with high normal BP, LVH, and left atrial dilatation, should undergo testing for hypertension with BP monitoring equipment approved for use in the presence of AF.
- The incidence of incident and recurring AF is decreased with antihypertensive therapy. The thresholds and treatment goals for reducing blood pressure are the same as for people with hypertension in general.

- It is possible to employ all main antihypertensive medication groups to stop the occurrence or recurrence of AF. To stop recurrent AF, people with AF may choose to consider RAS-blockers and BBs.
- In individuals with AF, treating hypertension lowers the risk of stroke and other CV events. The same as for the general hypertensive population, the BP threshold and targets, as well as pharmacological treatment strategies, should be used.
- To consider the fluctuating BP levels, it is advised that patients with AF receive at least three office BP measurements by auscultation.
- Because automated oscillatory methods accurately measure SBP and only slightly overestimate DBP, they can be utilized to measure blood pressure in patients with AF.
- For individuals with AF, BBs are the primary medication class for controlling heart rate. Particularly in individuals who are symptomatic, the resting heart rate should be reduced to under 110 beats per minute, with an ECG-based target heart rate of 80 beats per minute.
- Digoxin may be added to BBs to improve HR control in AF.
- Even when hypertension is the only extra risk factor (CHA2DS2-VASc score of 1 in men and 2 in women), oral anticoagulants for the prevention of stroke should be taken into consideration in patients with AF who have hypertension.
- The BP thresholds and targets for AS patients should be the same as those for the general hypertensive population, as should the pharmacological treatment techniques.
- Low BP should be used more cautiously in patients with high-grade AS, especially those with a history of syncope, to prevent an excessive drop in BP and repeated syncope.
- The BP targets and thresholds for patients with Aortic Incompetence should be the same as those with hypertension.
- In individuals with Aortic Incompetence, afterload-reducing medications such as RAS-blockers and CCBs are advised.
- Antihypertensive therapy is advised to prevent MI and lessen its symptoms by lowering the left ventricular afterload.

Ophthalmological Disorders

- In hypertensive patients with glaucoma, ABPM and closer ophthalmologic examinations should be frequently done, especially in patients with unexplained visual field deterioration.
- In patients with glaucoma, very low and very high BP should be avoided, particularly at night.
- In patients with glaucoma, bedtime administration of antihypertensive drugs should be avoided as it may increase the risk of excessive lowering of BP and, thus, visual field loss.
- BBs have been associated with lower intraocular pressure and decreased risk of primary open-angle glaucoma and may be preferred in hypertensive patients with glaucoma.

Bleeding Disorders

- It is advised to lower blood pressure to lower the risk of significant bleeding, including cerebral hemorrhage if SBP is greater than 160 mmHg. Oral anticoagulants should only be added when SBP is reduced to < 160 mmHg.
- Use caution while using non-DHP CCBs for rate control, such as Diltiazem and Verapamil, as they may interact with oral anticoagulants and increase bleeding risk.

Cerebrovascular Disorders

- A BP 140/90 mmHg is advised in individuals with hemorrhagic stroke and within 6 hours of the onset of symptoms to prevent hemorrhage expansion.
- An SBP of more than 220 mmHg may be carefully decreased with intravenous treatment to 180 mmHg in patients with hemorrhagic stroke and in >6 hours after the beginning of symptoms. Slow and moderate BP reductions are superior to aggressive BP reductions to 140/90 mmHg if SBP is 220 mmHg or less than that.
- Patients with acute ischemic stroke who are eligible for mechanical thrombectomy (MT) or intravenous thrombolysis (IVT) should have their blood pressure carefully decreased and kept at or below 180/105 mmHg for the first 24 hours following the intervention.
- Clinical judgment should be used when considering pharmacological therapy to lower blood pressure by 15% during the first 24 hours following surgery in patients who are not candidates for IVT or MT and have a BP of more than 220/120 mmHg.
- In acute ischemic stroke patients, it is not advised to reduce blood pressure with antihypertensive medication regularly if it's less than 185/105 during first three days
- Patients who have elevated BP and are otherwise eligible for treatment with IV alteplase should have their BP carefully lowered so that their SBP is <185 mmHg and their diastolic BP is <110 mmHg before IV fibrinolytic (alteplase) therapy is initiated.
- In patients for whom mechanical thrombectomy is planned and who have not received IV fibrinolytic therapy, it is reasonable to maintain BP ≤185/110 mmHg before the procedure.
- In patients who undergo mechanical thrombectomy, it is reasonable to maintain the BP at ≤180/105 mmHg during and for 24 hours after the procedure.
- In patients with AIS, early treatment of hypertension is indicated when required by comorbid conditions (e.g.,

concomitant acute coronary event, acute heart failure, aortic dissection, post fibrinolysis sICH, or preeclampsia/eclampsia)

- In patients with BP ≥220/120 mmHg who did not receive IV alteplase or mechanical thrombectomy and have no comorbid conditions requiring urgent antihypertensive treatment, the benefit of initiating or reinitiating treatment of hypertension within the first 48 to 72 hours is uncertain. It might be reasonable to lower BP by 15% during the first 24 hours after the onset of a stroke.
- In patients with BP <220/120 mmHg who did not receive IV alteplase or mechanical thrombectomy and do not have a comorbid condition requiring urgent antihypertensive treatment, initiating or reinitiating treatment of hypertension within the first 48 to 72 hours after an AIS is not effective to prevent death or dependency.
- In patients with spontaneous ICH of mild to moderate severity presenting with SBP between 150 and 220 mmHg, acute lowering of SBP to a target of 140 mmHg with the goal of maintaining in the range of 130 to 150 mmHg is safe and may be reasonable for improving functional outcomes.
- In patients with spontaneous ICH presenting with large or severe ICH or those requiring surgical decompression, the safety and efficacy of intensive BP lowering are not well established.
- In patients with spontaneous ICH of mild to moderate severity presenting with SBP >150 mmHg, acute lowering of SBP to <130 mmHg is potentially harmful.
- For secondary prevention, In patients with spontaneous ICH, it is reasonable to lower BP to an SBP of 130 mmHg and diastolic BP (DBP) of 80 mmHg for long-term management to prevent hemorrhage recurrence
- All antihypertensive medication groups can prevent strokes if blood pressure is kept under control.
- Even with Grade 1 hypertension, pharmacological treatment should be started in patients with a history of stroke or transient ischemic attack (TIA) to lower systolic blood pressure to less than 140 mmHg. An initial medication is an ACE inhibitor/ARB.
- Avoid giving antihypertensive medication for the first 72 hours after an ischemic stroke because too much blood pressure reduction can worsen the ischemia.
- Extreme blood pressure readings, such as systolic readings over 220 mmHg or diastolic readings over 120 mmHg, should be treated with medications that lower mean arterial pressure by no more than 25% in the first 24 hours and by about 15% in the first hour in patients who are not receiving thrombolytic therapy for ischemic stroke. Patients who are candidates for thrombolytic therapy should be managed cautiously and kept below blood pressure readings of 110 mmHg diastolic and 185 mmHg systolic.
- Treatment with thiazide diuretics, angiotensin-converting enzyme inhibitors, or angiotensin II receptor blockers helps lower blood pressure and minimize the risk of recurrent stroke in individuals with hypertension who suffer a stroke or TIA.
- To lower the risk of recurrent stroke and vascular events in patients with hypertension who have had a stroke or TIA, an office BP goal of 130/80 mmHg is advised for most patients.

Kidney Disorders

- Continuous monitoring of blood pressure (BP) is essential at all stages of chronic kidney disease (CKD) because hypertension stands as the second most critical risk factor for end-stage kidney disease (ESKD).
- In individuals with CKD, who often experience non-dipping or elevated nighttime BP, it is advisable to use ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM) to keep track of these fluctuations.
- < UNK> In diabetic or non-diabetic CKD patients dealing with hypertension, lowering BP through treatment can slow down the progression of kidney dysfunction and reduce the chances of ESKD (end-stage kidney disease) and cardiovascular (CV) complications.
- For most CKD patients, regardless of the stage of CKD, immediate interventions involving lifestyle adjustments and antihypertensive drug therapy are recommended if systolic BP (SBP) is equal to or exceeds 140 mmHg or diastolic BP (DBP) is equal to or exceeds 90 mmHg.
- The primary objective for all CKD patients is to achieve office BP levels below 140 mmHg for systolic BP and below 90 mmHg for diastolic BP.
- In a majority of CKD patients, which includes younger individuals and those with an albumin-to-creatinine ratio (UACR) greater than or equal to 300 mg/g, as well as those at high cardiovascular risk, the target office BP should ideally be reduced to levels below 130/80 mmHg if it's well-tolerated.
- Kidney transplant recipients facing hypertension should aim for office BP levels below 130 mmHg for systolic BP and below 80 mmHg for diastolic BP.
- Regardless of the presence of albuminuria, it's important to avoid lowering BP excessively below 120/70 mmHg in CKD patients.
- In patients with CKD who exhibit moderate (UACR 30 to 300 mg/g) or severe (UACR > 300 mg/g) albuminuria, it's advisable to use either an ACE inhibitor (ACEi) or an angiotensin receptor blocker (ARB), with doses adjusted to the maximum tolerable levels.
- The use of a dual combination of both an ACE inhibitor and an ARB is not recommended.

- BP control can be challenging in CKD, and cases of resistant hypertension are quite common. Consequently, combination therapy is typically recommended.
- In individuals with diabetic or non-diabetic nephropathies associated with CKD, SGLT-2 inhibitors are a recommended treatment option when the estimated glomerular filtration rate (eGFR) is at least 20 or 25 mL/min/1.732.
- The non-steroidal mineralocorticoid receptor antagonist (MRA) finerenone is suggested for CKD patients with albuminuria related to type 2 diabetes when the eGFR is at least 25 mL/min/1.732 and serum potassium levels are below 5.0 mmol/L.
- In CKD patients with hyperkalemia, a potassium-binding agent can be employed to maintain serum potassium levels at normal or near-normal levels (below 5.5 mmol/L). This allows for the optimal continuation of treatment with a RAS blocker or an MRA
- Therapy for renal sympathetic denervation has also been studied. This procedure involves radiofrequency ablation of the sympathetic plexus surrounding the renal arteries.
- As a result, renal denervation therapy is still being studied and is not recommended for use in typical clinical settings.
- The non-steroidal mineralocorticoid receptor antagonist (MRA) finerenone can be considered for its kidney and heart protection properties in patients with diabetic chronic kidney disease (CKD) and moderate to severe albuminuria. Finerenone also contributes to lowering BP.
- Limited data regarding the potential benefits of combining SGLT2is and finerenone necessitates further investigation.

Diabetes Mellitus

- It is crucial to routinely check blood pressure (BP) in all individuals with diabetes as hypertension is a common accompanying condition, elevating the risk of cardiovascular (CV) issues and kidney-related events.
- Non-dipping or increased nighttime BP frequently occurs in type 2 diabetes, and monitoring using ambulatory BP monitoring (ABPM) or home BP monitoring (HBPM) is advisable.
- In the context of type 2 diabetes, it is recommended to employ antihypertensive treatments to safeguard against both macrovascular and microvascular complications.
- In individuals with type 2 diabetes, if their office systolic BP (SBP) is equal to or exceeds 140 mmHg and diastolic BP (DBP) is equal to or exceeds 90 mmHg, prompt action is needed, including lifestyle adjustments and antihypertensive medication.
- While the strategies for drug treatment in patients with type 2 diabetes should align with those for patients without diabetes, the primary goal is to lower BP to levels below 130/80 mmHg.
- Managing BP in diabetes can be challenging, often requiring combination therapy to achieve effective control.
- SGLT2 inhibitors (SGLT2is) are recommended for individuals with type 2 diabetes to reduce the occurrence of cardiac and kidney-related events. These medications also have a BP-lowering effect.

Obesity

- For adults with elevated blood pressure who are overweight or obese, it is advisable to pursue weight reduction as a means to lower blood pressure and enhance cardiovascular outcomes.
- Thiazide diuretics and beta-blockers (BBs) can have certain unfavorable metabolic effects. However, given that achieving optimal blood pressure control is the primary objective of antihypertensive therapy combining these drug classes is often necessary and recommended.
- Prescribing dual GIP/GLP-1 receptor agonists (RA) or GLP-1 RAs alone is not recommended for managing blood pressure in patients with obesity.
- Bariatric surgery should not be considered a referral for controlling blood pressure in obese patients.
- Dual GIP/GLP-1 RAs or GLP-1 RAs, as well as bariatric surgery, indirectly lower blood pressure concurrently with reducing body weight, contributing to blood pressure management in obese individuals.
- In obese patients with diabetes and hypertension, treatment with anti-diabetic medications capable of reducing both body weight and blood pressure might be preferable**.**

Cancer

- Patients with cancer should follow the same hypertension definition, thresholds, targets, lifestyle adjustments, and medication strategies recommended for the general population with hypertension.
- If a patient's hypertension is uncontrolled and their blood pressure readings reach or exceed 180 mmHg for systolic or 110 mmHg for diastolic, it is not advisable to initiate anticancer treatment.
- In cases of uncontrolled hypertension with blood pressure levels of 180 mmHg or higher for systolic or 110 mmHg or higher for diastolic, a team-based multidisciplinary approach should be initiated to promptly manage blood pressure and associated symptoms. This is to enable the initiation of anticancer therapy as early as possible.

- Thiazide or thiazide-like diuretics should only be used when necessary for blood pressure control and in patients with fluid retention. Their use in cancer patients should be cautious due to potential adverse effects, such as increasing serum calcium levels in patients with bone metastases, a heightened risk of cardiac arrhythmias by extending the QT interval through inducing hypokalemia, an increased chance of hyponatremia, and the potential to worsen hypovolemic conditions or dehydration.
- Non-DHP calcium channel blockers should be avoided in cancer patients who are concurrently receiving anticancer medications susceptible to pharmacokinetic interactions mediated by CYP3A4 and/or P-gp.
- Hypertension caused by VEGF inhibitors in cancer treatment can be managed with either RAS inhibitors (ACEIs or ARBs) or DHP-CCBs.
- In severely ill cancer patients, hypertension treatment should be tailored to the individual's symptoms, existing medical conditions, and the complexity of their medication regimen. This should be done through a shared decision-making process.
- It is advisable to perform BP assessments before initiating anticancer therapy, whether patients have a history of hypertension or not. This is crucial because anticancer medications can lead to sudden BP increases and associated complications, including emergencies.
- Paying attention to pain and anxiety management before taking BP measurements is particularly important in cancer patients and is recommended.
- Whenever feasible, the use of ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM) is advised during active cancer treatment and subsequent follow-ups, especially for patients receiving anticancer drugs that can trigger hypertension.
- Hypertensive cancer patients should undergo screening for hypertensive-mediated organ damage (HMOD) and cardiovascular risk before commencing anticancer therapy. This screening may include ECG, echocardiography, kidney function assessments, and signs of heart failure.
- Patients treated with cardiotoxic anticancer drugs should undergo echocardiographic evaluations at various stages, including baseline, during treatment, and during follow-up.
- Monitoring blood pressure is recommended post-active cancer treatment and during long-term follow-up because BP levels may decrease after discontinuing anticancer drugs, potentially necessitating adjustments or discontinuation of BP-lowering medications.
- Cancer survivors face an elevated risk of developing hypertension, along with other cardiovascular and renal complications. Periodic BP measurements and information regarding increased cardiovascular risk are advised for these individuals.

Patient Follow-up

- Patient follow-up is a vital aspect of hypertension management. It involves evaluating BP control, considering lifestyle and medication adjustments, identifying HMOD, addressing risk factors, and assessing adherence to treatment.
- During the initial three months after starting treatment, when interventions are made to achieve BP control, physician visits (including virtual ones) are recommended monthly or more frequently based on factors like hypertension severity, cardiovascular risk, prior unsuccessful BP control attempts, and challenges in antihypertensive treatment.
- Follow-up visits should involve standard office BP measurements, updates to medical histories (with a focus on treatment side effects), and physical examinations. Laboratory tests should be conducted as needed based on clinical conditions and patient risk levels. Collecting ECG and blood test data annually seems reasonable for low-risk patients. Adherence should be assessed during each visit.
- ABPM can be incorporated into follow-up examinations whenever possible. While yearly intervals may seem appropriate, the frequency should depend on hypertension severity, BP variability between visits, and previous ABPM records indicating BP patterns.
- Encouraging home blood pressure monitoring (HBPM), ideally using automated electronic devices with automated data storage and asynchronous data transfer to healthcare providers via mobile phones, personal computers, internet links, or cloud-based systems, is strongly recommended. HBPM data can guide physician visits and decisions about treatment and overall management.
- Periodic checks for HMOD are also recommended. Patients without preexisting HMOD may undergo less frequent checks, such as every three years. Conversely, patients with preexisting HMOD should have more frequent checks, depending on HMOD type, sensitivity to change detection, or HMOD-related symptoms.
- Embrace novel telehealth technologies and virtual care options to enhance hypertension management during follow-up.
- Simplify treatment regimens by utilizing long-acting drugs that can be administered once daily to improve adherence.
- Monitor regimen efficacy both at the clinic and community levels. Patients who have not reached their target BP may need follow-up visits at 1-2 weeks until BP control is achieved. Subsequently, visit frequency depends on hypertension severity, comorbidities, target organ damage, and other factors.

- Streamlined methods to dispense medications should be allowed to facilitate patient compliance.
- Monitor patients for drug side effects. For instance, CCBs may cause dose-dependent peripheral edema, which could improve with dose reduction or combined with ACE inhibitors. Newer CCB options like Cilinidipine have a lesser tendency for pedal edema and tachycardia and can be preferred.
- Diuretics may lead to metabolic side effects like hypokalemia and hyperglycemia, although these are less common when used at low doses (e.g., 12.5 mg) and in combination with ACE inhibitors. Thiazide-induced hyponatremia, especially in the elderly or those with low body weight, is a particular concern, requiring prompt intervention.
- ACE inhibitors may induce a dry cough, potentially necessitating discontinuation of therapy. Be cautious about hypotension when initiating ACE inhibitors in patients on diuretics or strict low-sodium diets. A slight rise in serum creatinine levels from ACE inhibitors is usually reversible. Hyperkalemia is more likely with high ACE inhibitor doses, renal insufficiency, diabetes, concurrent use of potassium-sparing diuretics, and among the elderly. Angiotensin receptor blockers have a lower incidence of drug-induced cough but a higher rate of hypotension.
- Consider various strategies like pill counts, involving family members in medication supervision, periodic counseling, and providing patient information leaflets to enhance adherence and BP control.
- All hypertension patients should undergo an annual review, assessing BP control, lifestyle modifications (e.g., weight maintenance), target organ damage (such as proteinuria), treatment evaluation, and drug side effects.
- Individuals with high-normal blood pressure should also receive an annual review and advice on suitable lifestyle modifications, such as dietary changes, weight management, and tobacco cessation.
- Screening for non-adherence to treatment is recommended for all patients with apparent resistant hypertension. Before screening for secondary hypertension, consider evaluating adherence in patients on combination therapy (at least two drugs) who exhibit inadequate BP responses to this treatment.
- Verify adherence before screening for secondary hypertension while considering the limitations of all adherence assessment methods.
- Employ single-pill combinations to enhance adherence and persistence in antihypertensive treatment.
- Consider a range of strategies to enhance adherence and favor a multidimensional team-based care approach.

Recommendations for Community-based Management

- The diagnosis and management of hypertension in India should be integrated into the primary care system. A team-based approach involving physicians, allied staff, and community-based health workers is essential.
- Community-based health workers can receive training to play a pivotal role in addressing the challenges of undetected, untreated, and uncontrolled hypertension in India. They can improve detection, promote lifestyle changes, monitor treatment responses, ensure therapy adherence, and advise appropriate lifestyle modifications for individuals with high-normal blood pressure (130-139 mmHg systolic and 85-89 mmHg diastolic).
- Establishing a hypertension registry at the primary health center (PHC) and community health center (CHC) levels is strongly recommended for patient tracking and implementing recall systems involving community-based health workers.
- Encourage hypertension patients to consider home blood pressure monitoring using validated automated devices, which align with clinic-based measurements.

Section 11 - SPECIAL CIRCUMSTANCES

11.0.1 Resistant Hypertension

Resistant hypertension is a condition where blood pressure remains above the desired target (>140/90 mmHg) even though the patient is on aminimum of 3 medications with distinct mechanisms of action.[196,197] These medications should be prescribed at the highest doses the patient can tolerate, and it's recommended to include a prolonged-release calcium channel blocker (CCB), along with either an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB), as well as a diuretic. An alternative definition of resistant hypertension is when blood pressure is well-managed using a minimum of 4 antihypertensive medications.[196,197]

This condition impacts roughly 10% of the population and indicates a substantial susceptibility to cardiovascular ailments, damage to vital organs, and overall mortality.[38,198] A systematic review and meta-analysis (91 studies, n=3207911) conducted by Noubiap*et al.*[199] reported a global prevalence of 10.3 % (true-resistant), 14.7% (apparent treatment-resistant), and 10.3% (pseudo-resistant hypertension). Jaipur heart watch study by Gupta et al. reported a prevalence of 19.4% (uncontrolled BP > 140/90 mmHg, using any 3 drug classes) and 6.3% (uncontrolled BP, using 4 drugs).[200]

11.0.2 Secondary Hypertension

The prevalence of secondary hypertension in India is approximately 4-5% (renal parenchymal [2-3%], renovascular [1-2%], endocrine causes [0.3-1%], oral contraceptives [0.5%, and miscellaneous [0.5%]) of all the hypertensives.[205] Diagnosis of secondary

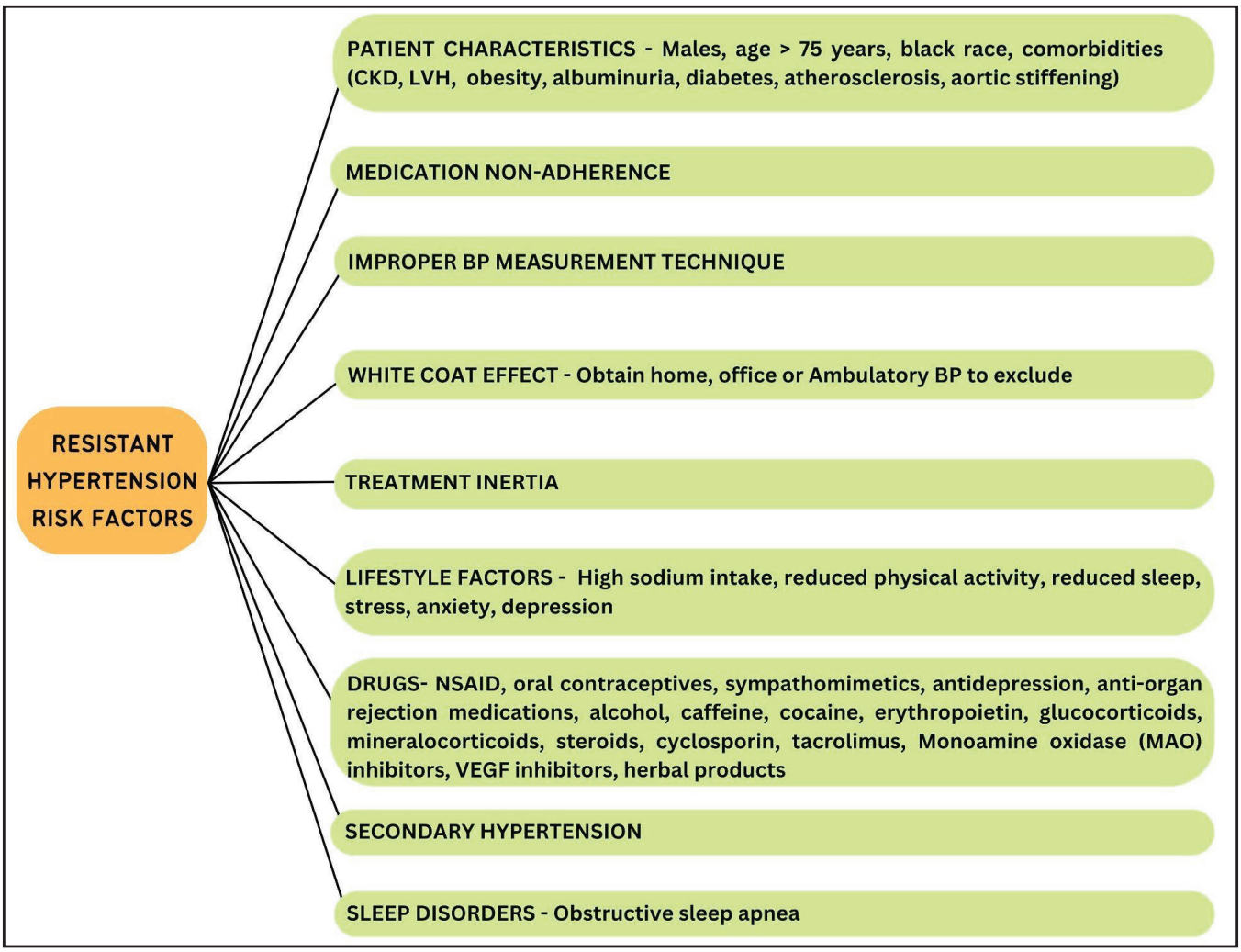


Figure 5: Resistant Hypertension - Risk factors.[197,201–203]

hypertension should be based on strong clinical and biochemical features.[198,203,206,207] Patients with early onset of hypertension (<30 years of age), especially in the absence of hypertension risk factors (obesity, metabolic syndrome, familial history, etc.), should be promptly screened for causes of secondary hypertension. Additional indications for detailed assessment and screening for secondary hypertension include pediatric cases of Grade 2 hypertension, patients with malignant hypertension, patients with HMOD, in cases with sudden deterioration of blood pressure, unprovoked or excessive hypokalemia, or metabolic alkalosis. ABPM can also be used for identifying causes of secondary hypertension and non-dipping or reverse-dipping patterns can be identified in such observations. Typically, blood pressure is lower at night than daytime, creating a noticeable 'dip' in nocturnal blood pressure levels. However, the lack of this nocturnal 'dip,' or the occurrence of a 'reverse dipping' pattern – where the 'dip' occurs during the day instead of at night – can signal the potential presence of a secondary underlying factor contributing to hypertension(Tables 4 and 5).[208]

11.0.3 Hypertensive Crises (Emergencies & Urgencies)

In the Indian population, hypertensive crisis has a prevalence ranging from 0.5 to 2%. Noncompliance with antihypertensive therapy, chronic hypertension, secondary causes, antihypertensive drug withdrawal, preeclampsia and eclampsia, pseudo-hypertension, and some medications such as oral contraceptives, linezolid, NSAIDS, amphetamines, Phencyclidine have been associated with hypertensive crisis (Tables 6 and 7).

The diagnostic workup[203] for hypertensive emergencies and urgencies includes the following common tests:

- Fundoscopy
- ECG 12 leads
- Hemoglobin, platelet count, fibrinogen, peripheral smear
- Creatinine, eGFR, electrolytes, LDH, haptoglobin
- UACR, urine microscopy for red blood cells, leukocytes and/or casts

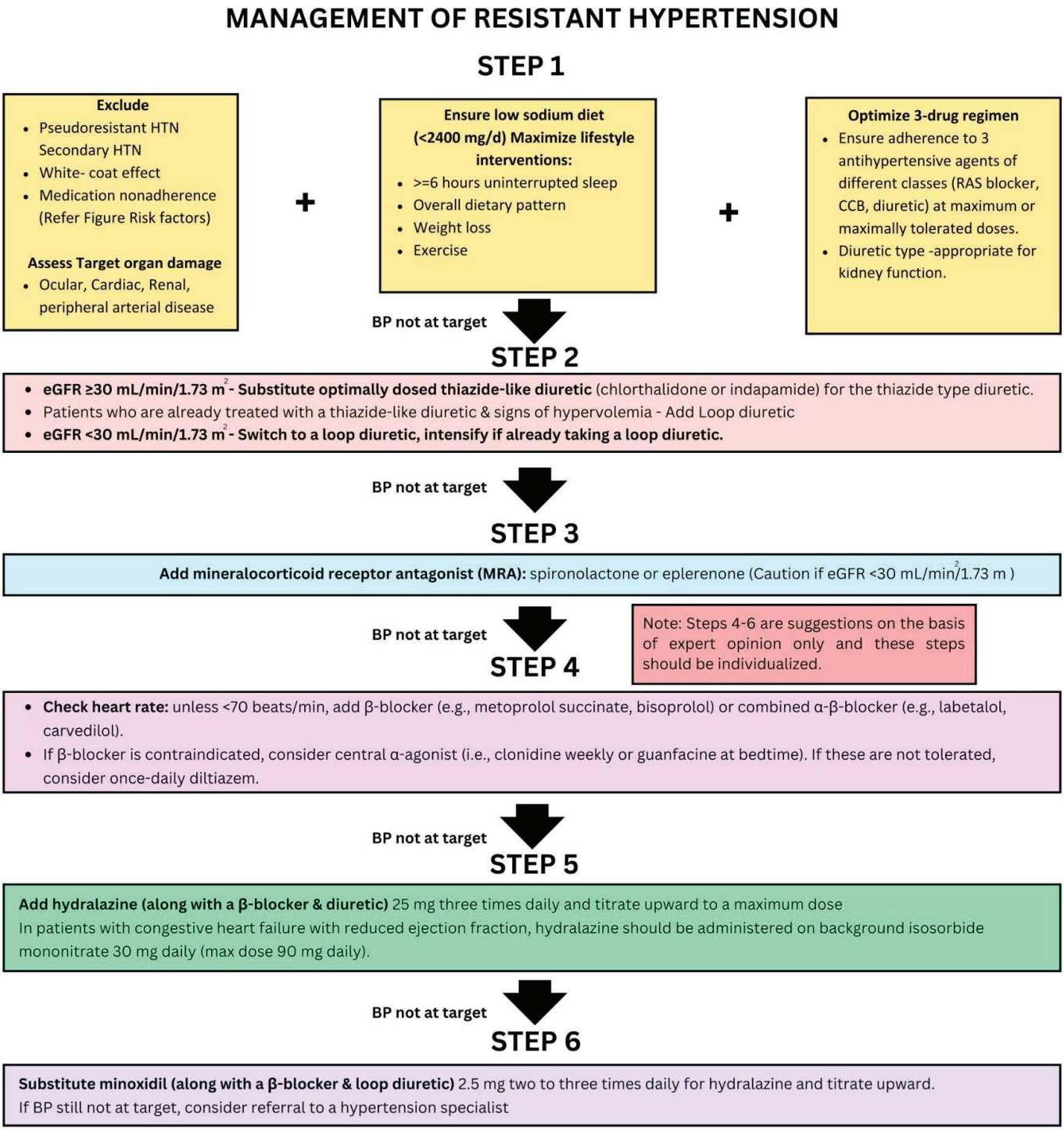


Figure 6: Management of Resistant hypertension.[203,204]

- Pregnancy test in women of childbearing age

In specific circumstances the following specific tests have also been recommended:

- Troponin, (suspected heart failure and/or acute coronary syndrome) NT-proBNP
- Chest X-ray or ultrasound (pulmonary congestion and fluid overload)
- Echocardiography (heart failure, acute ischemia, aortic dissection)
- CT angiography of thorax and/or abdomen in suspected aortic disease (aortic dissection)

Table 5: Classification of Secondary hypertension.[209,210]

ENDOCRINAL	RENAL PARENCHYMAL	RENOVASCULAR	VASCULAR	NEUROGENIC	DRUGS & TOXINS
• Adrenal-dependent causes • Parathyroid-dependent causes • Pituitary-dependent causes • Secondary hyperaldosteronism • Thyroid-dependent causes • Vitamin D deficiency	• Polycystic kidney disease • Chronic kidney disease • Urinary tract obstruction • Renin-producing tumor • Liddle syndrome • Chronic glomerulonephritis • Chronic interstitial nephritis • Analgesic nephropathy • Gout with renal failure	• Renal artery stenosis • Fibromuscular dysplasia or atherosclerosis	• Coarctation of aorta • Vasculitis • Collagen vascular disease	• Brain tumor • Autonomic dysfunction • Sleep apnea • Intracranial hypertension	• Alcohol • Cocaine • Cyclosporine, tacrolimus • NSAIDs • Erythropoietin • Adrenergic medications • Decongestants containing ephedrine • Herbal remedies containing licorice or ephedrine • Nicotine

Table 6: Secondary hypertension - Non-endocrine causes.

CLINICAL CONDITION	SCREENING	CLINICAL FEATURES	DIAGNOSTIC TESTS	TREATMENT
RENAL PARENCHYMAL	Urinary tract infections, Hematuria, Urinary frequency and nocturia, Analgesic abuse, Family history of polycystic kidney disease, elevated serum creatinine, abnormal urinalysis	Abdominal mass (polycystic kidney disease), skin pallor	Proteinuria, hematuria, leukocyturia on dipstick urine analysis, decreased estimated GFR, renal ultrasonography or biopsy and other tests to evaluate the cause of renal disease	Reduced salt intake, physical activity, RAS inhibitors & CCBs, diuretics
RENOVASCULAR	Resistant hypertension, hypertension of abrupt onset, worsening or increasingly difficult to control, flash pulmonary edema (atherosclerotic), early-onset hypertension, especially in women (fibromuscular hyperplasia)	Abdominal or renal bruit, bruits over other arteries (i.e., carotid & femoral arteries), drop in estimated GFR >30% after exposure to ACE-inhibitors/ ARBs	Imaging of renal arteries (duplex ultrasound, abdominal CT, or magnetic resonance angiograms, bilateral selective renal intra-arterial angiography, decrease in estimated GFR	RAS inhibitors - Calcium channel blockers (CCB), ACE inhibitors, ARBs, diuretics, and β-blockers, percutaneous transluminal renal angioplasty (PTRA), Angioplasty or surgical revascularisation.
OBSTRUCTIVE SLEEP APNEA	Resistant hypertension, snoring, fitful sleep, breathing pauses during sleep, daytime sleepiness	Increased BMI, snoring, daytime sleepiness, gasping or choking at night, witnessed apneas during sleep, nocturia, Mallampati class III–IV	Berlin Questionnaire, Epworth Sleepiness Score, overnight oximetry, Polysomnography	Anti-hypertensive therapy, weight loss, oral appliances, continuous positive airway pressure (CPAP), surgery (Nasal & Bariatric)
COARCTATION OF AORTA	Young patient with hypertension (<30 years of age)	BP higher in upper extremities than in lower extremities, absent femoral pulses, continuous murmur over patient's back, chest, or abdominal bruit, left thoracotomy scar (postoperative)	Echocardiogram, Computational Tomography Angiogram or Magnetic Resonance Angiogram	Surgery, ACE inhibitors, ARBs, β-blockers

Table 7: Hypertensive urgency *vs*. Hypertensive emergency.

	HYPERTENSIVE URGENCY	HYPERTENSIVE EMERGENCY
DESCRIPTION	• Blood pressure levels exceeding 180/120 mmHg • Evidence of target organ damage	• Extremely high blood pressure, exceeding 220/140 mmHg • Damage to vital organs • May be associated with serious complications such as acute myocardial infarction, hypertensive encephalopathy, intracranial hemorrhage, dissecting aneurysm, acute renal failure, and pulmonary edema. • Hypertensive emergency in pregnant women is identified when blood pressure reaches or surpasses 169/109 mmHg
SIGNS & SYMPTOMS	• Headache • Chest pain • Dyspnea • Epistaxis, faintness • Psychomotor agitation	• Neurologic deficits • Signs of heart failure (elevated jugular venous distention, rales on lung auscultation, or a gallop on heart auscultation) • Papilloedema
MANAGEMENT	• Patient admission and reduce BP to 160/100 mm Hg over hour, with gradual BP control over 12- 48 hours. BP should not be lowered rapidly to their normal baseline. • Low-dose, short-acting oral medications are preferred. Parenteral route & high dose to be avoided to protect hypoperfusion of major arterial beds.	• Patient admission and reduce BP < 25% within 2-6 hours & stabilize to 160/100 mm Hg, then 25% within 48 hours. • Admission to ICU for prompt BP control. Once stabilized patient may be shifted to the general ward. • Rapid-acting, parenteral titrable agents with continuous monitoring of BP, neurological status, and urine output. • Aggressive reduction of BP may aggravate hypoperfusion & worsening of end-organ damage. However, in patients with aortic dissection rapid reduction of BP <120/80 mm Hg should be achieved within 5-10minutes initially with beta-blockers.
PHARMACOLOGY	• Captopril - 12.5-25 mg PO • Nifedipine (extended-release - 10-20 mg PO • Labetalol - 200-400 mg PO • Clonidine - 0.1-0.2 mg PO • Prazosin - 1-2 mg PO • Amlodipine - 5-10 mg	• Nicardipine - 5–15 mg/h i.v. infusion, starting dose 5 mg/h, increase every 15–30 min with 2.5mg until goal BP, maximum 15 mg/h • Sodium nitroprusside - 0.3–0.5mg/kg/min i.v. infusion, increase by 0.5mg/ kg/min every 5 min until goal BP (maximum dose 10mg/kg/min) • Esmolol - 0.5–1 mg/kg i.v. bolus; 50–300 mg/kg/min i.v. infusionMetoprolol - 2.5–5mg i.v. bolus over 2 min; may repeat every 5 min to a maximum dose of 15mg • Labetalol - 10–20mg i.v. bolus in 1 min incremental doses 20mg may be administered i.v. at 10 min intervals (max 80 mg) or 1–3 mg/min i.v. infusion until goal BP is reached • Fenoldopam - 0.1–0.3mg/kg/min i.v. infusion, increase every 15 min with 0.1 mg/kg/min increments until goal BP is reached.Nitroglycerine - 5–200 mg/min i.v. infusion, 5mg/min increase every 5min • Enalaprilat - 0.62–1.25mg i.v. bolus given over 5 min every 6 hClonidine - 0.2–0.5mg/kg/min i.v. • Phentolamine - 1–5mg i.v. bolus or continuous i.v. infusion at a rate of 0.5–20mg/kg/min • Hydralazine - 10-20 mg i.v. bolus may be repeated every 30 min till goal BP is reached.

Table 8: Hypertensive emergencies requiring immediate BP-lowering with i.v. drug therapy.[203]

CLINICAL PRESENTATION	TIMING AND BP TARGET	FIRST-LINE TREATMENT	ALTERNATIVE
Malignant hypertension with or without acute renal failure	• Reduce Mean Arterial Pressure (MAP) by 20–25% over several hours	• Labetalol • Nicardipine	• Nitroprusside • Urapidi
Hypertensive encephalopathy	• Immediately reduce MAP by 20–25%	• Labetalol • Nicardipine	• Nitroprusside
Acute coronary event	• Immediate reduce SBP to <140 mmHg	• Nitroglycerine • Labetalol	• Urapidil
Acute cardiogenic pulmonary edema	• Immediately reduce SBP to <140 mmHg	• Nitroprusside or nitroglycerine (with loop diuretic)	• Urapidil (with loop diuretic)
Acute aortic dissection	• Immediately reduce SBP to <120mmHg and heart rate to <60 bpm	• Esmolol & nitroprusside • Ornitroglycerine or nicardipine	• Labetalol or metoprolol
Eclampsia and severe preeclampsia/ HELLP	• Immediately reduce SBP to <160mmHg & DBP to <105mmHg	• Labetalol or nicardipine • Magnesium sulphate	• Consider delivery

- CT or MRI brain (nervous system involvement)
- Kidney ultrasound (renal impairment or suspected renal artery stenosis)
- Urine drug collection (cocaine or methamphetamine use)

11.0.4 Hypertension in Asthma and Chronic Obstructive Pulmonary Disease (COPD)

Co-occurrence of hypertension and asthma is frequent, and research indicates that elevated blood pressure is linked to worsened asthma severity, decreased lung function, and reduced forced expiratory volume in 1 second (FEV1), which serves as a marker for cardiovascular mortality.[211,212] This condition often arises due to the usage of systemic steroids, β-agonists, or nasal decongestants. Stress also significantly contributes to hypertension development in these cases.[213] Additionally, COPD fosters harmful vascular modifications such as endothelial dysfunction, atherosclerosis, and damage to the heart and kidneys (HMOD).[214] Adopting lifestyle adjustments that are relevant to both conditions is imperative. Pharmacotherapy of hypertension in patients with COPD may be considered as follows (Table 8).

11.0.5 Hypertension in Elderly

Isolated systolic hypertension (ISH), defined by SBP greater than 140 mmHg and diastolic blood pressure DBP below 90 mmHg, becomes the prevailing form of hypertension after the age of 50 years, and it is prevalent in people 70 years or older.[215] According to the National Family Health Survey (NFHS), the prevalence of ISH and IDH in India was found to be 1.2% and 5.7%, respectively.[216] Another study reported a prevalence of 4.3% (5.1% in men and 3.6% in women).[217] Asian populations are at a heightened risk of systolic hypertension compared to Western populations, which amplifies the susceptibility to cardiovascular disorders, declining renal function, and mortality.[218] CCBs and thiazide-like diuretics are the preferred drugs for managing ISH. ACEIs and ARBs exhibit less efficacy, indicating that they should be prioritized as primary treatment options when compelling indications such as heart failure, coronary artery disease, chronic kidney disease, metabolic syndrome, or diabetes are present.[219] Statins are known to lower cholesterol levels, which can reduce the risk of atherosclerosis and subsequent cardiovascular events.

11.0.6 Hypertension in Acute Stroke

Hypertension prominently contributes to the risk of developing two significant categories of brain-related diseases - stroke and dementia.[220,221] Potential mechanisms contributing to hypertension-related cerebral dysfunction encompass impaired cerebral autoregulation, heightened blood-brain barrier permeability, endothelial dysfunction, oxidative stress, compromised functional hyperemia, and alterations in both small and large blood vessels.[222] RAS blockers, CCBs, and diuretics are the primary drug choices for initial treatment. In cases of ischemic stroke, it is essential to institute lipid-lowering treatment, aiming for a low-density lipoprotein cholesterol (LDL-C) target below 70 mg/dL (1.8 mmol/L).[198]

Table 9: Asthma, and COPD Pharmacology.

	SAFE	USE WITH CAUTION	AVOID
ASTHMA	Calcium channel blockers, ARBs	Diuretics, Clonidine	Beta blockers, ACEi
COPD	Calcium channel blockers, ARBs	Cardioselective Beta blockers, Diuretics	ACEi

Blood pressure management in acute stroke

- Acute ischemic stroke (AIS) not eligible for thrombolysis[223]
  - Routine BP lowering in AIS before hospital admission must be avoided.[224]
  - Withhold antihypertensives in AIS unless BP > 220/120 mmHg or MAP > 120 mmHg
  - BP must not be lowered more than 15% in the first 24 hours
  - Unless significant large artery stenosis is suspected, antihypertensives may be restarted after 48 hours if the blood pressure is more than 140/90 mmHg.[225]
  - Avoid sublingual therapy
  - Pre-existing antihypertensive therapy may be withheld until a few days after the stroke when the patient can safely swallow.Immediate administration of antihypertensives confers no additional benefit.[225]
- AIS eligible for thrombolysis[226,227]
  - If thrombolysis is planned, BP must be lowered to < 180/110 mmHg using one of the following agents:
  - Injection labetalol 20 mg i.v. given over 2 minutes may be repeated every 20 minutes to a maximum dose of 200 mg.
  - Labetalol infusion at 1-8 mg/minute
  - Nitroglycerine infusion 5 mcg/minute increase every 5 minutes toa maximum of 200mcg/minute
- During/after thrombolysis BP must be maintained at < 180/105 mmHg
- Precipitous drops in systolic blood pressure must be avoided

Acute Haemorrhagic stroke

Intensive blood pressure lowering in patients with acute cerebral hemorrhage improves outcomes[224] SBP must be maintained between 140 and 160 mmHg.[228]

- If BP measured on occasions at least 2 minutes apart more than an SBP of 200 mmHg or a MAP of 150 mmHg, BP must be lowered with parenteral antihypertensives (labetalol, nitroglycerin, sodium nitroprusside (SNP) or nicardipine)
- If SBP is180–200 mmHg or MAP130–150 mm oral agents may lower Hg BP as follows:
  i. Clonidine 0.2 mg hourly to a maximum of 3 doses
  ii. Labetalol 200 mg every 2 hours

11.0.7 Hypertension in Diabetes

The prevalence of hypertension is more pronounced in individuals with diabetes mellitus (DM), with about half of hypertension cases coinciding with a diagnosis of type 2 diabetes mellitus (T2D).[229] This susceptibility is particularly notable among the elderly population, where both DM and hypertension increase the risk of complications encompassing macro- and microvascular diseases.[230] In India, those with diabetes exhibit a 1.5 to 2.0 times higher prevalence of hypertension than those without diabetes.[231] Among patients grappling with both diabetes and hypertension, the risk of isolated systolic hypertension is particularly heightened due to autonomic neuropathy.[232]

In individuals with type 2 diabetes, the occurrence of non-dipping patterns or elevated nighttime blood pressure (BP) levels is frequent and necessitates monitoring through ABPM or HBPM.[203]

Treatment

1. Lifestyle measures:
   a. < 1500 mg salt intake per day
   b. Weight reduction
   c. A diet rich in fruits, vegetables & low-fat dairy
   d. Regular exercise
   e. Smoking cessation
   f. Curtailing alcohol intake
2. Target BP < 130/80 mmHg and less than 140/80 mmHg in elderly patients
3. Pharmacotherapy must be initiated if BP> 130/80 mmHg in a patient with diabetes
4. Initiate with monotherapy with ACEI/ARB/CCB/thiazide
5. In the presence of microalbuminuria, initiate therapy with ACEI/ARB
6. If BP remains 20/10 mmHg above goal, then a long-actingnon-dihydropyridine calcium channel blocker may be added (diltiazem/verapamil) as they decrease albuminuria
7. In patients with recent MI, a beta blocker may be added. Carvedilol is preferred to metoprolol. Avoid combinations of ACEI/ARB/ARNIs as this increases the risk of hyperkalemia and may increase mortality [233,234]
8. For primary prevention, a statin may be included in the treatment regimen if the low-density lipoprotein cholesterol (LDL-C) level is above 70 mg/dL (1.8 mmol/L) in cases of patients with target organ damage or above 100 mg/dL (2.6 mmol/L) in uncomplicated diabetes.[198]

Cardiac Autonomic Neuropathy (CAN) & Orthostatic Hypotension (OH)

Multiple studies have shown a prevalence of 30–70% of Cardiovascular autonomic neuropathy (CAN) in patients with diabetes.[235-237] Notable clinical manifestations of diabetic autonomic neuropathy (DAN) encompass resting tachycardia, reduced

exercise tolerance, orthostatic hypotension (OH), constipation, gastroparesis, erectile dysfunction, sudomotor dysfunction, impaired neurovascular function, "brittle diabetes" and autonomic failure during hypoglycemia.[235,236,238] CAN associated with diabetes results in damage to autonomic nerve fibers that innervate the heart and blood vessels, leading to disruptions in heart rate and vascular dynamics, ultimately affecting blood pressure regulation.[239] Treating CAN is a multifaceted endeavor encompassing lifestyle changes, improving insulin resistance, tight glycemic control, addressing dyslipidemia, and utilizing antioxidants like α-lipoic acid (ALA), aldose reductase inhibitors, acetyl-L-carnitine, and specific vitamins such as fat-soluble vitamin B1.[240]

Orthostatic hypotension refers to a significant drop in blood pressure (a decrease of >20 mmHg systolic or >10 mmHg diastolic) within 3 minutes of standing up, often accompanied by symptoms like lightheadedness, weakness, dizziness, palpitations, blurred vision, and even nausea and fainting. All antihypertensive drugs may produce OH as a side effect. However, this occurs more commonly with diuretics, α blockers, vasodilators, and ACE inhibitors.[213]Non-pharmacological approaches for OH involve physical maneuvers like squatting, gradual posture changes, and lifestyle modifications such as adjusting meals and fluid intake. Medications such as midodrine, erythropoietin, desmopressin, somatostatin analogs, and nonselective beta-blockers can be employed to manage symptomatic hypotension.[241]

11.0.8 Hypertension and Human Immunodeficiency Virus (HIV)

Patients living with HIV (PLHIV) undergoing antiretroviral therapy (ART) display a heightened prevalence of hypertension compared to individuals without HIV infection.[247] This elevated prevalence in PLHIV can be attributed to several factors, including persistent inflammation, increased microbial translocation, renal dysfunction, and blood vessel impairment due to prolonged exposure to ART.[248,249] Conversely, there are factors that contribute to a potentially reduced burden of hypertension among PLHIV. Better blood pressure management may stem from the heightened healthcare support that individuals with HIV often receive. Moreover, a decrease in behavioral risk factors among PLHIV, possibly due to health-conscious behaviors and interventions, can also play a role in mitigating hypertension prevalence.[250] Under many antiretroviral therapies, there's a potential for drug interactions with CCBs.

11.0.9 Hypertension & Corona virus-19 (COVID-19)

COVID-19 exerts a significant impact on the cardiovascular system, giving rise to complications like acute coronary syndrome, myocardial infarction, fluctuations in blood pressure, and the exacerbation of pre-existing cardiovascular diseases.[251] Studies consistently highlight that hypertension and cardiovascular diseases are the most prevalent co-existing conditions in individuals afflicted with COVID-19.[252,253] The association likely involves the dysregulation of the RAAS and ACE2 system, along with the strain caused by acute lung injury, which increases the workload on the heart.[254] Lifestyle modifications and continuation of the prescribed antihypertensive therapy is recommended.

11.0.10 Hypertension in Collagen Vascular Diseases

11.0.10.1 Rheumatoid Arthritis (RA)

Individuals diagnosed with RA experience higher cardiovascular morbidity and mortality rates. Hypertension emerges as a conventional cardiovascular risk factor with an increased prevalence and is also influenced by the presence of RA. RAS inhibitors and CCB can be used as first-line treatment. Beta-blockers are given with caution in insulin resistance patients.

11.0.10.2 Scleroderma Crisis

Scleroderma renal crisis (SRC), a severe and life-threatening complication of scleroderma, manifests with sudden and severe hypertension, rapidly progressing renal failure, hypertensive encephalopathy, congestive heart failure, and/or microangiopathic hemolytic anemia.[255] Typically, over 90% of SRC patients present with blood pressure readings exceeding 150/90 mmHg and a substantial decrease in kidney function (a reduction of ≥30% in estimated glomerular filtration rate or eGFR).[256,257] The disorder's

Table 10: Antihypertensive prescription in OH.[242–246]

DRUG	INDICATION	CAUTION
ACEi/ARBs	Use as first line	Be mindful of possibility of hypotensionafter first dose
Alpha blockers	Administer as bedtime dose	Avoid in elderly
Beta blockers	Use only if specific indications like recentMI/HF	Avoid mixed alpha/beta blockers likecarvedilol
Diuretics	Start with lowest possible dose and then up-titrate	Use with caution in combination withSGLT2i
Nitrates	Start with lowest possible dose and then up-titrate	Do not combine with PDE I - Phosphodiestarase inhibitors
CCB	Use dihydropyridines without negativechronotropic effect	-

early stages involve endothelial cell injury, resulting in structural changes in blood vessels (intimal thickening, proliferation, fibrin deposition). The rapid increase in blood pressure damages renal blood vessels, initiating a damaging cycle that ultimately culminates in malignant hypertension.[255,256] This cascading effect underscores the critical nature of early intervention and management for individuals with scleroderma renal crisis. ACE inhibitors are the preferred initial treatment for SRC. If blood pressure remains uncontrolled even after reaching the maximum ACEi dose, CCBs can be introduced as an additional therapeutic option to enhance blood pressure management.[255]

11.0.10.3 Systemic Lupus Erythematosus (SLE)

In patients diagnosed with Systemic Lupus Erythematosus (SLE), there is a notably elevated prevalence of cardiovascular risk factors in comparison to the general population. CVD plays a pivotal role in the morbidity and mortality of SLE patients, stemming from a complex interplay of factors that possess both prothrombotic and atherogenic properties. Systemic inflammation and the therapies commonly administered to manage SLE can contribute to this heightened cardiovascular risk.[203] Treatments involving corticosteroids, immunosuppressants, and non-steroidal anti-inflammatory drugs, frequently employed to control inflammatory symptoms, can lead to various complications. Lupus nephritis classes IV and V are typically associated with hypertension, primarily due to decreased glomerular filtration rates resulting from vasoconstriction.[258] Lupus-related hypertension is thought to be linked to changes in vascular endothelial cell function and increased levels of endothelin-1. Antihypertensive drug therapy should be considered when BP levels reach or exceed 140/90 mmHg in patients without any hypertensive-related organ involvement. The initiation of antihypertensive drug therapy typically begins with first-line agents, which include thiazide diuretics, CCBs, as well as ACE inhibitors or ARBs.[203,259]

11.0.11 Sickle Cell Anemia

Patients with Sickle cell disease (SCD), a hereditary autosomal recessive condition resulting from mutations in the β-globin gene (HBB), face an elevated risk of developing high blood pressure. Hypertension places additional strain on the heart, potentially leading to complications.[260] Notably, relative systemic hypertension in sickle cell disease patients is linked to heightened susceptibility to pulmonary hypertension and renal dysfunction.[261,262] Increased hemolysis, increased arginase activity, and reduced arginine-ornithine ratios with attendant reduced nitric oxide bioavailability lead to increased vasoconstriction and higher blood pressures.[263]

11.0.12 Psychiatric Disorders

In individuals with psychiatric disorders, depression, stress, and anxiety have all been linked to a higher prevalence of Hypertension, cardiovascular morbidity, and mortality, underscoring the importance of blood pressure (BP) management in these cases.[198,264,265] For BP control in patients with psychiatric conditions, using RAS inhibitors and diuretics is preferable, as they tend to have fewer pharmacological interactions with antidepressants. Caution should be exercised when considering CCBs and alpha1-blockers, especially in patients with orthostatic hypotension (e.g., serotonin reuptake inhibitors or SRIs). Beta-blockers (excluding metoprolol) may be appropriate in the presence of drug-induced tachycardia, often associated with the use of antidepressant and antipsychotic drugs.[198,264,265]

Section 11.1 - Hypertension in Women

Globally, there is a prevailing notion that women exhibit lower susceptibility to cardiovascular diseases (CVD), including hypertension.[266-268] Unfortunately, this belief has contributed to medical professionals conducting fewer tests and administering lesser treatment to females for conditions like hypertension and other cardiovascular ailments.[269] The majority of Indian studies indicate a higher prevalence of hypertension among males.[270-274] Analysis of data from the National Family Health Survey 4, Study of Ageing and Health Wave 2 datasets (NFHS-SAGE), and the Longitudinal Ageing Study of India (LASI) dataset revealed a distinct trend: males demonstrated a higher prevalence of hypertension until the age of 50, after which females exhibited higher rates.[275] Based on the WHO-SAGE study, hypertension was more prevalent in tribals, poor, Sikhs, and older women.[276] Child brides and adolescent mothers have been reported to be more likely to have hypertension later in life.[277] Younger age at first childbirth, early menarche, oral contraceptive pill use, hysterectomy, and domestic violence have also been associated with hypertension.[278,279]

11.1.1 Premenopausal Women

Before entering menopause, women tend to exhibit slightly lower blood pressure levels and a reduced likelihood of developing hypertension. Estrogen, in particular, is believed to yield favorable effects on the cardiovascular system, potentially safeguarding women of reproductive age by amplifying nitric oxide (NO) mediated vasodilation and modulating the potent vasoconstrictor actions of endothelin-1.[280] Estrogen is also known to elevate angiotensinogen levels while simultaneously reducing renin levels, ACE activity, angiotensin AT-1 receptor density, and aldosterone production.[281] Noteworthy contributors to secondary hypertension among younger women include obesity, polycystic ovarian syndrome, obstructive sleep apnea, aortic coarctation, Turner syndrome, autoimmune disorders, endocrine irregularities (such as hyperaldosteronism, hypothyroidism, hyperthyroidism, hyperparathyroidism, pheochromocytoma, and diabetes mellitus), renal ailments, and the use of certain medications (e.g., corticosteroids, hormonal contraceptives, etc.).[282-284]

11.1.2 Postmenopausal Women

During menopause women exhibit a heightened occurrence of left ventricular hypertrophy and a greater vulnerability to the development of diastolic dysfunction when compared to younger adult women. The presence of isolated systolic hypertension among postmenopausal women is intricately linked to aortic

stiffness, which is potentially attributed to the proliferation of smooth muscle cells, accumulation of collagen, and heightened levels of vasoconstrictor molecules within the blood vessel walls—consequences stemming from the absence of estrogen's protective influence.[285] A noticeable escalation in the concentration of the potent vasoconstrictor, endothelin, is observed in postmenopausal women, which normally is inhibited by estrogens.[280,286] The decline-in progesterone levels, a vasoactive hormone, may be partially linked to the emergence of arterial hypertension in postmenopausal women.[287-290] Postmenopausal hypertension might also be associated with changes in the autonomic nervous system that occur with age.[291] Secondary data from the longitudinal aging study of India reported a prevalence of 51.68% (postmenopausal hypertension), out of which19.14% of women were unaware. Studies conducted in other parts of India (Delhi and Kerala) reported the prevalence of systolic (27.2–32%) and diastolic blood pressure (41.1–44%).[292-294]

11.1.3 Hypertension in Pregnancy

Hypertensive disorders during pregnancy encompass a range of conditions, starting from pre-existing chronic hypertension in the current pregnancy and extending to intricate multi-system disorders such as preeclampsia. These conditions can give rise to various complications, including eclampsia, HELLP syndrome, acute renal failure, pulmonary edema, stroke, and left ventricular failure.[295] As the World Health Organization (WHO) outlined, the lethal trifecta of pregnancy are hemorrhage, hypertensive disorders of pregnancy (HDP), and infections. These elements play a substantial role in maternal mortality and morbidity, leading to the loss of at least one woman's life every 7 minutes.[296] A systematic review and meta-analysis conducted by Dhinwa *et al.* in 2021 estimated a prevalence of 11% in India (1/11 women suffer from pregnancy-induced hypertension).[297] Multiple studies conducted all over India showed a 10–13% prevalence.[297-300]

11.1.3.1 Classification

Pregnant women should undergo a comprehensive screening for preterm preeclampsia during the early stages of pregnancy. Screening should be conducted as a one-step procedure, and the best-combined test is one that includes maternal risk factors, measurements of mean arterial pressure (MAP), serum placental growth factor (PLGF), and uterine artery pulsatility index (UTPI). MAP is calculated from systolic (SBP) and diastolic blood pressure (DBP) readings. (MAP = DBP + (SBP-DBP)/3).[234] Women who develop preeclampsia exhibit notably lower maternal PLGF concentrations in the first trimester compared to those with pregnancies that progress normally.[302,303] Three consecutive waveforms of a similar nature are acquired using a transabdominal ultrasound scan, and the UTPI is determined. Subsequently, the mean UTPI of both the left and right arteries is computed.[304]

11.1.3.2 Investigations

- Blood Pressure measurement - After reaching 20 weeks of gestation, the recommended posture for the expectant mother involves either sitting upright or resting on her left side, aligning the zero level with the heart's height.

Table 11: Classification- Pregnancy hypertension.[295,301]

	TYPE	FEATURES
1.	**GESTATIONAL HYPERTENSION**	• BP reaching or exceeding 140/90 mmHg • identified after the 20th week of gestation • Normalizes by the 42nd day after childbirth • additional signs of preeclampsia or proteinuria absent
2.	**CHRONIC HYPERTENSION**	• Hypertension before the 20th week of gestation • Absence of neoplastic trophoblastic disease or multiple pregnancies • Either primary or secondary
3.	**PREECLAMPSIA** **NONSEVERE, SEVERE, EARLY AND LATE-ONSET**	• Presents as a multi-system inflammatory disorder occurring after the 20th week of pregnancy • Features proteinuria, edema, and marked by the de-novo hypertension • Atypical variant (Severe Preeclampsia) - neurological, hematological, hepatic, renal manifestations, or fetal growth restriction without proteinuria
4.	**ECLAMPSIA**	• Occurrence of seizures in association with preeclampsia • Hypertensive encephalopathy, cerebral edema, infarction, hemorrhage, endothelial dysfunction, etc.
5.	**SUPERIMPOSED PREECLAMPSIA**	• Preeclampsia in women with chronic hypertension.
6.	**OTHER TYPES**	• Resistant hypertension • Chronic hypertension • Unclassified hypertension • Whitecoat hypertension • Masked hypertension • Transient hypertension

Table 12: Risk factors.[295,301,305-307]

	PREECLAMPSIA (MATERNAL RISK FACTORS)	PREGNANCY-INDUCED HYPERTENSION (MATERNAL RISK FACTORS)	PREGNANCY-INDUCED HYPERTENSION FETAL RISK FACTORS

RISK FACTORS	• Maternal age
	• Weight, height,
	• Past obstetric history
	  ○ nulliparous
	  ○ parous without prior preeclampsia (PE)
	  ○ parous with prior PE
	  ○ interpregnancy interval in years between the birth of the last child
	  ○ gestational age at delivery
	  ○ birthweight of previous pregnancy beyond 24 weeks
	  ○ family history of PE in mother
	  ○ method of conception
	  ○ smoking
	  ○ chronic hypertension
	  ○ diabetes mellitus (type 1, type 2, insulin intake)
	  ○ systemic lupus erythematosus
	  ○ antiphospholipid syndrome
		• Pulmonary edema
		• Congestive cardiac disorders,
		• Acute left ventricular failure (ALVF)
		• Venous thromboembolism
		• Posterior reversible encephalopathy syndrome (PRES)
		• Visual disturbances such as temporary amaurosis
		• Cerebral edema
		• Hemorrhage
		• Stroke
		• End-stage renal disease (ESRD)
		• Placental abruption
		• Postpartum hemorrhage
		• HELLP syndrome
			• Fetal growth restriction (FGR)
			• Premature birth (iatrogenic)
			• Small for age
			• Oligohydramnios
			• Perinatal death

- Proteinuria[308,309] - Urinary dipstick method (≥+2), Spot urine protein: creatinine ratio (≥30 mg/mmol)
- Kidney function tests, Liver function tests, Coagulation profile (platelet count is < 1,00000 /mm^3), Serum Electrolytes
- Chest X-ray, Maternal and Fetal Ultrasonography, Fundoscopy, 2D ECHO, MRI.[295]

11.1.3.3 Management

Recommendations

- It is advised to screen premenopausal women for secondary hypertension.
- When prescribing a combination of oral contraceptives, monitoring their use and effects throughout the therapy is essential.
- For women experiencing hypertensive disorders during pregnancy, it is advisable to commence or enhance drug therapy when the systolic blood pressure (SBP) reaches or exceeds 140 mmHg and/or the diastolic blood pressure (DBP) reaches or exceeds 90 mmHg.
- In cases of pre-existing hypertension, whether with or without superimposed pre-eclampsia, gestational hypertension, or preeclampsia, the goal is to maintain blood pressure below 140/90 mmHg.
- It is important to exercise caution in women with hypertensive disorders during pregnancy to avoid overly aggressive lowering of blood pressure. Specifically, lowering the on-treatment DBP below 80 mmHg is not recommended.
- During pregnancy, avoiding ACE inhibitors, ARBs, or direct renin inhibitors is advisable.
- For pregnant women who are at a high or moderate risk of developing preeclampsia, it is recommended to administer aspirin at a dosage of 100–150 mg at bedtime between weeks 11 and 35 of gestation.

Table 13: Lifestyle modifications

TYPE	FEATURES
Patient Education	Education regarding the associated risks with high blood pressure, Advantages ofmaking lifestyle adjustments, Education regarding necessity of long-term treatmentadherence, and the importance of consistent monitoring and therapy. In women withchronic hypertension - Prenatal counseling, Assessment of potential end-organ damage,Medication adjustments when needed, Suitable lifestyle changes, Exploration ofsecondary factors contributing to hypertension
Lifestyle modifications	Lifestyle modifications including proper diet (rich in vegetables and fruits whileeliminating high-fat dairy products) and regular exercise. Salt intake - Consumingexcessive amounts of salt (>2 g/day) and not consuming enough potassium (<3.5 g/day)and Weight reduction

Table 14: Pharmacological management.

TYPE	FEATURES
Target	SBP: 130–150 mmHg and DBP: 80–100 mmHg
Mild or moderatehypertension	Blood pressure to be monitored regularly
Severe Hypertension	Oral labetalol 200 mg orally (every 4 hours, maximum 1200 mg/day) or 40 mg IV over 2 minutes as a first-line agent till the BP falls to SBP <150 mmHg and DBP is80-100 mmHg If BP >180/110 mmHg: Alternatives include methyldopa and nifedipine (10 mg orally, repeat at 20-minute intervals up to a maximum of 40 mg)
Preexisting hypertension	To be avoided in the second and third trimesters - Angiotensin-converting enzymeinhibitors (ACEIs) inhibitors, angiotensin receptor blockers (ARBs), and diuretics. Aspirin (75 mg OD from 12 weeks till delivery).
Women with chronicand gestational hypertension	Methyldopa (0.5 to 3.0 g/d in 2 divided doses) Second-line agents are labetalol (200 to1200 mg/d in 2 to 3 divided doses) and nifedipine (30 to 120 mg/d) of a slow-release preparation
Seizures	4g Magnesium sulfate IV over 10 minutes
Corticosteroids	Women delivering before 34 completed weeks or in case of elective cesarean deliverybefore 38 completed weeks.
Postpartum care	Closely monitor the first 48 hours for eclampsia, Postpartum hemorrhage (PPH),hemolysis, elevated liver enzymes, low platelets (HELLP), pulmonary edema, cardiovascular, cerebrovascular events, and thrombo-embolic complications. The patientrequires a 2-week postdelivery follow-up. Antihypertensive medication may beneeded for 2 to 6 weeks. If complications arise, readmission might be necessary. A finalpost-partum assessment at 6 weeks is vital.

Section 11.2 - ENDOCRINE HYPERTENSION

Primary hypertension, often referred to as essential or idiopathic hypertension, accounts for most cases of hypertension. However, a subset of around 10–15% is attributed to secondary hypertension, and this prevalence might be underestimated.[310] Endocrine causes include pheochromocytoma (0.2 to 0.6%), primary aldosteronism (4.6 to 13.0%), Cushing's syndrome (<0.1%), hyper-and hypothyroidism (<0.1%), etc. (Table 14).[207]

Recommendations

- Consider **screening for endocrine hypertension** in new onset or uncontrolled hypertension(moderate/severe hypertension (BP >150/100mmHg on three separate occasions)

Table 15: Endocrine hypertension – Etiology.[209,310]

Adrenal-dependent causes	Pheochromocytoma and sympathetic paraganglioma, Primary aldosteronism, Hyperdeoxycorticosteronism - Congenital adrenal hyperplasia :11β-Hydroxylase deficiency, 17α-Hydroxylase deficiency. Deoxycorticosterone-producing tumor, Primary cortisol resistance, Cushing syndrome, Chrousos syndrome, Genetic, Acquired - Licorice or carbenoxoloneingestion, Cushing syndrome
Parathyroid-dependent causes	Hyperparathyroidism
Pituitary-dependent causes	Acromegaly, Cushing syndrome
Secondary hyperaldosteronism	Renovascular hypertension, Renin-producing tumor, Renal arterystenosis, Edematous disorders like left ventricular heart failure,Pregnancy, Cor-pul-monale, Cirrhosis with ascites
Thyroid-dependent causes	Hypothyroidism Hyperthyroidism
Vitamin Deficiency	Vitamin D deficiency
Complex effects	Obstructive sleep apnea

Table 16: Secondary hypertension - Endocrine

CLINICAL CONDITION	WHO SHOULD BE SCREENED	CLINICAL FEATURES	DIAGNOSTICTESTS	TREATMENT
Pheochromocytoma & Paragangliomas Prevalence (0.2–0.6%.)	Spontaneous or provoked occurrence, Cardiovascular incidents presenting with PPGL symptoms, including Takotsubo cardiomyopathy, Elevated blood pressure variability. Individuals under 50 yearsof age with type 2 diabetes despite a BMI below 25kg/m^2, Adrenal incidentaloma with a density sur passing 10 HU, even in the absence of hypertension. Adrenal mass that is > 4cm is cystic or has hemorrhagic changes. Presence of genetic disorders ormutations associated with heightened PPGL risk or a family history of PPGL. Resistant or severehypertension Indications of cervical, abdominal, orpelvic mass.	Menard Triad - Head ache (60–90%), palpitations (50–70%), and sweating (55–75%). Skin stigmata of neurofibromatosis (café-au-lait spots, neurofibromas). Orthostatic hypotension. Non-specific headaches, dizziness, hyperhidrosis, anxiety. Blood pressure (labileor paroxysmal)	24-h urinaryfractionated metanephrines or plasmametanephrines understandard conditions (supine positionwith indwelling IV cannula). Contrast-enhanced CT orMRI. Genetic testing	Alpha-adrenergic blockade, followed by a β-adrenergic blockade. Tyrosine kinase inhibitors (selected patients). Surgicalre section
Primary aldosteronism (PA) Prevalence (4.6–13.0%)	Resistant hypertension: SBP ≥ 140 mmHg or DBP≥ 90 mmHg despite three medications including thiazides, RAS blockers, and CCB. Grade 3 HTN:SBP ≥ 180 mmHg or DBP≥ 110 mmHg. Grade 2HTN, especially with poortreatment response, asprevalence increases with HTN severity. HTN at ayoung age (< 40 years). Hypokalemia, regardless of diuretic use. Presence of adrenal incidentaloma. Family history of PA (monogenic forms arerare). Unexplained atrial fibrillation bystructural heart disease orhyperthyroidism. Earlystroke ordisproportionaterenal/cardiovascular complications relative to age or HTN severity. HTN and obstructive sleep apnea	Symptoms of hypokalemia: muscle weakness, muscle crampstetany. Hypertension, incidentally discovered adrenalmass, Arrhythmias, especially atrialfibrillation. Polyuria	Plasma aldosterone (PA) and plasmarenin activity (PRA). Elevated PA/ PRA ratio (ARR) under standard conditions. Oral Salt Suppression. Test Intravenous Saline Infusion Test. Captopril Challenge Test, Fludrocortisone Suppression Test, Oral Salt Suppression Test, Intravenous SalineInfusion Test, CTscan & adrenal veinsampling, Genetictesting	SpironolactoneUnilateralPA - Laparoscopicunilateraladrenalectomy

Cushing's syndrome Prevalence (2–5%)	Young individuals with atypical medical conditions, like osteoporosis and resistant hypertension Patients exhibit classic manifestations such aseasy bruising, weight gain, facial redness, and purplestriae. Children experiencing a decline in height percentile coupled with rising weight Individuals withadrenal incidentalomassuggestive of adenomas	Truncal obesity, Moonface, Hypertension, Skinatrophy, and bruising, purple striae, Diabetes or glucoseintolerance, Gonadal dysfunction, muscleweakness, hirsutism, Acne, mood disorders, insomnia, depression, Osteoporosis, Fungal infections	Overnight 1-mg Dexamethasone suppression test 24-hours Urinary freecortisol. Midnightsalivary/plasmacortisol. Morningplasma Adrenocorticotropic hormone(ACTH). ACTHstimulation by corticotropin-releasinghormone (CRH) ordesmopressin. CTimaging	Spironolactone ordiuretics totreat hypokalemia (ec topic ACTH production). Surgical resection
Hyperthyroidism Prevalence- < 1%	Warm, moist skin Heatintolerance, Nervousness, Tremulousness, Insomnia, Weight loss, Diarrhea & proximal muscle weakness	Tremor, Tachycardia, Atrial fibrillation, Weight loss, Goiter, Pretibial myxedema	Thyroid-stimulatinghormone, Free thyroxine, Radioactiveiodine uptake andscan	Antithyroid medications. Beta-blockers
Hypothyroidism Prevalence - < 1%	Dry skin, Cold intolerance, Constipation, Hoarseness, Weight gain	Fatigue & Cold intolerance, Weight gainnon-pitting edema, Periorbital puffiness, slow speech, Coarsevoice and skin, Constipation, Enlargedtongue, Brittle hair, Delayed ankle reflex, Bradycardia	Thyroid-stimulating hormone, Freethyroxine	Levothyroxine
Primary Hyperparathyroidism (PHTP)	Hypercalcemia	Bones, stones, abdominal groans, and psychic moans. Polyuriaand polydipsia	PTH Calcium Phosphate Albumin Vitamin D 24 hurinary calcium excretion	Surgical excision of gland Vitamin Dsupplements
Growth Hormone (GH)	Hypertension, incidentally discovered pituitary tumors Patients with typical clinical manifestations of acromegaly	Acral features, largehands and feet, Frontalbossing, Progressivedental malocclusion. Degenerative arthritis Low-pitched sonorousvoice, Excessive sweating, and oilyskin. Perineural hypertrophy leadingto nerve entrapment. Cardiac dysfunction	Serum growth hormone ≥1 ng/mL-during oral glucoseload. Elevated ageand sex-matchedIGF-1 level MRI. scan of the pituitary	Somatostatin analogs GH receptor antagonist. Dopamine agonists. Surgical resection of tumor
Congenital Adrenal Hyperplasia (CAH)	Children, adolescents andyoung adults with HTN, Spontaneous hypokalemia, low levels of aldosterone and renin. Girls with virilization and boys with pseudoprecocious puberty, Primary amenorrhea, andpseudohermaphroditism	*Girls*: HTN, Hypokalemia, Acne, Hirsutism, Virilization, Primary amenorrhea, and Pseudohermaphroditism. *Boys*: HTN, Hypokalemia, Pseudo precocious puberty	Hypokalemia with low or normal aldosterone and renin Elevated DOC, 11-deoxycortisoland androgens De creased androgens and estrogen. Germline mutationtesting	Glucocorticoid replacement. Bilateral adrenalectomy

- **Reconsider screening for endocrine hypertension in**
  - New onset or uncontrolled hypertension (Moderate/ severe hypertension (BP >150/100 mmHg on three separate occasions)
  - Resistant hypertension (BP >140/90 mmHg on three antihypertensive medications and anyone on four or more antihypertensives) or drug-induced.
  - Abrupt onset of hypertension and family history of early onset
  - Onset of hypertension in young persons (aged <30 years)
  - Exacerbation of previously controlled hypertension
  - Disproportionate target organ damage for the degree of hypertension
  - Accelerated or malignant hypertension
- Onset of diastolic hypertension in older adults (aged ≥65 years)
- Unprovoked or excessive hypokalemia
  - Initial screening for endocrine hypertension should **encompass a comprehensive evaluation of the patient's medical history,** a thorough physical examination focusing on clinical indicators, and basic blood biochemistry tests.
  - Subsequent investigations aimed at **diagnosing endocrine hypertension, including additional biochemistry, imaging studies, and other relevant tests, should be selected thoughtfully.** This selection process should be guided by the information gleaned from the patient's medical history, findings from the physical examination, and the results of initial basic clinical assessments.
  - Should an adult with persistent hypertension exhibit indications of a particular type of endocrine-related hypertension during screening, it could be **prudent to consider referring them to a specialist physician well-versed in managing that specific form of hypertension.** This step aims to ensure accurate diagnostic confirmation and the initiation of appropriate treatment measures.

Section 11.3 - OBESITY AND HYPERTENSION

The rise of industrialization, sedentary habits, genetic predisposition, dietary patterns, lack of awareness/education, and swift urbanization has led to a substantial increase in individuals

Table 17: Normal Cut-off values

Body Mass Index (BMI) (kg/m^2)	Consensus statement Asian Indians[318]	WHO – Asian population[317]
	Normal BMI: 18.0-22.9	Underweight: <18.5
	Overweight: 23.0-24.9	Normal: 18.5-22.9
	Obesity: >25	Overweight: 23.0-24.9
		Pre-obese: 25.0-29.9
		Obese: ≥30.0
		Type 1 (obese): 30.0-40.0
		Type 2 (morbidly obese): 40.1-50.0
		Type 3 (super obese): >50.0

Waist Circumference (WC) (cm)	Consensus statement Asian Indians[318]	National Family Health Survey (NFHS)- 5[319]
	Men: >90	Men: >94
	Women: >80	Women: >80
Waist Hip Ratio (WHR)[207]	Men < 0.90	
	Women < 0.85	

Body Fat Percentage (%)[319,320]	Male	Female
	Essential fat: 2–5	Essential fat: 10–13
	Athletes: 6–13	Athletes: 14–20
	Fitness: 14–17	Fitness: 21–24
	Acceptable: 18–24	Acceptable: 25–31
	Obese: ≥25	

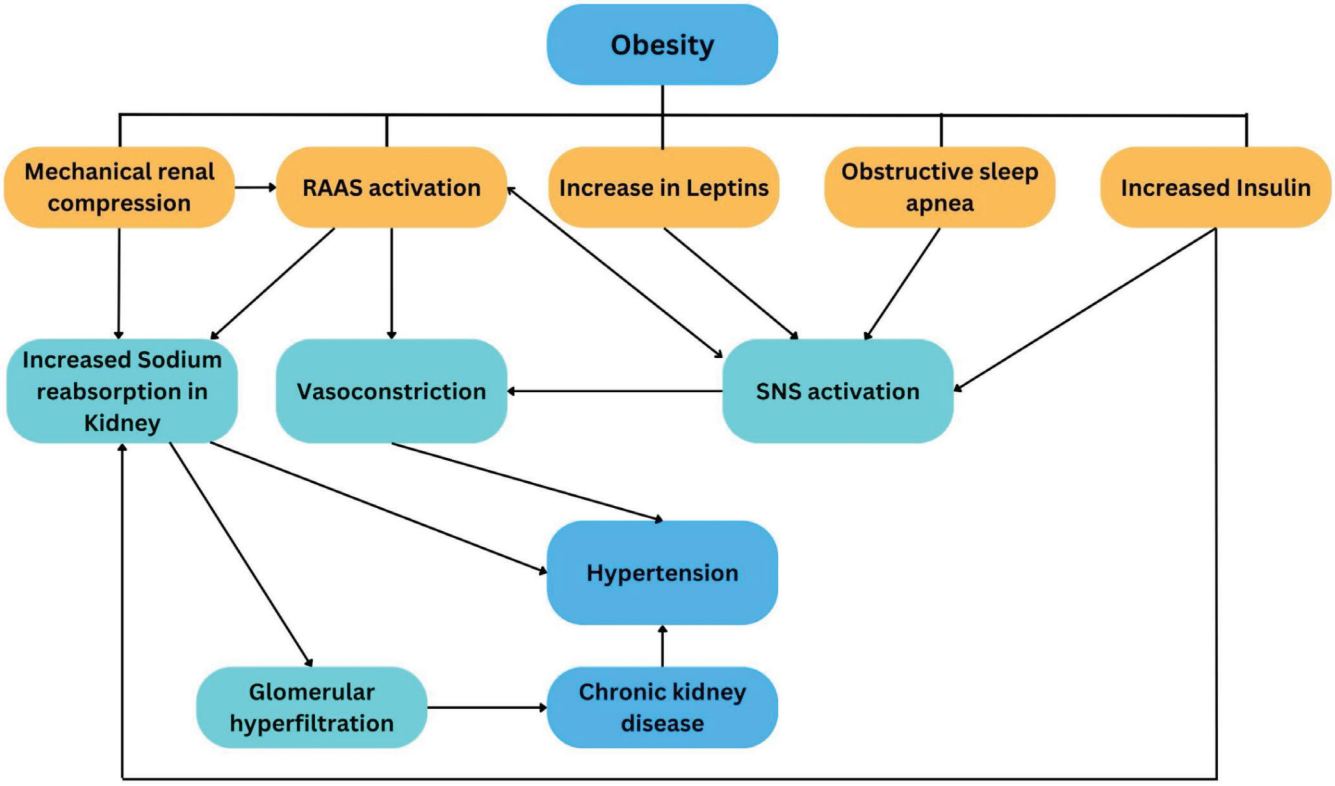


Figure 7: Possible pathways connecting obesity, hypertension, and chronic kidney disease[321-323] (RAAS-Renin-angiotensin-aldosterone system; SNS-sympathetic nervous system)

grappling with overweight or obesity, along with elevated blood pressure and blood glucose levels.[311] ICMR-INDIAB national cross-sectional study (ICMR-INDIAB-17) has projected the prevalence of generalized obesity at 28·6% (254.2 Mn) and abdominal obesity at 39·5% (351.1 Mn). The 2016 report from the World Health Organization (WHO) characterized overweight and obesity as a pandemic in India, owing to a rise in prevalence from 8.4% in 2006 to 11.8% in 2016, marking a 3.4% increase over the decade.[312] The National Nutrition Monitoring Bureau survey revealed higher prevalence rates of hypertension among individuals classified as overweight or obese (39.7%), those with abdominal obesity (39%), and those with truncal obesity (27.8%).[313]

According to the ICMR-INDIAB study (phase 1), 30% of hypertensive patients had generalized obesity (GO: BMI ≥ 25 kg/m^2), 34.9% of hypertensive patients had abdominal obesity (AO: WC ≥ 90 cm for men, and ≥ 80 cm), and 25.2% of hypertensive patients had combined obesity (CO: GO+AO).[314] The Asian Indian phenotype is characterized by a substantial body fat percentage combined with a comparatively lower body mass index (BMI), reduced lean body mass—especially in the lower limbs—and an elevated BF/BMI ratio, indicating greater body fat relative to BMI.[315] This group tends to present a greater body fat percentage (BF%) than other ethnicities, even with lower BMI measurements–a phenomenon commonly known as the Yajnik and Yudnik (Y-Y) paradox.[316,317] The Asian Indian phenotype encompasses heightened insulin resistance and increased abdominal adiposity, as evident from elevated waist circumference and waist-to-hip ratio.

Table 18: Obesity and hypertension - Management

PATIENT EDUCATION	• Regarding the enduring financial consequences of various conditions associated with obesity and hypertension. • Regarding obesity being a complex issue and not a cosmetic issue • Encouraged to lose weight, have a proper diet, and start moderate-intensity physical activity
LIFESTYLE AND DIETARY MODIFICATIONS	Sufficient consumption of fruits and vegetables Reduced intake of unhealthy food Yoga asanas should be encouraged. 60 min of physical activity daily or ≥ 300 min of weekly moderate-intensity physical activity Reduced calorie intake Increased consumption of complex carbohydrates, proteins, fruits, vegetables, berries, pulses, whole grain cereals, and nuts

PHARMACOTHERAPY FOR WEIGHT LOSS	• Indications
	  ○ BMI ≥ 27 kg/m2 without co-morbidities
	  ○ ≥ 25 kg/m2 with co-morbidities
	  ○ WC is 10 cm above the upper limit of gender-specific normal values
	• Obese patients with diabetes –
	  ○ Metformin
	  ○ SGLT-2 inhibitors
	  ○ GLP1RAs
	  ○ Pancreatic lipase inhibitor

PHARMACOTHERAPY FOR HYPERTENSION	• Initiate antihypertensive therapy with ACEis,ARBs, or CCBs - they do not worsen insulin sensitivity or adiposity • Thiazide/Thiazide-like diuretics may be used in combination therapy (can worsen glucose and lipid metabolism at higher doses) • Comorbidities such as postmyocardial infarction or heart failure with reduced ejection fraction (HFrEF) - Beta-blockers (promote weight gain, have dyslipidemic effects, and may also increase the risk of type 2 diabetes)

BARIATRIC SURGERY	• Indications
	  ○ BMI of ≥ 32.5 kg/m2 with co-morbidities
	  ○ BMI ≥ 37.5 kg/m2 without co-morbidities
	• Laparoscopic adjustable gastric banding (LAGB)
	• Laparoscopic sleeve gastrectomy (LSG)
	• Laparoscopic Roux-en-Y gastric bypass (LRYGB)
	• Biliopancreatic diversion with duodenal switch (BPDS)

11.3.1 Management

The main objective in managing hypertension linked to obesity is achieving weight loss, as it effectively counteracts the underlying pathophysiological processes contributing to hypertension. The blood pressure-lowering benefits of weight loss exhibit a linear relationship, with an approximate reduction of 1-mmHg per kilogram of weight loss.[324] However, this effect might diminish over extended periods, revealing a decrease of approximately 6 mmHg for every 10 kilograms of weight loss.[325] Lifestyle modifications, pharmacotherapy, and metabolic surgeries are the next effective strategies (Table 17).

Recommendations

- For adults experiencing high normal blood pressure and overweight, it is advisable to **prioritize weight reduction** as a means to lower blood pressure and enhance cardiovascular results.
- Through **integrating lifestyle modifications and weight reduction**, a significant decrease in hypertension is observed in most instances.
- In cases where obesity coexists with diabetes and hypertension, it is preferable to consider **treatment strategies involving antidiabetic medications that have the dual benefit of reducing both body weight and blood pressure (GLP1RA, SGLT2i).**

Section 12 - TECHNOLOGY

The future of hypertension management lies in digital solutions and wearable blood pressure monitoring technology. These innovations hold the promise of significantly reducing and possibly even eliminating cardiovascular events in patients with hypertension. Emerging technologies such as Wrist-based Oscillometric Measurement, Information/Communication Technology (ICT) multisensor blood pressure monitoring systems, application trigonometry method, and Photoplethysmography represent exciting prospects for the future of blood pressure monitoring.[326–328]

12.1 Digital Aids

12.1.1 Telemedicine

Though telemedicine in India was formally launched in 2000,[329] it has gained more importance during the post-coronavirus disease-2019 (COVID-19) era.Telemedicine has the advantage of being fast, easy to access, saving time (no long-distance travel) and efforts of the patient, better documentation, and safety.[330]

It can be used as a tool to interactively educate the young and old patients alike. Telemedicine, using trained non-physician health workers equipped with electronic tablets and point-of-care devices, improved blood pressure control in rural areas through remote consultations, benefiting known hypertensive patients.[332] Electronic health records (EHRs) can significantly improve hypertension control by providing quick access to patient data, optimizing treatment, enhancing patient-physician communication, and promoting preventive care.[333,334]

12.1.2 Mobile and Mobile Applications

Mobile health is increasingly used for healthcare services and patient education. Mobile apps for managing hypertension are becoming popular, offering features like data tracking, personalized guidance, and smartphone interactive communication. However, challenges include a lack of clinical validation, poor quality, data privacy concerns, and limited adoption among elderly populations.[335]

A nurse-facilitated smartphone or tablet-based clinical decision support software (DSS) was used to generate prescriptions for patients in Himachal Pradesh (mPower Heart Project), which significantly helped reduce systolic (-12.9 to -14.6 mmHg) and diastolic blood pressure (-7.1 to -7.7 mmHg) in patients.[336] Community health workers (SIMCARD Trial) supported by local physicians equipped with mobile health technology reported a 25.5% increase in patient-reported antihypertensive medication use and a reduction in systolic blood pressure (-2.7 mmHg).[337] Although promising, more studies must be conducted to establish sustainability and long-term outcomes.

A study revealed a six-fold rise in the likelihood of developing hypertension among individuals who had used mobile phones for a minimum of eight years and a four-fold increase among those who used them for more than 60 minutes daily.[338] A study involving adolescents in China unveiled mobile addiction as a novel risk element for hypertension. The prevalence of elevated blood pressure was substantial and linked to the rising prevalence of overweight/obesity, subpar sleep quality, and smartphone addiction.[339]Stalin *et al*.[341] reported a negative association between blood pressure and using mobile phones in South India. Some studies have indicated the absence of any connections between mobile phone usage and blood pressure.[342,343] More studies are required to assess the relationship between Hypertension and Mobile usage more accurately.

The **India Hypertension Control Initiative** (IHCI), initiated in November 2017, is a collaborative effort to address hypertension. Its goal is to reduce hypertension prevalence by 25% by 2025, with support from India's Ministry of Health and Family Welfare (MoHFW), the Indian Council of Medical Research (ICMR), and the World Health Organization's India chapter (WHO-India).[344] "Simple," a quick and cost-free mobile app, was collaboratively developed with IHCI for physicians and officials to handle hypertension and diabetes patients. This Android app empowers doctors to store and oversee vital patient data, such as blood pressure, blood glucose levels, medication schedules, and follow-up appointments.[345,346] According to progress brief reported in 2022, nearly half (47%) of the registered patients under care had BP under control during the most recent visit in the first quarter of 2021.[347]

12.2. Artificial Intelligence (AI) driven Approaches

Machine learning (ML) and Artificial Intelligence (AI) amalgamate computer science, statistics, and decision theory to identify intricate patterns within extensive datasets. Given that hypertension can lead to sudden blood pressure escalation, artificial intelligence techniques are harnessed to predict the onset of hypertension.[348] Emerging digital tech offers real-time health data, including social media, apps, and wearables. AI and big data can reveal hidden hypertension risk factors and build precise prediction models by combining cardiovascular, multi-omics, socioeconomic data, and personalized treatments.[349] An AI- and ML-driven risk stratification model customized to data from community-based screening initiatives can enhance accuracy in risk stratification for hypertension within resource-constrained settings.[350]

12.3. Digital Devices and Manual Sphygmomanometer

Accurately measuring and controlling blood pressure (BP) prevents conditions like hypertension, cardiovascular diseases, and strokes.[351] Ensuring precise BP readings, even with an error margin as small as 5 mmHg, holds immense significance, particularly amidst the increasing enigma of hypertensive disorders.[352] Mercury sphygmomanometers, once the gold standard, have faced global decline due to mercury toxicity, disposal issues, and observer bias concerns, impacting treatment guidelines.[353] Recently, there has been a notable shift towards automated BP devices like Aneroid and Digital sphygmomanometers. A key advantage of the aneroid instrument lies in its portability[354], while the digital counterpart excels in user-friendliness, eliminating the necessity for the examiner's auscultatory skills. The blood pressure measured by mercury, aneroid, and digital sphygmomanometers are comparable, but aneroids are considered more sensitive and specific when compared to digital apparatus.[351,352,355] However, regardless of the currently preferred digital or aneroid sphygmomanometers, it's mandatory to satisfy the standard techniques of blood pressure measurement (*Refer Section 6*: Blood pressure measurement).

12.4. Barriers to Implementing Digital Technology interventions to improve Hypertension Management in the Public Healthcare system in India

Barriers to implementing digital technology interventions to improve hypertension diagnosis andmanagement in India include a lack of healthcare infrastructure, a shortage of trained healthcare professionals, a lack of technology literacy, data privacy & security concerns, affordability, and resistance to change.[357,358]

Addressing these barriers requires a multi-faceted approach involving collaboration between stakeholders, including state and national governments, healthcare institutes, and healthcare device manufacturers.

Recommendations

- **Using digital devices for BP measurement is encouraged.**
- We recommend regular usage of **Electronic Health Records (EHRs)** as they facilitate quick retrieval of patient records and augment the efficacy of existing treatments.

Section 13 - PEDIATRIC AND ADOLESCENT HYPERTENSION

Neonatal hypertension occurs in approximately 0.2% of term newborn infants and can affect up to 3% of infants admitted to the Neonatal Intensive Care Unit (NICU). Various systematic reviews and meta-analyses have consistently reported a prevalence ranging from 5.54 to 7.6% in children and adolescents below the age of 18 years in India.[359-361] A secondary analysis of data obtained from the Comprehensive National Nutrition Survey found that the prevalence of high blood pressure was 35.1% among children aged 10 to 12 years and 25.1% among those aged 13 years and older.[362] All the studies point towards a high prevalence of hypertension in apparently healthy children.

Table 20 serves primarily as a screening tool to identify children and adolescents who require additional blood pressure (BP) assessment through repeated measurements. It should not be solely relied upon for diagnosing elevated BP or hypertension. To diagnose elevated BP or HTN accurately, referring to the specific cutoff values provided in the comprehensive BP tables is crucial.[363] This is imperative due to the potential variation in systolic blood pressure (SBP) and diastolic blood pressure (DBP) cutoffs, which can be elevated by up to 9 mmHg based on the individual's age andheight.[363]

Neonates - Defining hypertension in neonates is notably challenging due to the widely recognized fluctuations in blood pressure (BP) that transpire during the initial weeks of life.[366] These BP fluctuations can be particularly pronounced in preterm infants, wherein BP is influenced by many factors encompassing postmenstrual age, birth weight, and maternal health conditions(Refer to Table 21 for Neonatal BP values).[367] Direct intra-arterial measurements using indwelling catheters and indirect measurements using the oscillometric technique (in-office method) are the two methods for measuring BP in hospitalized neonates. It can be determined in the right upper arm with the infant in a supine position.[363]

Essential or primary HTN - where an underlying cause cannot be identified (usually ≥6 years).[368] Risk factors for primary hypertension include - overweight/obesity, suboptimal diet (high sodium diet, consumption of fewer fruits and vegetables), physical inactivity, poor sleep, environmental factors (air pollution, exposure to phthalates, compounds commonly found in plastics, etc.), hereditary, and low birth weight/intrauterine growth restriction, low socioeconomic status and food insecurity, tobacco use and males.[364,369-371]

Table 19: Definition and classification of Pediatric & Adolescent Hypertension[363-365]

BP/HTN	Age 1 to < 13 Years	Age > 13 Years
Normal BP	<90th percentile	< 120/< 80 mmHg
Elevated BP	≥90th percentile to <95th percentile or 120/80 mmHg to <95th percentile (whichever is lower)	120/< 80–129/< 80 mmHg
Stage 1 HTN	≥95th percentile to <95th percentile + 12 mmHg or 130/80–139/89 mmHg (whichever is lower)	130/80–139/89 mmHg
Stage 2 HTN	≥95th percentile + 12 mmHg or ≥ 140/90 mmHg (whichever is lower)	≥140/90 mmHg
Hypertensive Crisis		
Hypertensive Urgency	>95th centile + 30 mmHg without symptoms/signs of target end organ damage	>180/120 without symptoms/signs of target end organ damage.
Hypertensive Emergency	>95th centile + 30 mmHg associated with encephalopathy (headache, vomiting, vision changes, and neurological symptoms (facial nerve palsy, lethargy, seizures, coma) +/- target-end organ damage.)	>180/120 associated with encephalopathy (headache, vomiting, vision changes, and neurological symptoms (facial nerve palsy, lethargy, seizures, coma) +/- target-end organ damage)

Table 20: Screening BP values - As proposed by the Indian Academy of Pediatrics[363]

Age (yr)	BP percentile	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile							Height percentile						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7.	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89

Age (yr)	BP percentile	Systolic BP (mm Hg)							Diastolic BP (mm Hg)						
		Height percentile							Height percentile						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	109	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	87	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

Table 21: Reference values for Neonatal BP values[366]

Postmenstrual Age		50th Percentile	95th Percentile	99th Percentile
44 weeks	Systolic	88	105	110
	Diastolic	50	68	73
	Mean	63	80	85
42 weeks	Systolic	85	98	102
	Diastolic	50	65	70
	Mean	62	76	81
40 weeks	Systolic	80	95	100
	Diastolic	50	65	70
	Mean	60	75	80
38 weeks	Systolic	77	92	97
	Diastolic	50	65	70
	Mean	59	74	79
36 weeks	Systolic	72	87	92
	Diastolic	50	65	70
	Mean	57	72	71
34 weeks	Systolic	70	85	90
	Diastolic	40	55	60
	Mean	50	65	70
32 weeks	Systolic	68	83	88
	Diastolic	40	55	60
	Mean	48	62	69
30 weeks	Systolic	65	80	85
	Diastolic	40	55	60
	Mean	48	65	68
28 weeks	Systolic	60	75	80
	Diastolic	38	50	54
	Mean	45	58	63
26 weeks	Systolic	55	72	77
	Diastolic	30	50	56
	Mean	38	57	63

Secondary HTN - is caused by an underlying disorder or the use of certain medications (Refer to sections 12.0.2 & 12.2) More prone to manifest at a younger age.[372,373]

13.1 Measurement of blood pressure

Normative values for blood pressure are established through auscultatory sphygmomanometry, which remains the preferred technique for blood pressure assessment (Figure 9).[368,370,374] A stethoscope is placed on the brachial artery, proximal and medial to the antecubital fossa, positioned below the cuff's lower edge, and blood pressure is measured and recorded.

13.2 Screening

Diagnosing hypertension in children often goes unnoticed due to the absence of symptoms or the inability to express discomfort. Screening for hypertension is imperative in pediatric care. In cases with no identifiable underlying cause, blood pressure should be assessed annually starting from the age of 3.

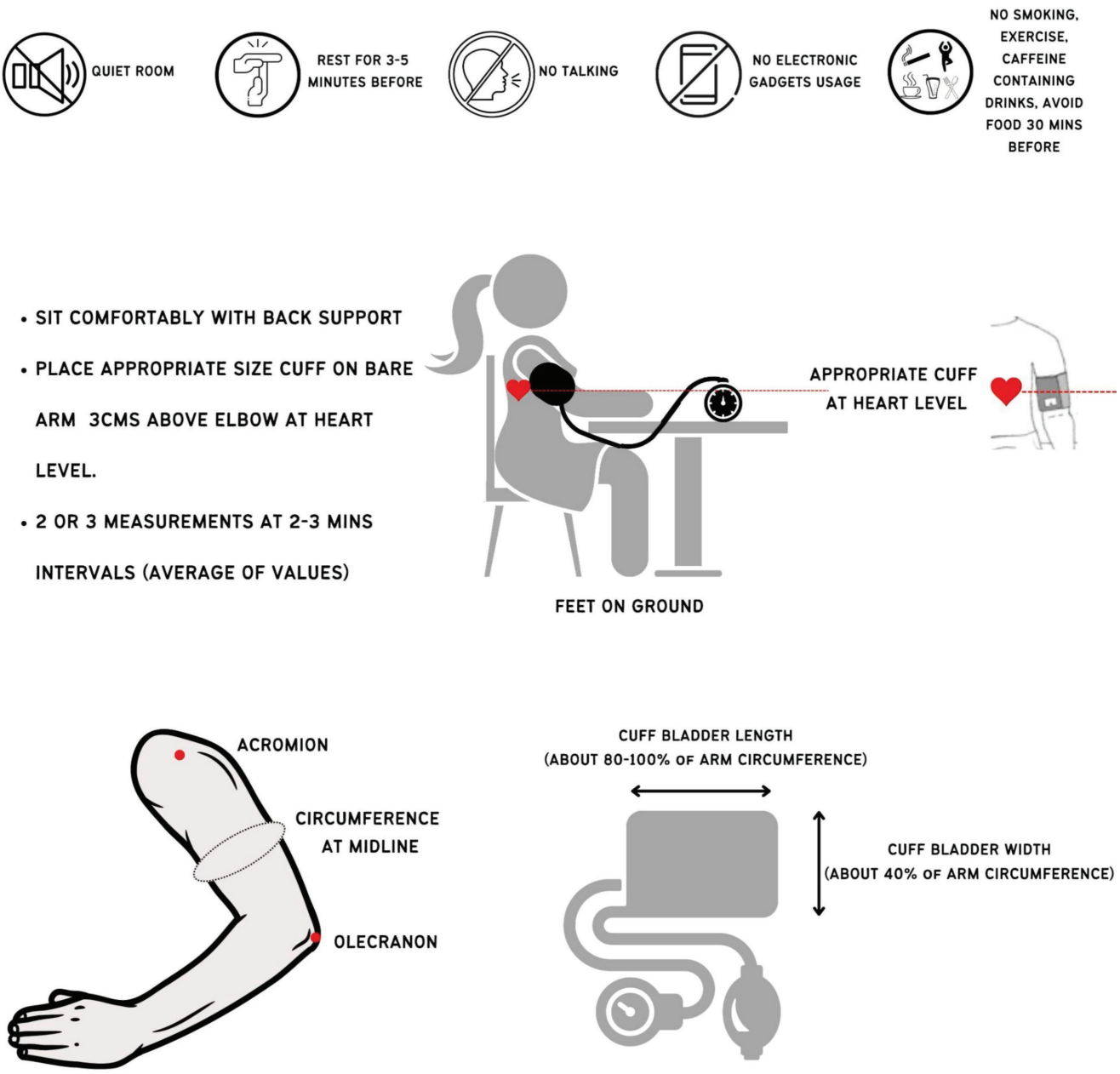


Figure 8: BP measurement in children.

However, when any risk factors are present—such as prematurity <32 weeks gestation, small for gestational age or low birth weight, history of umbilical artery line, congenital heart disease, recurrent urinary tract infections, or abnormal urinalysis, known renal disease or urologic malformations, family history of renal disease, history of solid-organ transplant, malignancy or bone marrow transplant, treatment with medications known to increase BP, a BMI ≥ 95th percentile[375], diabetes, aortic arch obstruction or coarctation—blood pressure measurements should be taken during every clinic visit, regardless of the child's age.[363,372,376,377]

13.3 Examination

Diagnosing hypertension in a child necessitates a comprehensive approach encompassing several key steps. These steps include compiling the medical history, conducting a thorough clinical examination (Table 22), performing relevant laboratory tests, and radiological evaluations (Table 23). Initiating the clinical examination involves the measurement of fundamental parameters, including weight, height, and BMI. These measurements provide essential baseline data for assessing the child's growth and overall health status.[371,378,379]

13.4 Management

The objectives for managing pediatric hypertension should encompass preventing damage to target organs and the development of adult hypertension. Maintaining optimal blood pressure levels in hypertensive children and adolescents is a vital goal (Figure 10). The whole family has to be involved to adapt to the lifestyle changes.[368,384,385]

13.4.1 Lifestyle modifications

- Healthy diet - children should follow the DASH (dietary approach to stop hypertension) diet, which includes minimally processed foods, whole grains, fresh legumes, vegetables, fruits, low-fat dairy, fish, and lean red meat. This diet reduces refined sugar and avoids excessive salt, sugar, and refined white wheat flour. The goal is to limit daily sodium intake to less than 2.3g. A potassium-rich diet is recommended instead of high sodium intake. Coffee, caffeinated, carbonated drinks, and junk food should be avoided.
- Weight reduction
- Physical activity - Promote outdoor activities that involve moderate to vigorous physical activity for 40-60 minutes, at least 3-5 times per week. Decrease the time spent on sedentary video games and ensure age-appropriate sleep duration.
- Stress reduction (Yoga & meditation), avoiding smoking and alcohol use.[380,381,383]

Table 22: Physical examination.[374,380-382]

History	*Birth or Antenatal history* - Maternal history of HTN, low birth weight, gestational age, etc.
	Family history - HTN, ischemic heart disease, familial hyperlipidemia, diabetes, sudden cardiac death, hereditary renal or endocrine syndromes (< 55 years).
	Family Structure - Nuclear/ joint/both parents working. May determine ease of following dietary or activity advice given.
Environmental factors	Smoking, alcohol consumption, drug/substance intake.
Diet	Daily intake of high sodium, high-fat junk food, and caffeine-containing drinks, gym formulations
Physical activity	Physical exercise/leisure time
Screen time	Time spent on mobile phone/ laptop/ tablet/television (Inversely proportional to physical & mental activity level)
Sleep	*Obstructive sleep apnea* - Sleeplessness, snoring, day time sleepiness
Symptoms	Headache, epistaxis, vertigo, visual impairment, strokes, low school performance, attention defects, dyspnoea, chest pain, palpitations, and syncope.
Physical examination	*General* - Stunted growth, pallor, edema, obesity
	Endocrine - cushingoid features, dysmorphology
	Skin - Rash, vasculitis, axillary freckling, acne, acanthosis nigricans, xanthelasma, xanthomas, café au lait spots
	Coarctation of Aorta (COA), Aortoarteritis, hyperthyroidism - Pulse rate and volume in both upper and lower limbs
	Thyroid - Enlargement
	Cardiovascular - Apical heave, murmur, bruits (LVH), weak femoral pulses, tachycardia
	Genetalia - Virilization (Congenital adrenal hyperplasia)
	Renal - Bruit over flanks (renal artery), Renal mass
	Joints - Arthritis in certain autoimmune causes of glomerulonephritis
	Abdominal - Check for masses, hepatosplenomegaly

Table 23: Investigations.[380,381,383,384]

Blood chemistry	Complete haemogram, Electrolytes (serum sodium, potassium, chloride levels), thyroid function tests, cortisol, aldosterone.
	Renal disease- serum blood urea nitrogen, serum creatinine,estimated eGFR.
	Cardiovascular disorders - Lipid profile (especially Cardiolipins).
	Obesity - fasting blood sugar, HbA1c, serum alanine aminotransferase, serum aspartate aminotransferase (AST)
Bilateral upper arm and single leg blood pressure measurement	To rule out COA
Drug screening	To rule out substances causing increase in heart rate & BP.
Urine analysis	Routine and microscopic examination
Echocardiography	Cardiac organ damage, LVH
Retinal fundus examination	To rule out fundal edema and hemorrhages.
Renal Doppler and Ultrasound	To assess underlying renal disease.
Computed Tomography (CT) and Magnetic Resonance (MR) Angiography	Mass, complete visualization of the aorta and branches, including renal vessels.
Polysomnography	Obstructive sleep apnea
Genetic testing	To test a few secondary causes (pheochromocytoma, etc.)

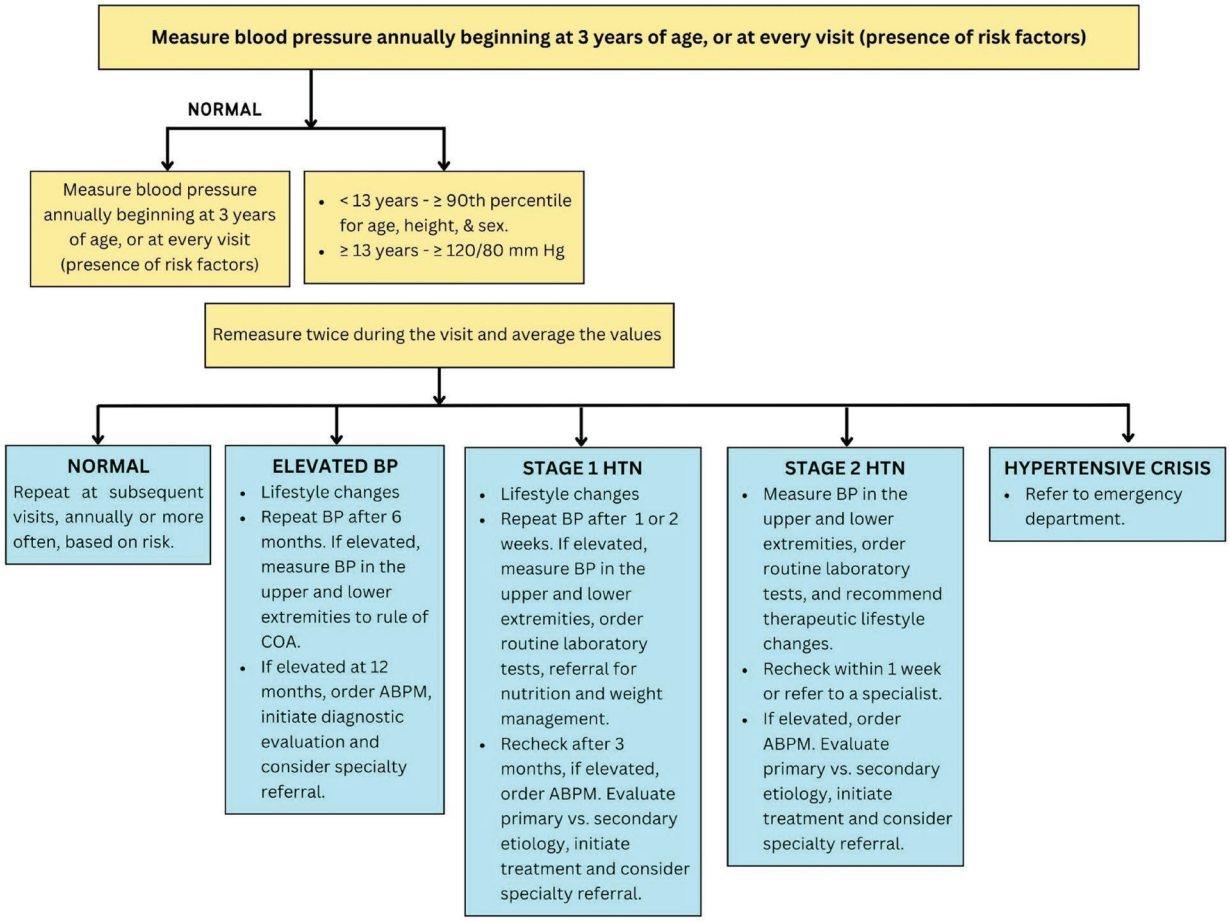


Figure 9: Algorithm for management of elevated BP in children and adolescents.[383]

13.4.2 Pharmacological interventions

The decision to start pharmacological therapy is advised when signs or symptoms linked to hypertension, hypertensive organ damage (HMOD), stage 2 HTN, concurrent comorbidities, or resistance to lifestyle changes are present. The recommended first-line antihypertensive agents are (ACEi) angiotensin-converting enzyme inhibitors (but contraindicated in renal artery stenosis), angiotensin receptor blockers (ARB), calcium channel blockers (CCB), and thiazide diuretics (Beta blockers are avoided due to side effects). Initiation with a low dose is preferable; if ineffective, a single full dose or low-dose combination is considered. If needed, a full-dose combination is preferred.[383] (Table 24) Mechanism of action of different antihypertensive drug classes is given in Table 26.

If a child remains consistently hypertensive despite being on three different antihypertensive medications (resistant hypertension), a trial of spironolactone may be considered.[363,380] When a non-functioning kidney contributes to hypertension, a nephrectomy can be performed by blocking the renal artery using coil closure, obviating the need for surgery. Similarly, if resistant hypertension is caused by renal artery stenosis, the condition can be addressed through balloon angioplasty to open the artery and potentially implant a stent for improved blood flow.[376,378]

Neonates

In neonatal hypertension, addressing correctable causes usually resolves the condition. Mild hypertension can be monitored, with treatment options including thiazide or loop diuretics if needed. For moderate hypertension (95th to 99th percentiles), diuretics, hydralazine, or propranolol may be considered. Severe hypertension (>99th percentile) requires cautious IV drug infusion for treatment. Surgical intervention is considered in specific cases, such as coarctation of the aorta or renal artery obstruction, etc. (Table 25).[388]

Table 24: Pharmacological therapy for HTN in pediatric cases[381,386,387]

Drug	Dose Range (Initiating to Maximum)	Doses Per Day	Remarks
First Line Oral Anti-Hypertensive for Pediatric Htn			
Enalapril	0.08 to 0.6 mg/kg/dose	Twice	Age > 1 month (max dose range: 5 mg to 40 mg/day)
Lisinopril	0.07 to 0.6 mg/kg/dose	Once	Age > 6 years (max dose range: 5 mg to 40 mg/day)
Ramipril	1.6 to 6 mg/m^2/dose	Once	Max dose in adults: 2.5 mg to 20 mg/day. Has been used in children above 18 months of age.
Candesartan	0.2 mg/kg/dose	Once	Age 1-6 years (max dose range: 0.4 mg/kg up to 4 mg/day)
	< 50 kgs - 4-8 mg (max dose - 16 mg) > 50 kgs - 8-16 mg (max dose - 32 mg)	Once	Age 6 - 17 years
Olmesartan	10 to 20 mg/dose	Once	Age > 6 years, weight < 35 kg
	20 to 40 mg/dose	Once	Age > 6 years, weight >35 kg
Losartan	0.7 to 1.4 mg/kg/dose	Once	Age > 6 years (max dose range: 50 to 100 mg/day)
Valsartan	0.4 to 3.4 mg/kg/dose	Once	Age: 1-5 years and weight > 8 kg Max dose: 40 mg (< 18 kg)to 80 mg (> 18 kg /day)
	1.3 to 2.7 mg/kg/dose	Once	Age: > 6 years Max dose range: 40 to 160 mg/day
Hydrochlorothiazide	0.5 to 1 mg/kg/dose	Twice	Max dose range: 25 to 75 mg/day
Chlorothiazide	5 to 10 mg/kg/dose	Twice	Max dose for age <2 years: 375 mg/day Max dose for 2-12 years: 1000 mg/day Max dose for > 12 years: 2000 mg/day

Amlodipine	0.1 to 0.6 mg/kg/dose	Once	Age 1 to 5 years. (max dose 5 mg/day)
	2.5 to 10 mg/dose	Once	Age > 6 years. (max dose 10 mg/day)
Nifedipine (extended-release)	0.2 to 0.5 mg/kg/dose	Once or Twice	Max dose: 3 mg/kg/day - 120 mg/day
Second Line Oral Anti-Hypertensive for Pediatric HTN			
Atenolol	0.5 to 1 mg/kg/dose	Once or Twice	Max dose: 2 mg/kg/day up to 100 mg/day
Metoprolol	1 to 2 mg/kg/dose	Twice	Max dose: 6 mg/kg/day up to 200 mg/day
Metoprolol (extend-ed- release)	1 to 2 mg/kg/dose	Once	Max dose range: 50 to 200 mg /day
Propranolol	1.0 mg/kg/dose	Twice or Thrice	Max dose: 8mg/kg/day up to 640 mg/day
Labetalol	2 to 3 mg/kg/dose	Twice	Max dose: 10 - 12 mg/kg/day up to 1.2 g/day
Prazosin	0.02 to 0.15 mg/kg/dose	Thrice	Max dose: 2 to 20 mg/day
Clonidine	5-10 mcg/kg/dose	Twice or Thrice	Max dose: 25 mcg/kg/day up to 0.9 mg/ day
Hypertension Emergencies & Urgencies			
DRUG	**DOSE**		**REMARKS**
Nicardipine infusion	0.5 to 4 mcg/kg/min		Reflex tachycardia is a side effect. Can be used even in infants.
Labetalol infusion	0.25 to 3 mg/kg/hour		Bolus or infusion is contraindicated in asthma and frank heart failure
Labetalol bolus	0.2 to 1 mg/kg/dose Max 40 mg/dose		Can be repeated every 10 minutes.
Sodium Nitroprusside	0.5 to 3 mcg/kg/min Max dose 10 mcg/kg/min		Avoid in chronic renal disease
Hydralazine bolus	0.1–0.2 mg/kg/dose. Max 0.4 mg/kg/dose		Onset of action is slower. Can be repeated every 4 hours. Can be given intramuscularly as well. Tachycar-dia is a side effect. Can be used in infants.

Table 25: Management of Neonatal hypertension[388,389]

Drug	Dose	Remarks
Chlorothiazide	PO 20-40 mg/kg/ day every 12 hours	Monitor for hypercalcemia & electrolyte abnormalities
Spironolactone	PO 1-3 mg/kg/day every 12-24 hours	Monitor for hyperkalemia and renal failure
Amlodipine	PO 0.1-0.5 mg/kg/day once daily	Peripheral edema

Hydralazine	PO 0.25-1 mg/kg/ dose every 6-8 hours. Maximum 7.5 mg/kg/day	Tachycardia
Lisinopril	PO 0.07-0.1 mg/kg/dose once daily. Maximum 0.5 mg/kg/day PO	Avoid in preterm infants Use with caution in decreased renal function.
Propranolol	PO 0.25 mg/kg/dose every 6 to 8 hours. Maximum 5 mg/kg/day PO	Bradycardia, hyperkalemia, Use with caution in bronchospastic disease.
INTRAVENOUS		
Nicardipine	0.5-2 mcg/kg/dose infusion	Edema & Tachycardia
Sodium Nitroprusside	Initial 0.2 mcg/kg/min infusion. Not exceeding 10 mcg/kg/min	Cyanide and thiocyanate toxicity, renal failure
Hydralazine	0.1-0.5 mg/kg/dose every 6-8 hours not exceeding 2 mg/kg/dose	Monitor for tachycardia & edema.
Enalaprilat	5-10 mcg/kg/dose every 8-24 hours	Do not use it in preterm infants and if GFR < 30 ml/min. Monitor serum electrolytes and creatinine levels.
Esmolol	Term infant 0-7 days of life: 50 mcg/kg/min. At 8-28 days old - Start with 75 mcg/kg/min. Do not exceed 500 mcg/kg/min	Hyperkalemia and bronchospasm
Propranolol	0.01 mg/kg/dose every 6-8 hours. Maximum 0.15 mg/kg/dose every 6-8 hours	Bradycardia
Labetalol	0.1-1 mg/kg/dose every 4-6 hours or 0.25-3 mg/kg/hour infusion	Use with caution in bronchospastic disease and congestive heart failure.

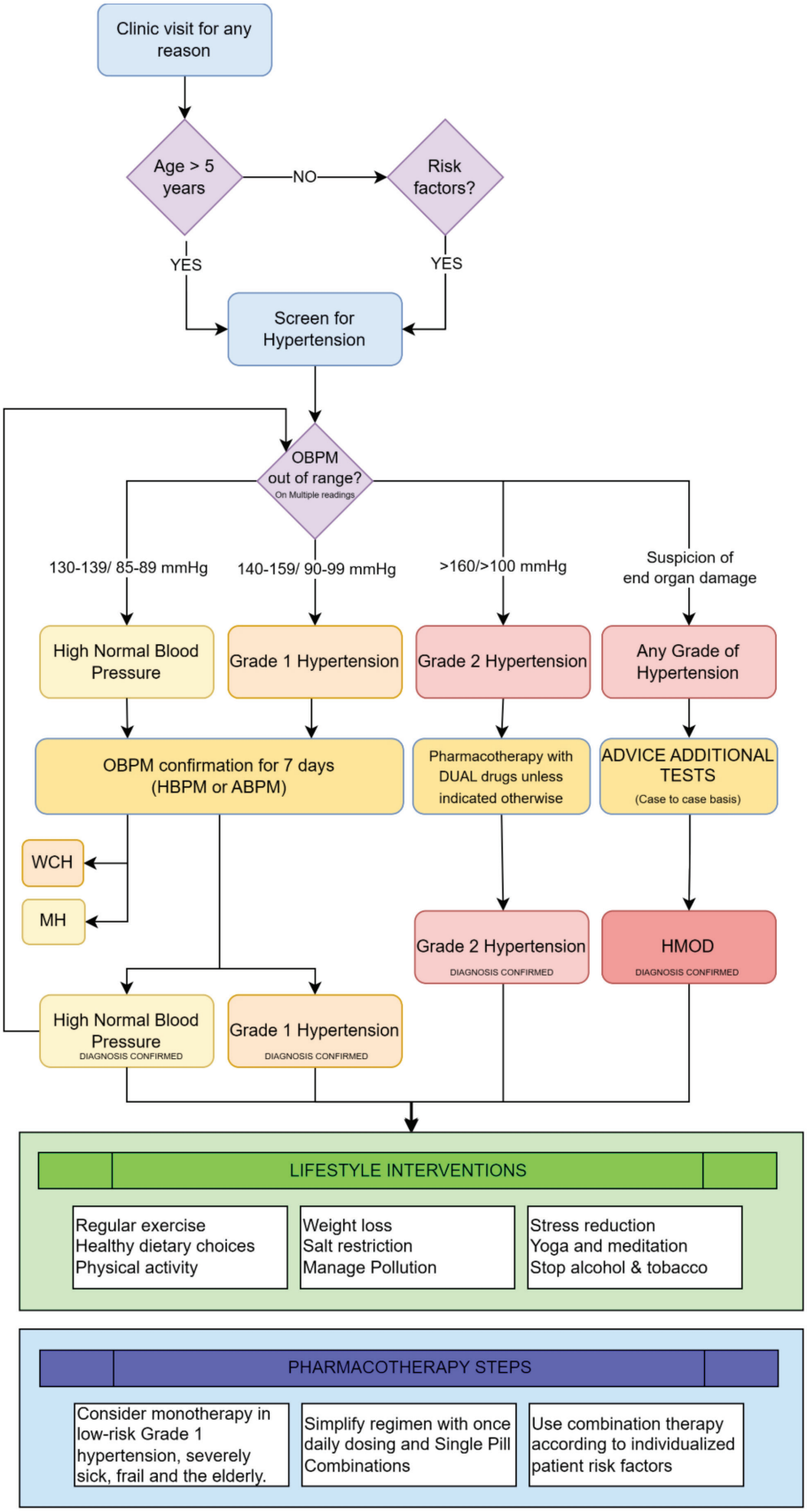
Table 26: Mechanism of action of various antihypertensive medications[390]

Diuretics (Chlorothiazide, Spironolactone)	Block sodium reabsorption at various levels of the renal tubules
Adrenergic blockers (Propranolol,	Competitively inhibit the catecholamines.
Angiotensin-converting enzyme (ACE) inhibitors (Lisinopril, Enalapril)	Block the conversion of angiotensin I to angiotensin II
Angiotensin II receptor blockers (Candesartan, Losartan)	Interfere with the binding of angiotensin II to angiotensin I receptors.
Calcium-channel blockers (Amlodipine, Nicardipine)	Block calcium entry into the cells, producing vasodilation.
Vasodilators (Hydralazine)	Dilate blood vessels.

Recommendations

- Blood pressure levels **should be evaluated in children from three years old.**
- Screening for blood pressure in children under the age of three is advised when there is COA or other risk factors for elevated blood pressure, such as **chronic kidney disorders** (contracted kidney, nonfunctioning kidney), **solid organ transplantation,** use of blood pressure-raising medications, a history of preterm birth, and other relevant factors.
- **Hypertension diagnosis should be confirmed through multiple measurements using a manual auscultatory device.**

Section 14 - HYPERTENSION MANAGEMENT AT A GLANCE



HISTORY AND PHYSICAL EXAMINATION

- Chronic illnesses
- Ongoing treatments
- CV Risk factors
- Evaluate for organ damage
- Symptoms/ signs of secondary hypertension
- Check adherence

LABORATORY TESTS

ESSENTIAL

- Renal Tests:
  - Microscopic urinalysis
  - Albumin excretion
  - Serum BUN and/ or creatinine
- Endocrine Tests:
  - Serum sodium
  - Serum potassium
  - Serum calcium
  - TSH
- Metabolic Tests:
  - HbA1c
  - Total cholesterol
  - HDA and LDL cholesterol
  - Triglycerides
- Other Tests:
  - Hematocrit
  - ECG

ADDITIONAL

On case to case basis

- Complement levels and autoimmune profile such as hsCRP, LP(a), 24 hour urinary fractionated metanephrines and non metanephrine
- 24 hour urinary free cortisol or low dose dexamethasone suppression test
- Fundus examination

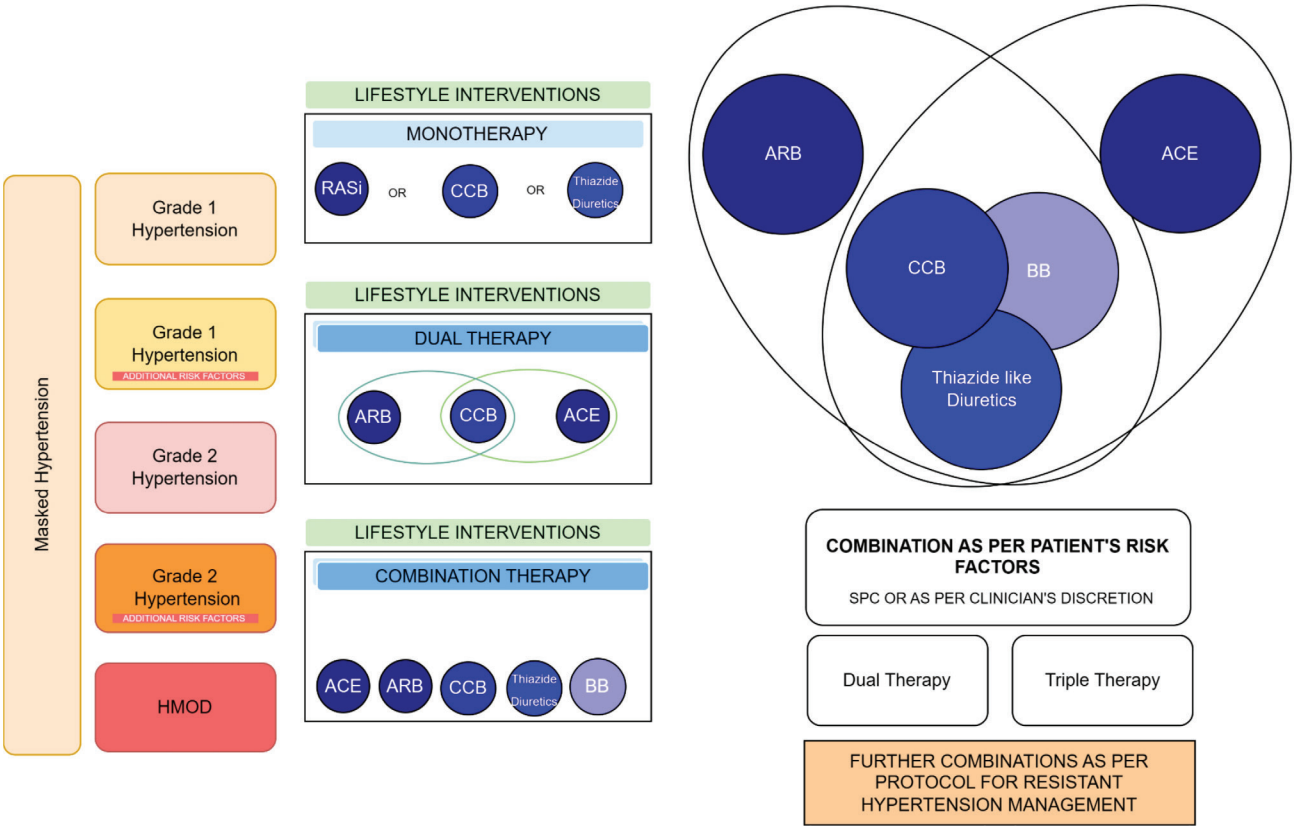


Figure 10: Hypertension management at a glance

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