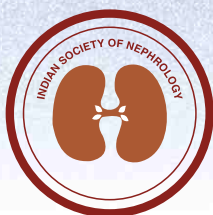


INDIAN HYPERTENSION GUIDELINES-II

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Convenor : Dr. Siddharth Shah

INDIAN HYPERTENSION GUIDELINES-II

CONTENTS

	Page
PREAMBLE	1
LIST OF MEMBERS	2-4
DEFINITION AND CLASSIFICATION	5
• Definition	5
• Classification	5
EPIDEMIOLOGY	7-9
MEASUREMENT OF BLOOD PRESSURE	10-11
• Clinic Measurement	10
• Home Measurement	11
• Ambulatory Blood Pressure Monitoring	11
EVALUATION	12-14
• Medical History	12
• Physical Examination	12
• Laboratory Investigations	13
• Factors Influencing Risks and Risk Stratification	13



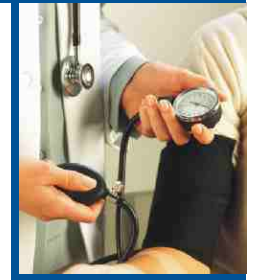
INDIAN HYPERTENSION GUIDELINES-II



MANAGEMENT OF HYPERTENSION	15-26
• Goals of Therapy	15
• Management Strategy	15
• Non-pharmacologic Therapy	16
- Principles of diet in hypertension	17
• Pharmacologic Therapy	19
- Principles of drug treatment	19
- Antihypertensive drugs	19
- Diuretics	19
- Beta-blockers	20
- Calcium channel blockers (CCBs)	20
- Angiotensin converting enzyme inhibitors (ACE inhibitors)	20
- Angiotensin II receptor blockers (ARBs)	20
- Alpha-blockers	21
- Other drugs	21
- Antihypertensive drug combinations	23
• Drug Interactions	24
• Maintenance and Follow-up of Therapy	25
• Adverse Drug Reactions	26
• Associated Therapies	26
SECONDARY HYPERTENSION	27-28
• Prevalence	27
• Presentation	27
• Important Causes	28

INDIAN HYPERTENSION GUIDELINES-II

COMPLICATIONS	30
HYPERTENSION IN SPECIAL SITUATIONS	31-39
• Hypertension with Diabetes Mellitus	31
• Hypertension with Renal Disease	31
• Hypertension with Cerebrovascular Disease	32
• Hypertension in Women	33
• Hypertension in Pregnancy	33
• Hypertension in the Elderly	34
• Isolated Systolic Hypertension	35
• Hypertension with Congestive Cardiac Failure	35
• Hypertension with Chronic Obstructive Airway Disease	35
• Hypertension with Coronary Artery Disease	36
• Hypertension with Dyslipidemia	36
• Hypertension with Obesity and Metabolic Syndrome	37
• Resistant Hypertension	38
• Hypertensive Crises	39
REFERENCES	40-46



INDIAN HYPERTENSION GUIDELINES-II

PREAMBLE

Hypertension is a major contributor to cardiovascular morbidity and mortality in India and worldwide. In view of our special geographical, ethnic, climatic conditions, dietary habits, literacy levels and socio-economic variables, there could be some areas where significant differences need to be addressed. With this in mind, the Association of Physicians of India (API), Cardiological Society of India (CSI), the Indian College of Physicians (ICP), and the Hypertension Society of India (HSI) developed the "FIRST INDIAN GUIDELINES FOR THE MANAGEMENT OF HYPERTENSION - 2001."

Significant new data has emerged in last 6 years in areas of epidemiology, classification of hypertension and management strategies. Guidelines such as the JNC, BHS, ESH/ESC, NICE, and WHO-ISH have been revised based on emerging evidence from large, randomized controlled clinical trials. It was, therefore, felt necessary to update the Indian guidelines to align them with the current best evidence. Henceforth, the first Indian guidelines have been revised and updated and the second guidelines IGH II -2007 are being published under the stewardship of API.

These guidelines have been prepared as a reference for treating physicians. The current level of practice patterns based on evidence-based medicine have been presented. We understand that with the evolving knowledge in the field of hypertension, these guidelines will need to be modified from time to time. The intention is not to cover the topic of hypertension in totality but to give useful information based on literature after extensive reference to Medline search and other latest guidelines (JNC VII, ESH/ESC, NICE-BHS, WHO-ISH) available to date. These guidelines do not include hypertension in children and adolescents.

The primary aim of these guidelines is to offer balanced information to guide clinicians, rather than rigid rules that would constrain their judgement about the management of individual patients, who will differ in their personal, medical, social, economic, ethnic and clinical characteristics.

Methodology

The first Indian guidelines were formulated by a core committee who in turn, were supported by a working group. The document was then circulated to about 250 doctors whose inputs were incorporated in the final version. The updated guidelines have been reviewed by a panel of experts so as to arrive at a consensus. There have been three meetings at which the evidence since 2001 and the US, European, British and WHO guidelines were reviewed. Relevant portions of the first Indian guidelines were revised. New data from the latest gold standard clinical trials was added as well as data from Indian studies wherever applicable. Once the document was drafted, it was circulated to a group of 25 reviewers. The final document has been endorsed by the API, CSI, HSI, Indian Society of Nephrology (ISN) and Indian Medical Association (IMA).

We hope these guidelines will help the practising physicians to address to a very important public health problem. Treatment of essential hypertension is a life-long commitment and should not be stopped even when the blood pressure is stabilised without consulting the physician.

The core committee recognizes that the responsible physician's judgment remains paramount for individual patients.

INDIAN HYPERTENSION GUIDELINES-II

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INDIAN HYPERTENSION GUIDELINES-II

DEFINITION AND CLASSIFICATION

Definition

There is a continuous relationship between the level of blood pressure and the risk of complications. Starting at 115/75 mmHg, CVD risk doubles with each increment of 20/10 mmHg throughout the blood pressure range.^{1,2} All definitions of hypertension issued by various international authorities are arbitrary. While it is possible that the risk of cardiovascular events in Asian Indians is higher at relatively lower levels of blood pressure (BP), in the absence of any such data from India, it would be prudent to avoid any further confusion and maintain the same definition proposed in the first Indian guidelines on management of hypertension (2001).³

Hypertension in adults age 18 years and older is defined as systolic blood pressure (SBP) of 140 mm Hg or greater and/or diastolic blood pressure (DBP) of 90 mm Hg or greater or any level of blood pressure in patients taking antihypertensive medication.^{2,3}

Classification

The positive relationship between SBP and DBP and cardiovascular risk has long been recognized. This relationship is strong, continuous, graded, consistent, independent, predictive, and etiologically significant for those with and without coronary heart disease.^{4,5} For persons over age 50, SBP is more important than DBP as a CVD risk factor.⁶ SBP is more difficult to control than DBP.^{7,8} SBP needs to be as aggressively controlled as DBP. Therefore, although classification of adult blood pressure is somewhat arbitrary, it is useful to clinicians who make treatment decisions based on a constellation of factors including the actual level of blood pressure. Table 1 provides a classification of blood pressure for adults (age 18 and older).^{3,9} This classification is for individuals who are not taking antihypertensive medication and who have no acute illness and is based on the average of two or more blood pressure readings taken at least on two subsequent occasions, one to three weeks apart, after the initial screening. When SBP and DBP fall into different categories, the higher category should be selected to classify the individual's blood pressure.

It is felt that the more recently coined term “prehypertension”² includes a wide range from normal to high normal. The high normal group needs to be treated in presence of family history of hypertension and concomitant diseases like diabetes and target organ damage (TOD).¹⁰ Also, the term prehypertension introduced in the JNC VII guidelines is more likely to create anxiety in a large subset of population. Hence, we do not recommend the use of the term “pre-hypertension.”⁹

INDIAN HYPERTENSION GUIDELINES-II

Table 1: Classification of blood pressure for adults age 18 and older^{*3,9}

Category	Systolic (mm Hg)		Diastolic (mm Hg)
Optimal**	<120	and	<80
Normal	<130	and	<85
High-normal	130-139	or	85-89
Hypertension***			
Stage 1	140-159	or	90-99
Stage 2	160-179	or	100-109
Stage 3	≥180	or	≥110
Isolated systolic hypertension			
Grade 1	140-159	and	<90
Grade 2	≥160	and	<90
<p>* Not taking antihypertensive drugs and not acutely ill. In addition to classifying stages of hypertension on the basis of average blood pressure levels, clinicians should specify presence or absence of target organ disease and additional risk factors.</p> <p>** Optimal blood pressure with respect to cardiovascular risk is below 120/80 mm Hg. However unusually low readings should be evaluated for clinical significance.</p> <p>*** Based on the average of two or more blood pressure readings taken at least on two visits after an initial screening.</p>			

INDIAN HYPERTENSION GUIDELINES-II

EPIDEMIOLOGY

Cardiovascular diseases caused 2.3 million deaths in India in the year 1990; this is projected to double by the year 2020. Hypertension is directly responsible for 57% of all stroke deaths and 24% of all coronary heart disease deaths in India. There is a strong correlation between changing lifestyle factors and increase in hypertension in India. The nature of genetic contribution and gene-environment interaction in accelerating the hypertension epidemic in India needs more studies. Pooling of epidemiological studies shows that hypertension is present in 25% urban and 10% rural subjects in India. At an underestimate, there are 31.5 million hypertensives in rural and 34 million in urban populations. A total of 70% of these would be Stage I hypertension (systolic BP 140-159 and/or diastolic BP 90-99 mmHg). Recent reports show that borderline hypertension (systolic BP 130-139 and/or diastolic BP 85-89 mmHg) and Stage I hypertension carry a significant cardiovascular risk and there is a need to reduce this blood pressure.¹¹

According to a recent review on “the global burden of hypertension”, the estimated prevalence of hypertension (in people aged 20 years and older) in India in 2000 was 20.6% among males and 20.9% among females and is projected to increase to 22.9% and 23.6% respectively in 2025.¹² The estimated total number of people with hypertension in India in 2000 was 60.4 million males and 57.8 million females and projected to increase to 107.3 million and 106.2 million respectively in 2025.¹²

There are multiple single centre studies on prevalence of hypertension available from across the country. However, there is no multicentric national prevalence data. Over the years with changing definition, a lower level of pressure (140/90) is being used as a cut-off point to define hypertension as compared to previous studies, which used higher levels of pressure (160/95). This vitiates any assessment of trends of hypertension prevalence over the past few decades. Nevertheless, there appears to be a steady increase in hypertension prevalence over the last 50 years, more in urban than in rural areas. It is well recognized that hypertension is now a major health problem in India. The various epidemiological studies published from India over the last 5 decades are tabulated in Tables 2 and 3. A review of this data shows that prevalence of hypertension has progressively increased over the last 5 decades, particularly in the urban areas. Majority of these studies have shortcomings, in that they have used differing examination techniques, differing diagnostic criteria and only screening blood pressure values for defining hypertension. The fact that hypertension is a major health problem in our country calls for large, nationwide, multi-centric, prospective and supervised epidemiological studies.

INDIAN HYPERTENSION GUIDELINES-II

Table 2: Studies on prevalence of hypertension in Urban Indian population^{11,13-17}

Author	Place	Year	Age Group (Years)	Hypertension Criteria (mm Hg)	Men		Women	
					%	Sample size	%	Sample size
Mathur	Agra	1963	>20	≥160/95	3.98	(1408)	6.64	(227)
Malhotra	Railways	1970	20-58	≥160/95	6.2 ^a	(2638)	—	—
					15.2 ^b	(1594)		
Gupta SP	Rohtak	1978	>20	≥160/95	6.00	(1151)	7.00	(872)
Dalal	Mumbai	1980	>18	Variable	15.63	(3148)	15.38	(2575)
Wasir	New Delhi	1984	20-60	≥160/95	3.80	(1767)	1.45	(688)
Ahmed	Karnataka	1988	>21	DBP > 90	10.20	(698)	2.00	(102)
Hussain	Rajasthan	1988	20-60	≥140/90	6.15	(1561)	7.33	(1103)
Chaddha	New Delhi	1990	25-64	≥160/90	11.66	(637)	13.68	(7351)
Gupta R	Jaipur	1995	>20	≥140/90	30.00	(1415)	34.00	(797)
Anand*	Mumbai	2000	28-65	≥140/90*	26.78	(1512)	27.65	(141)
Shanthirani	Chennai	2003	>20	≥140/90	22.8	(557)	19.7	(705)
Gupta R	Jaipur	2002	≥20	≥140/90	36.36	(550)	37.52	(573)
Bharucha	Mumbai	2003	≥20	≥140/90	32.8	(1099)	39.4	(1316)
Deepa	Chennai	2004	≥20	≥140/90,	22.1 [#]	(1262) [#]	—	—
Ashavaid	Mumbai	2004	—	≥140/90	22.5 [#]	(39940) [#]	—	—

^a North Indians

^b South Indians

* Diagnosis of hypertension based on the average of three readings on the 2nd occasion after the initial screening

[#] Overall prevalence and total sample size for men and women

INDIAN HYPERTENSION GUIDELINES-II

Table 3: Studies on prevalence of hypertension in Rural Indian population ^{13,18,19}								
Author	Place	Year	Age Group (Years)	Hypertension Criteria (mm Hg)	Prevalence			
					Men		Women	
					%	Sample size	%	Sample size
Gupta SP	Haryana	1977	20-69	≥160/95	3.50	(1154)	3.69	(891)
Wasir	Delhi	1983	>20	≥160/95	3.20	(441)	7.50	(464)
Baldwa	Rajasthan	1984	21-60	≥141/91	6.93	(447)	8.81	(465)
Puri	Himalayas	1986	15-82	≥160/95	2.44	(1592)	2.38	(1511)
Hussain	Rajasthan	1988	20-60	≥140/90	5.72	(1328)	6.43	(1150)
Kumar	Rajasthan	1991	>21	≥160/95	4.00	(3742)	3.60	(3098)
Joshi	Maharashtra	1993	>16	≥160/95	4.85	(227)	3.17	(221)
Jajoo	Maharashtra	1993	>20	≥160/95	2.89	(2247)	4.06	(1798)
Agarwal	Uttar Pradesh	1994	>20	≥160/95	1.57	(3760)	—	—
Malhotra	Haryana	1999	16-70	≥140/90	3.00	(2559) [#]	5.80	—
Hazarika	Assam	2004	>30	JNC-VI	33.3 [*]	(3180) [#]	—	—
Thankappan	Kerala	2006	>30	JNC VII	36	(2159)	37.2	(2796)

[#] Total sample size for men & women

^{*} Overall prevalence for men and women

In India and its surrounding countries, awareness level for hypertension is $\leq 45\%$.^{20,21} Only half of these are on treatment and adequacy of control of blood pressure is very poor and in one such study, it has been observed in $<10\%$ of the total hypertensive population.¹⁹ Thus, there is a need to increase awareness, detection and adequate control of blood pressure.

INDIAN HYPERTENSION GUIDELINES-II

MEASUREMENT OF BLOOD PRESSURE

Clinic measurement

- Blood pressure (BP) is characterized by large spontaneous variations, therefore the diagnosis of hypertension should be based on multiple BP measurements taken on several separate occasions.
- Standard mercury sphygmomanometer should be used. Use a standard cuff with a bladder that is 12 cm X 35 cm. Use a large bladder for fat arms and a small bladder for children. The bladder should encircle and cover two-thirds of the length of the arm. Proper maintenance and calibration of the sphygmomanometer should be ensured. Whenever aneroid sphygmomanometer is used, its accuracy should be checked against standard mercury sphygmomanometer at regular intervals.
- For measurement, inflate the bladder quickly to a pressure 20 mm Hg higher than the point of disappearance of the radial pulse. Deflate the bladder slowly by 2 mm Hg every second.
- The first appearance of the sound (Phase I Korotkoff) is the systolic BP. The disappearance of the sound (Phase V Korotkoff) is the diastolic BP. For children and in those with high output states, muffling of the sound (Phase IV Korotkoff) is taken as diastolic pressure.

Precautions

The following precautions are required for correct measurement of blood pressure:

- At the initial visit, an average of three readings, taken at intervals of 2-3 minutes should be recorded.
- For confirmation of diagnosis of hypertension, record at least 3 sets of readings on different occasions, except in Stage III hypertension.
- Patients should be asked to refrain from smoking or drinking tea/coffee, exercise for at least 30 minutes before measuring the BP.
- Allow the patient to sit for at least five minutes in a quiet room before beginning blood pressure measurement.
- Measurement should be done preferably in a sitting or supine position. Patient's arm should be fully bared and supported at the level of the heart.
- Measure the blood pressure in both arms at the first visit and use higher of the two readings.
- In older persons aged 60 years and above, in diabetic subjects and patients on antihypertensive therapy, the BP should be measured in both, supine/sitting and in standing positions to detect postural hypotension.
- If atrial fibrillation is present, additional readings may be required to estimate the average SBP and DBP.
- Occasionally, thigh BP (popliteal) has to be measured with appropriately large cuff, especially in younger persons with hypertension. Normally thigh SBP is higher and DBP a little lower than the arm BP because of the reflected pulse wave. This is important for suspected coarctation and non-specific aortoarteritis.

INDIAN HYPERTENSION GUIDELINES-II

Home BP measurement

Measurement of blood pressure outside the clinic may provide valuable information for the initial evaluation of patients with hypertension and for monitoring the response to treatment. Home measurement has the advantage that it distinguishes sustained hypertension from "white-coat hypertension", a condition noted in patients whose blood pressure is elevated in the physician's clinic but normal at other times. There is no universally agreed upper limit of normal home blood pressure, but readings of 135/85 mm Hg or greater should be considered elevated.

In our country, considering the socioeconomic and educational level, this method has limitations and may not be generally advocated.

Although the mercury sphygmomanometer is still the most accurate device for clinical use, it is generally less practical for home use. The electronic devices when used should be periodically checked by simultaneous recordings taken with mercury sphygmomanometer. Finger monitors are inaccurate and are not recommended. The patient should be educated not to change medication without consulting their physician.

Self-measurement although ensures patient compliance due to participation, carries a risk of generating greater anxiety and thereby self-modification of treatment.

Ambulatory blood pressure monitoring

It has been found that at least 20-25% of patients diagnosed with stage I-II hypertension (DBP 90-104 mm Hg) are normotensive outside the physician's clinic. Ambulatory blood pressure monitoring (ABPM) has been found to be clinically useful only in the following settings: to identify non-dippers and white-coat hypertension, evaluate drug resistant hypertension, episodic hypertension, evaluate antihypertensive drugs and in individuals with hypotensive episodes while on antihypertensive medication. However, this procedure should not be used indiscriminately in the routine work-up of a hypertensive patient because of its high cost.

BP has a reproducible circadian profile with higher values while awake and mentally and physically active, whereas, much lower values during rest and sleep. Different values have been suggested for definition of hypertension with ABPM for day time average BP (>140/90 mm Hg) and the night-time average (>125/75 mm Hg). Early morning surge in BP for 3 or more hours during transition from sleep to wakefulness, can be an independent risk factor and needs to be managed effectively.²²

Table 4: Blood pressure thresholds (mm Hg) for definition of hypertension with different types of measurement.²³

	SBP (mm Hg)	DBP (mm Hg)
Office or Clinic	140	90
Home (self)	135	85
ABPM (24-hour average)	125	80

SBP: Systolic Blood Pressure; **DBP:** Diastolic Blood Pressure

INDIAN HYPERTENSION GUIDELINES-II

EVALUATION

Evaluation of patients with documented hypertension has three objectives:

- To identify known causes of high blood pressure
- To assess the presence or absence of target organ damage
- To identify other cardiovascular risk factors or concomitant disorders that may define prognosis and guide treatment

Data for evaluation is acquired through medical history, physical examination, laboratory tests, and other special diagnostic procedures

Medical history

- Duration and level of elevated blood pressure, if known
- Symptoms of coronary artery disease (CAD), heart failure, cerebrovascular disease, peripheral vascular disease and CKD
- Diabetes mellitus, dyslipidaemia, obesity, gout, sexual dysfunction and other co-morbid conditions
- Family history of high blood pressure, obesity, premature CAD and stroke, dyslipidaemia and diabetes
- Symptoms suggesting secondary causes of hypertension
- History of smoking or tobacco use, physical activity, dietary assessment including intake of sodium, alcohol, saturated fat and caffeine
- Socioeconomic status, professional and educational levels
- History of use / intake of all prescribed and over-the-counter medications, herbal remedies, licorice (*Yashtimadhu/Jestamadha*), illicit drugs, corticosteroids, NSAIDs, nasal drops. These may raise blood pressure or interfere with the effectiveness of antihypertensive drugs
- History of oral contraceptive use and hypertension during pregnancy
- History of previous antihypertensive therapy, including adverse effects experienced, if any
- Psychosocial and environmental factors

Physical examination

- Record three blood pressure readings separated by 2 minutes, with the patient either supine or sitting position and after standing for at least 2 minutes.
- Record height, weight and waist circumference.
- Examine the pulse and the extremities for delayed or absent femoral and peripheral arterial pulsations, bruits and pedal oedema.
- Look for arcus senilis, acanthosis nigricans, xanthelasma and xanthomas.
- Examine the neck for carotid bruits, raised JVP or an enlarged thyroid gland.
- Examine the heart for abnormalities in rate and rhythm, location of apex beat, fourth heart sound and murmurs.
- Examine the lungs for rales and rhonchi.
- Examine the abdomen for bruits, enlarged kidneys, masses and abnormal aortic pulsation.
- Examine the optic fundus and do a neurological assessment.

INDIAN HYPERTENSION GUIDELINES-II

Laboratory investigations

- Routine:
 - Urine examination for protein and glucose and microscopic examination for RBCs and other sediments.
 - Haemoglobin, fasting blood glucose, serum creatinine, potassium and total cholesterol
 - 12-lead electrocardiogram
- Additional investigations in special circumstances can include
 - Fasting lipid profile and uric acid
 - Echocardiogram
- Other specific tests to rule out secondary causes of hypertension where there is a high index of suspicion are described under “secondary hypertension”.
- At the present state, tests for HS-CRP, serum homocysteine levels and microalbuminuria are not recommended for routine clinical use.
- The cost of investigations in the context of the needs of an individual patient and resources available is an important consideration. In patients with essential hypertension where there is a resource crunch, one may be required to initiate therapy without carrying out any laboratory investigations.

Factors influencing risk

Before initiating therapy, patients’ overall risk should be assessed considering the presence or absence of additional risk factors; extent of target organ damage and other associated clinical conditions.

Table 5: Factors influencing risk of cardiovascular disease

Risk factors for coronary artery disease (RF)	Target organ damage (TOD)	Associated clinical conditions (ACC)
<ul style="list-style-type: none"> • Age > 55 years • Male sex • Post-menopausal women • Smoking and tobacco use • Diabetes mellitus • Family history of premature CAD (Males < 55 years, Female < 65 years) • Increased Waist hip ratio, High LDL or total cholesterol, Low HDL cholesterol and High triglycerides • High sensitivity C-reactive protein (HS-CRP) and homocysteine levels might evolve as markers for high risk of vascular damage • Estimated GFR <60 mL/min 	<ul style="list-style-type: none"> • Left ventricular hypertrophy detected by ECG and/or echocardiogram • Microalbuminuria/ proteinuria and/or elevation of serum creatinine (1.2-2.0 mg/dl) • Urinary ACR (albumin creatinine ratio) • Ultrasound or radiological evidence of atherosclerotic plaques in the carotids • Hypertensive retinopathy 	<ul style="list-style-type: none"> • Cerebrovascular disease <ul style="list-style-type: none"> - Ischemic stroke - Cerebral haemorrhage - Transient ischemic attack • Heart disease <ul style="list-style-type: none"> - Myocardial infarction - Angina - Coronary revascularization - Congestive heart failure • Renal disease <ul style="list-style-type: none"> - Diabetic nephropathy - Renal failure (serum creatinine > 2.0 mg/dl) • Vascular disease <ul style="list-style-type: none"> - Peripheral arterial disease including non-specific aortoarteritis - Aortic dissection • Advanced hypertensive retinopathy <ul style="list-style-type: none"> - Haemorrhages or exudates - Papilledema

INDIAN HYPERTENSION GUIDELINES-II

The prognosis of these patients and the choice and need for urgency of therapy, will be dependent on the overall risk stratification (Table 6)

Hyperhomocysteinemia (hyperHcy) has been associated with hypertension and higher CV risk.^{24,25,26} Whether the relation between total plasma homocysteine (tHcy) and cardiovascular disease is causal or not remains controversial.^{27,28} Large prospective controlled trials in patients with concomitant hypertension and hyperHcy should be conducted to evaluate the impact of tHcy lowering therapy on endpoints related to hypertension and its complications.

Table 6: Risk stratification of patients with hypertension				
		Blood pressure (mm Hg)		
Stage	Other risk factors and disease history	Stage 1	Stage 2	Stage 3 (severe hypertension)
		SBP 140-159 or DBP 90-99	SBP 160-179 or DBP 100-109	SBP \geq 180 or DBP \geq 110
I	No other risk factors	Low risk	Medium risk	High risk
II	1-2 risk factors ^a	Medium risk	Medium risk	Very high risk
III	3 or more risk factors or TOD ^b or diabetes	High risk	High risk	Very high risk
IV	ACC ^c	Very high risk	Very high risk	Very high risk

Risk strata (typical 10 year risk of stroke or myocardial infarction):
 Low risk = Less than 15%
 Medium risk = about 15-20%
 High risk = about 20-30%
 Very high risk = 30% or more

^a See Table 5
^b TOD: Target Organ Damage see Table 5
^c ACC: Associated clinical conditions, including clinical cardiovascular disease or renal disease see Table 5

INDIAN HYPERTENSION GUIDELINES-II

MANAGEMENT OF HYPERTENSION

Goals of therapy

The primary goal of therapy of hypertension should be effective control of BP in order to prevent, reverse or delay the progression of complications and thus reduce the overall risk of an individual without adversely affecting the quality of life.

Initiation of therapy

Having assessed the patient and determined the overall risk profile, management of hypertension should proceed as follows:

- In low risk patients, institute life style modifications and observe BP for a period of 3 months, before deciding whether to initiate drug therapy.
- In medium risk patients, institute life style modifications and monitor BP on a monthly basis. If after a period of 2-3 months, BP remains above 140/90, then initiate drug therapy.
- In high and very high-risk groups, initiate immediate drug treatment for hypertension and other risk factors.

Targets of therapy

- The earlier concern that lowering DBP too much may increase the risk of coronary events by lowering diastolic perfusion pressure in coronary circulation (J-curve hypothesis) has not been supported by recent studies.²⁹
- Gradual reduction of BP is a prudent therapeutic approach except in stage 3 hypertension.
- In Hypertension Optimal Treatment (HOT) study (target diastolic pressure less than 90, 85 or 80 mm Hg) there was no increase in cardiovascular risk in patients randomized to the lowest target group (DBP<80 mm Hg).
- Among diabetic patients participating in the HOT study, there was a significantly lower risk of CAD in patients with the lowest target DBP.²⁹
- The results of United Kingdom Prospective Diabetes Study (UKPDS) demonstrated that a tight control of BP (average achieved : 144/82 mm Hg) in diabetic patients conferred a substantial reduction in the risk of CAD compared to a less tight control of BP (average achieved: 154/87 mm Hg).³⁰
- The PROGRESS trial showed that in patients with a history of stroke or TIA, stroke risk was reduced not only in participants classified as hypertensive, but also among those classified as non-hypertensive, among whom the mean blood pressure at entry was 136/79 mm Hg.³¹
- In view of the above studies, it would seem desirable to achieve optimal or normal BP in young and middle aged. In diabetic subjects (below 130 / 80 mm Hg), or patients with stroke (below 130/85 mm Hg) and at least high normal BP in elderly patients (below 140/90 mm Hg). Antihypertensive therapy should achieve and maintain SBP below 140 mm Hg and DBP below 90 mm Hg and lower if tolerated, while controlling other modifiable risk factors.

Management strategy

- Recent evidence suggests that the level of SBP control correlates better with reduction of mortality than the level of DBP control.³¹⁻³⁹
- Impressive evidence has accumulated to warrant greater attention to the importance of SBP as a major risk factor for CVDs. The rise in SBP continues throughout life, in contrast to DBP, which rises until approximately 50 years old, tends to level off over the next decade, and may remain the same or fall later in life. Diastolic hypertension predominates before 50 years of age, either alone or in combination with SBP elevation. DBP is a more potent cardiovascular risk factor than SBP until age 50; thereafter, SBP is more important.²

INDIAN HYPERTENSION GUIDELINES-II

- Trials describe population averages for the purposes of developing guidelines, whereas physicians must focus on the individual patient's clinical responses".⁴⁰

Non-pharmacologic therapy

Life style measures should be instituted in all patients including those who require immediate drug treatment. These include:

- Patient education: Patients need to be educated about the various aspects of the disease, adherence to life style changes on long term basis and need for regular monitoring and therapy.
- Weight reduction: Weight reduction of even as little as 4.5 kg has been found to reduce blood pressure in a large proportion of overweight persons with hypertension.⁴¹
- Physical activity: Regular aerobic physical activity can promote weight loss, increase functional status and decrease the risk of cardiovascular disease and all cause mortality. A program of 30-45 minutes of brisk walking or swimming at least 3-4 times a week could lower SBP by 7-8 mm Hg. Isometric exercises such as weight lifting should be avoided as they lead to pressor effects.
- Alcohol intake: Excess alcohol intake causes a rise in blood pressure, induces resistance to antihypertensive therapy and also increases the risk of stroke.^{42,43}
- Salt intake: Epidemiological evidence suggests an association between dietary salt intake and elevated blood pressure. The total daily intake of salt should be restricted to 6 gms, however, in hot summer this may be relaxed. Patients should be advised to avoid added salt, processed foods, and salt-containing foods such as pickles, papads, chips, chutneys and preparations containing baking powder. In the Indian context, salt restriction is more important as Indian cooking involves a high usage of salt.

Table 7: Lifestyle interventions for blood pressure reduction (adapted from Chobanian, Hypertension 2003)		
Intervention	Recommendation	Expected systolic blood pressure reduction (range)
Weight reduction	Maintain ideal body mass index Below 23 Kg/m ²	5-20 mm Hg per 10 kg weight loss
DASH* eating plan	Consume diet rich in fruits, vegetables, low-fat dairy products with reduced content of saturated and total fat	8-14 mm Hg
Dietary sodium Restriction	Reduce dietary sodium intake to <100 mmol/day (<2.4 g sodium or <6 g sodium chloride)	2-8 mm Hg
Physical activity	Engage in regular aerobic physical activity, for example, brisk walking for at least 30 min most days	4-9 mm Hg
Alcohol moderation	Men≤60 ml per day, twice a week Women≤30 ml per day, twice a week. Abstinence is preferred	2-4 mm Hg
Tobacco	Total abstinence	—

* DASH= Dietary Approaches to Stop Hypertension

INDIAN HYPERTENSION GUIDELINES-II

- Smoking: Smoking or consumption of tobacco in any form is the single most powerful modifiable lifestyle factor for prevention of major cardiovascular and non-cardiovascular disease in hypertensives.⁴⁴⁻⁴⁶ Cardiovascular benefits of cessation of smoking can be seen within one year in all age groups.⁴⁶
- Yoga & Meditation: Yoga, meditation and biofeedback have been shown to reduce blood pressure.⁴⁷⁻⁵⁰
- Diet:
 - Vegetarians have a lower blood pressure compared to meat eaters⁵¹. This is due to a higher intake of fruit, vegetables, fibers coupled with a low intake of saturated fats and not due to an absence of intake of meat protein.⁵²
 - Intake of saturated fats is to be reduced since concomitant hyperlipidaemia is often present in hypertensives.
 - Regular fish consumption may enhance blood pressure reduction in obese hypertensives.⁵³
 - Adequate potassium intake from fresh fruits and vegetables may improve blood pressure control in hypertensives.⁵⁴
 - Caffeine intake increases blood pressure acutely but there is rapid development of tolerance to its pressor effect. Epidemiological studies have not demonstrated a direct link between caffeine intake and high blood pressure.⁴²
- Principles of diet in hypertension:^{55,56}
Low calorie, Low fat, Low sodium diet with normal protein intake (0.8 gm / kg body wt)
- Foods with low/moderate content of sodium are recommended. Intake of foods with high potassium content is advisable.

Table 8: Sodium content of foods per 100 gms^{55,56}

<25 mg Low		25-50 mg Moderate	50-100 mg Moderately High	>100 mg High
Amla	Cow pea	Raisins	Cauliflower	Amaranth
Bitter gourd	Horse gram	Broad beans	Fenugreek	Bacon
Bottle gourd	Ragi	Carrots	Lettuce	Egg
Brinjal	Vermicelli	Raddish white	Field beans	Lobster
Cabbage	Semolina	Black gram dal	Beetroot	
Lady finger	Wheat	Green gram dal	Water melon	
Colocasia	Maida	Red gram dal	Bengal gram dal	
Cucumber	Milk	Lentil whole	Red gram tender	
French beans	Grapes	Bengal gram whole	Liver	
Peas	Sweetlime	Banana	Prawns	
Onion	Papaya	Pineapple	Beef	
Potato	Orange	Apple	Chicken	
Tomato ripe	Sapota	Mutton		
Yam				

Reduce dietary sodium intake to not more than 6 gm sodium chloride

INDIAN HYPERTENSION GUIDELINES-II

Table 9: Food items to be avoided in hypertensives^{55,56}

A	B
Table Salt Mono sodium glutamate (Ajinomoto) Baking powder Sodium bicarbonate Fried foods Alcohol	Salt preserved foods: Pickles and canned foods Ketchup and sauces Prepared mixes Ready to eat foods Highly salted foods: Potato chips, cheese, peanut butter, salted butter, papads Bakery products: Biscuits, cakes, breads and pastries

Table 10: Foods with high potassium^{55,56}

Fruits :		Vegetables:	
Amla	Plums	Cabbage	Raddish white
Sapota	Lemon	Bitter gourd	Brinjal
Peaches	Sweetlime	Ladies finger	Pumpkin
Orange	Pineapple	Cauliflower	French beans
Papaya	Apple	Spinach	Colocasia
Banana	Watermelon	Potato	Tapioca
		Drumstick	

INDIAN HYPERTENSION GUIDELINES-II

Pharmacologic therapy

Principles of drug treatment

- Over the past decade, the goals of treatment have gradually shifted from optimal lowering of blood pressure, which is taken for granted, to patient's overall well being, control of associated risk factors and protection from future target organ damage.⁵⁷
- Achieve gradual reduction of blood pressure. Use low doses of antihypertensive drugs to initiate therapy.
- Five classes of drugs can be recommended as first line treatment for stage 1-2 hypertension^{1,2} These include :1) diuretics, 2) beta-blockers, 3) calcium channel blockers, 4) ACE inhibitors, 5) angiotensin II receptor blockers. With regard to lowering of blood pressure, all these five classes are equally effective. The Blood Pressure Lowering Treatment Trialists' Collaboration concluded that treatment with any commonly used regimen reduces the risk of total major cardiovascular events and larger reductions in blood pressure produce larger reductions in risk.⁵⁸
- Low dose diuretics may be preferred as initial therapy unless there are compelling or specific indications for other classes (Table 11).
- Choice of an antihypertensive agent is influenced by age, concomitant risk factors, presence of target organ damage, other co-existing diseases, socioeconomic considerations, availability of the drug and past experience of the physician.
- Combining low doses of two drugs having synergistic effect is likely to produce lesser side effects. In 60-70 % of patients, goal blood pressure will be achieved with two or more agents only.
- Use of fixed dose formulations may be considered to improve compliance.
- If a diuretic is not chosen as the first drug, it is usually indicated as a second step agent because its addition enhances the effects of other agents except dihydropyridine calcium channel blockers.
- Use of long acting drugs that provide 24-hour efficacy with once daily administration ensures smooth and sustained control of blood pressure; which in turn is expected to provide greater protection against the risk of major cardiovascular events and target organ damage. Once daily administration also improves patient compliance.
- Although antihypertensive therapy is generally lifelong, an effort to decrease the dosage and number of antihypertensive drugs should be considered after effective control of hypertension (step-down therapy).
- Due to a greater seasonal variation of temperatures in India, marginal alterations in dosages of drugs may be needed from time to time.
- If addition of a second agent controls blood pressure satisfactorily, an attempt to withdraw the first agent may be considered.

Antihypertensive drugs

Diuretics

Diuretics are widely used as first line agents. They are effective and inexpensive. Although high dose diuretic therapy was associated with side effects, currently recommended low dose diuretic therapy is generally well tolerated. Diuretics should be used in doses equivalent to 12.5 mg daily of hydrochlorothiazide to avoid adverse metabolic consequences. Indapamide use has been shown to be associated with minimal metabolic side effects.

INDIAN HYPERTENSION GUIDELINES-II

Beta-blockers

Beta-blockers are effective, inexpensive, and relatively well tolerated. These drugs should be avoided in patients with obstructive airway disease and peripheral vascular disease. They also have limitations in patients with dyslipidemia and impaired glucose tolerance. However, they are preferred in young hypertensives, those with stable and unstable angina and post-MI patients with hypertension. Cardioselective beta-blockers (metoprolol) should be preferred over non-selective ones (propranolol). Agents with intrinsic sympathomimetic activity and highly selective beta-blockers such as bisoprolol and nebivolol have lesser metabolic adverse effects. Emerging evidence suggests that beta-blockers are losing their pre-eminent place as first-line antihypertensive agents. This is based on the head to head trials where it was found that beta-blockers are less effective than ACEIs or CCBs at reducing the risk of diabetes and stroke. This was particularly true in patients taking beta-blockers and diuretics. It is observed that in most of these studies, the beta-blocker used was atenolol and in the absence of substantial data on other agents it would not be wise to apply this conclusion to all beta-blockers. The role of beta-blockers could be considered as compelling in certain situations like younger people, those intolerant to ACEIs and ARBs, women of child bearing potential, and people with evidence of increased sympathetic drive. Also, the role of beta-blockers in situations of cardiac decompensation and IHD is not in doubt.

Calcium Channel Blockers (CCBs)

The subgroups of CCBs are dihydropyridines (nifedipine and amlodipine) and non-dihydropyridines (verapamil and diltiazem). Besides blood pressure lowering effect, they also have antianginal effects and are devoid of metabolic side effects. CCBs are particularly recommended for elderly patients with isolated systolic hypertension. Verapamil and diltiazem reduce heart rate and have negative inotropic effects. In the Nordic diltiazem (NORDIL) study,⁵⁹ diltiazem was shown to be as effective as treatment based on diuretics, beta-blockers or both, in preventing the combined primary endpoints of stroke, myocardial infarction and cardiovascular deaths. The findings of the recent ASCOT-BPLA (Blood Pressure Lowering Arm) study show that an antihypertensive drug regimen starting with amlodipine (adding perindopril as required) is better than one starting with atenolol (adding thiazide as required) in terms of reducing the incidence of all types of cardiovascular events and all-cause mortality, and risk of subsequent new-onset diabetes.³⁹

Short acting dihydropyridines (nifedipine) should be avoided. Amlodipine has no effect on heart rate and cardiac contractility, and has been shown to be safe even in the presence of congestive heart failure.⁶⁰

Angiotensin Converting Enzyme inhibitors (ACE inhibitors)

ACE inhibitors such as enalapril, lisinopril, ramipril, perindopril, quinapril and others are effective in lowering blood pressure and are well tolerated. These drugs are particularly effective in reducing morbidity and mortality in patients with heart failure and myocardial infarction. In individuals with diabetes mellitus, they retard the onset and progression of renal disease. The HOPE trial (a primary prevention trial) showed that in high and average risk individuals, use of ramipril reduced overall mortality and cardiovascular endpoints, even with small reductions in blood pressure.⁶¹ As a class, they are metabolically favorable. The most common side effect is dry cough. ACE inhibitors are contraindicated in pregnancy. Serum creatinine and potassium should be monitored in patients receiving ACE inhibitors.

Angiotensin II Receptor Blockers (ARBs)

Angiotensin II receptor blockers (losartan, candesartan, valsartan, irbesartan and telmisartan) block the angiotensin II AT-1 receptors, and thus prevent the action of angiotensin II. In the LIFE trial, losartan was better than atenolol in reducing the frequency of the primary composite endpoint of stroke, myocardial infarction and cardiovascular death; this was due to a significant reduction in

INDIAN HYPERTENSION GUIDELINES-II

stroke.⁶² In the Valsartan Antihypertensive Long-term Use Evaluation (VALUE) trial, both valsartan and amlodipine reduced blood pressure in hypertensive patients at high cardiovascular risk, but the effects of the amlodipine-based regimen were more pronounced, especially in the early period. The main outcome of cardiac disease did not differ between the treatment groups. The findings emphasize the importance of prompt blood-pressure control in hypertensive patients at high cardiovascular risk.⁶³ Subgroup analyses of some studies suggests that angiotensin receptor blockers, may marginally increase the rates of myocardial infarction despite their beneficial effects on reducing blood pressure.⁶⁴ However, this needs further evaluation. These drugs have many features in common with ACE inhibitors, but do not cause an accumulation of bradykinin. Consequently, cough and angioedema are much less likely to occur than with ACE inhibitors.⁹

Alpha-blockers

Alpha-blockers such as prazosin, terazosin and doxazosin - effectively reduce blood pressure both as monotherapy and in combination. This class of drugs improves insulin sensitivity and has no adverse effects on lipid profile. They have a special place in the management of elderly hypertensives with benign prostatic hyperplasia (BPH).^{2,23,65} Since postural hypotension can occasionally occur, the dose of alpha-blockers should be carefully up-titrated. Data from the Antihypertensive and Lipid Lowering treatment to prevent Heart Attack Trial (ALLHAT) shows that patients in the doxazosin - based arm had 25% increase in the cardiovascular events and twice the risk of congestive heart failure.⁶⁶ Alpha-blockers are useful agents for add-on therapy in hypertensive patients with chronic renal failure, peripheral vascular disease, and metabolic disorders. If patients develop heart failure, they should be withdrawn.

Other drugs

Centrally acting drugs have been in use for several years. In particular, methyldopa remains an important agent for the treatment of hypertension in pregnancy. Clonidine, though a potent antihypertensive agent, is infrequently used these days due to side effects such as postural hypotension and problem of withdrawal-related rebound hypertension.

Direct vasodilators such as hydralazine and minoxidil are effective, but some of their side effects (such as tachycardia, headache, and retention of sodium and water) may make it difficult to use them in modern day treatment of hypertension.

Racemic forms of calcium channel blockers and beta-blockers are presently available. However, long-term studies regarding their efficacy and safety are not available.

Table 11 presents guidelines for selecting the most appropriate antihypertensive drugs

Table 12 presents commonly used anti-hypertensive drugs and their usual dosage

INDIAN HYPERTENSION GUIDELINES-II

Table 11: Guidelines for selecting the most appropriate antihypertensive drugs				
Class of drugs	Definite Indication/s	Possible indication/s	Definite contraindication/s	Relative contraindication/s
Diuretics	- Heart failure - Elderly patients - Systolic hypertension	- Diabetes	- Gout	- Dyslipidaemia
Beta-blockers	- Angina - Post-myocardial infarction - Tachyarrhythmia - Heart failure	- Pregnancy - Diabetes	- Asthma and chronic pulmonary disease - Heart block ^a	- Dyslipidaemia - Physically active - Peripheral vascular disease
CCBs	- Angina - Elderly - Systolic hypertension - Diabetes	- Peripheral vascular disease - CVA	- Heart block ^b	- Congestive heart failure ^c
ACE inhibitors	- Heart failure - Left ventricular dysfunction - Post-myocardial Infarction - Significant proteinuria - Diabetes	- CVA	- Pregnancy & lactation - Bilateral renal artery stenosis - Hyperkalemia	- Moderate renal failure (Creatinine levels >3 mg/dl)
Angiotensin II Receptor Blockers (ARBs)	- ACE inhibitor induced cough	- Heart failure - CVA	- Pregnancy & lactation - Bilateral renal artery stenosis - Hyperkalemia	- Moderate renal failure (Creatinine levels >3 mg/dl)
Alpha-blockers	- Prostatic hypertrophy	- Glucose intolerance - Dyslipidaemia	—	- Orthostatic hypotension - Congestive heart failure

^a Grade 2 or 3 atrioventricular block

^b Grade 2 or 3 atrioventricular block with verapamil or diltiazem

^c Verapamil or diltiazem

INDIAN HYPERTENSION GUIDELINES-II

Table 12: Commonly used anti-hypertensive drugs and their usual dosage

Class	Drug	Dosage (mg/day)
Diuretics	Hydrochlorothiazide	6.25-25
	Chlorthalidone	12.5-25
	Indapamide	1.5-2.5
	Amiloride	5-10
	Triamterene	50-100
	Spironolactone	25-50
Beta-blockers	Atenolol	25-100
	Metoprolol	25-100
	Bisoprolol	2.5-10
	Nebivolol	2.5-5
CCBs	Amlodipine	2.5-10
	Diltiazem	90-360
	Verapamil	80-240
ACE inhibitors	Enalapril	2.5-20
	Lisinopril	2.5-20
	Ramipril	1.25-10
	Perindopril	2-8
	Quinapril	10-80
ARBs	Losartan	50-100
	Candesartan	8-32
	Valsartan	40-160
	Irbesartan	150-300
	Telmisartan	40-160
Alpha-blockers	Prazosin	2.5-10
	Doxazosin	1-4
Centrally acting drugs	Clonidine	0.1-0.3
	Methyldopa	500-1500

Antihypertensive drug combinations

One often needs to combine different classes of drugs with different mechanisms of action to achieve effective control of blood pressure with minimal side effects. Combinations with additive hypotensive effects will produce greater blood pressure reductions than those obtained with monotherapy. A majority of patients will require two or more drugs for sustained and effective control of blood pressure.^{2,9} When a subject is in stage 2 or above, therapy can be initiated either with two drugs or as a fixed dose combination.

INDIAN HYPERTENSION GUIDELINES-II

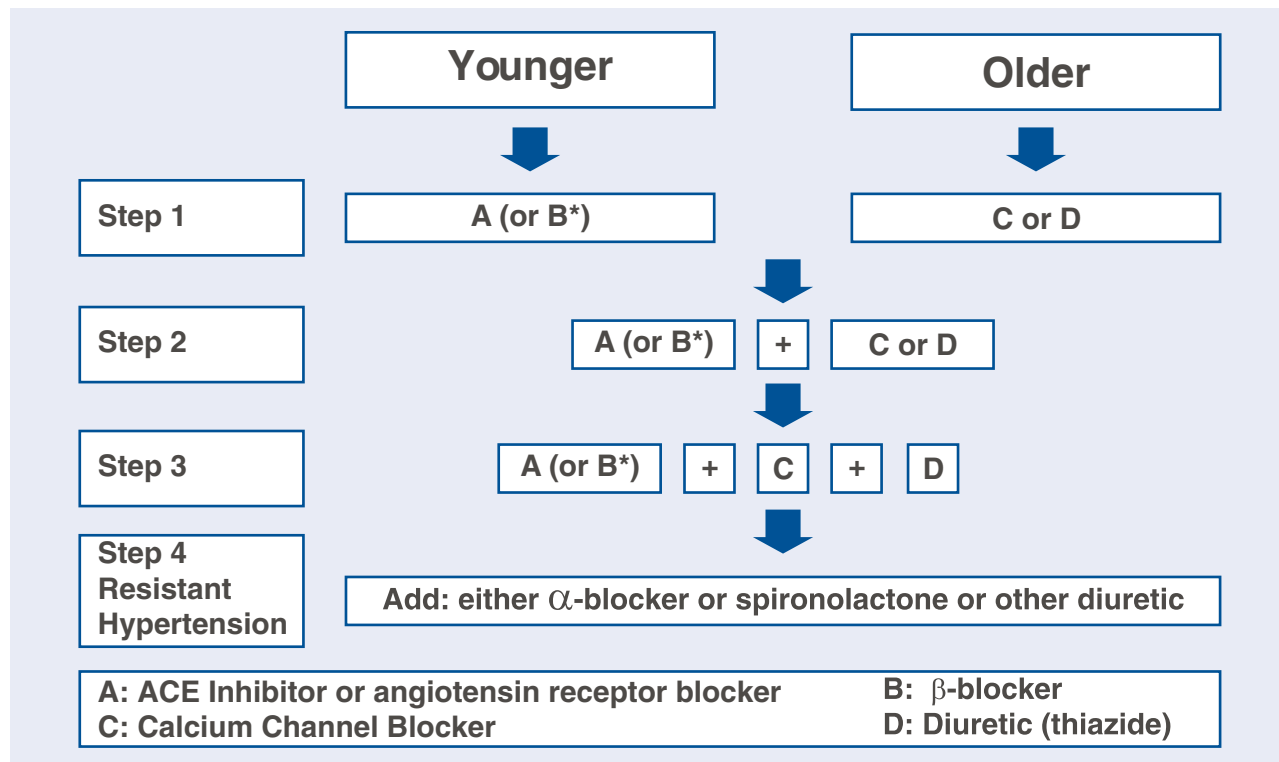
Younger individuals have high renin hypertension, hence ACE inhibitors/ARBs or beta-blockers are preferred; while older individuals have low renin hypertension and hence diuretics or CCBs are preferred as first line agents.

In combination, one out of the two groups A [ACE inhibitor/ ARB] or B [beta-blocker] is combined with C [calcium channel blocker] or D [thiazide diuretic] (step 2)

In refractory patients, when 3 agents are to be used, A+C+D is a good choice (step 3)

The combined use of diuretics and beta-blockers is discouraged due to a high incidence of new-onset diabetes.⁹

Figure 1: Algorithm for recommended drug combination



*Combination therapy involving B and D may induce more new onset diabetes compared with other combination therapies.

Table 13: Undesirable combinations

- Low dose diuretics and calcium channel blockers
- Beta-blocker and ACE inhibitor
- Beta-blocker and verapamil/diltiazem
- Two drugs from the same class

Drug interactions

Since multiple drugs are used in hypertensive patients and often these patients have other co-existing conditions, certain common drug interactions should be kept in mind.

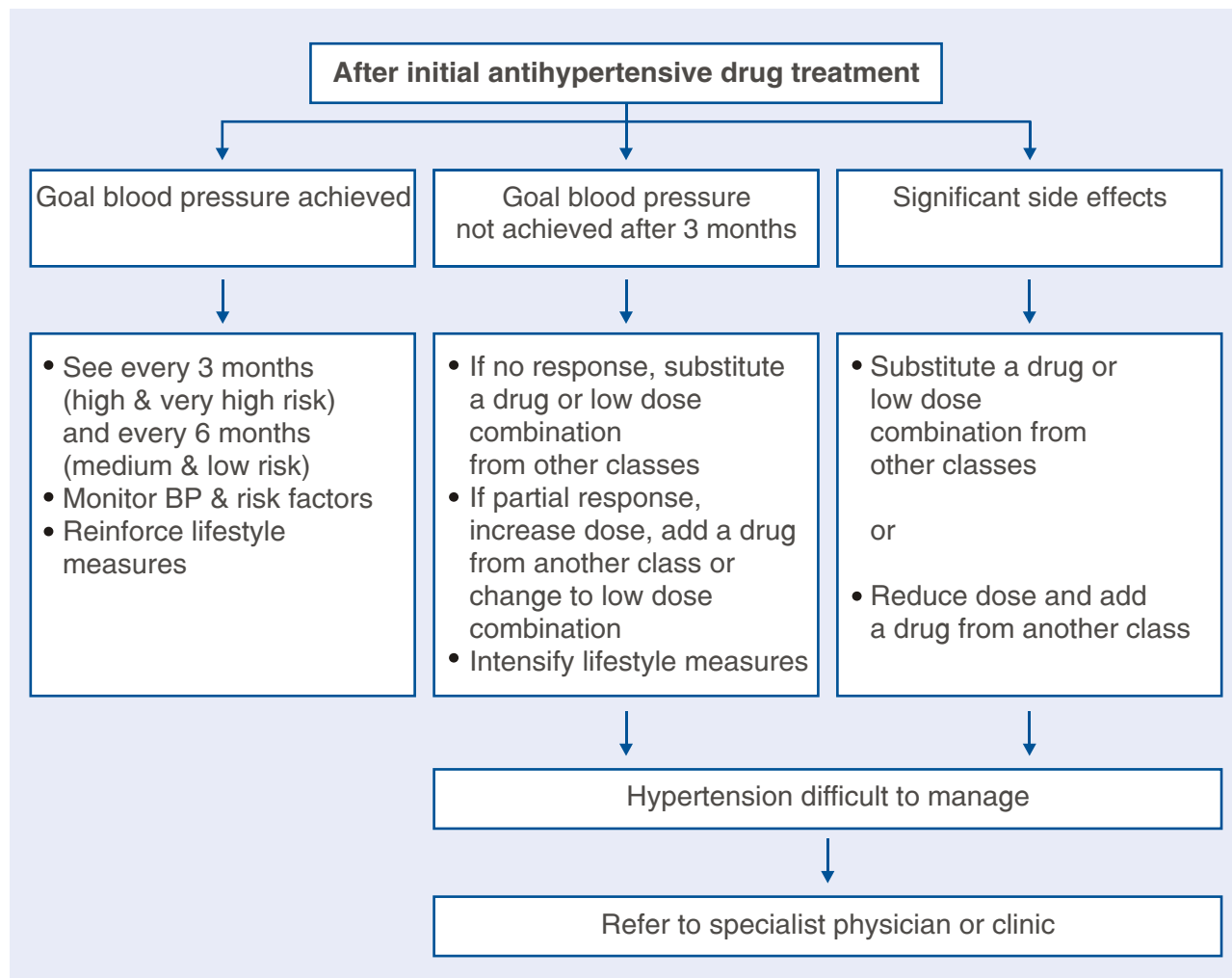
INDIAN HYPERTENSION GUIDELINES-II

Table 14 : Drug interactions

- NSAIDs including COX-2 inhibitors decrease efficacy of diuretics, beta-blockers and ACE inhibitors
- Concomitant use of beta-blockers and non-dihydropyridine CCBs can result in heart blocks
- Combined use of ACE inhibitors and potassium sparing diuretics may result in hyperkalemia
- Cyclosporin levels are increased with diltiazem and verapamil
- Concomitant use of tricyclic antidepressants with methyldopa is to be avoided

Maintenance and follow-up of therapy

Once therapy with particular antihypertensive drugs is instituted, patients need to be seen at frequent intervals during the period of stabilization in order to monitor changes in blood pressure and see whether non-drug measures are being strictly followed. At least once in a fortnight, blood pressure should be measured at the clinic or at home. Other CHD risk factors as well as co-existing diseases/conditions should be monitored. The overall risk category of a patient and the level of blood pressure decide the frequency of follow up visits to a large extent. The frequency can be reduced once blood pressure is stabilized and other risk factors are controlled. Tobacco avoidance must be promoted vigorously.



INDIAN HYPERTENSION GUIDELINES-II

Adverse drug reactions

Table 15: Checklist for known and common or important side effects with different classes of antihypertensive drugs

Common side effects	Diuretic	-blocker	Calcium channel blocker	ACE inhibitor	ARB	- blocker
Headache	-	-	+	-	-	-
Flushing	-	-	+	-	-	-
Lethargy	-	+	-	-	-	-
Impotence	+	+	-	-	-	-
Cough	-	-	-	+	+	-
Gout	+	-	-	-	-	-
Oedema	-	-	+	-	-	-
Postural hypotension	-	-	-	-	-	+
Cold hands and feet	-	+	-	-	-	-
Hyperkalemia	-	-	-	+	+	-

Associated therapies

In order to reduce the overall risk, patients with hypertension need therapies for control of other risk factors for secondary prevention and now with recent available data even for primary prevention. Low dose aspirin should be prescribed to all hypertensives with cardiovascular disease and stroke (secondary prevention). Hypertensive patients with no previous CV disease but aged >50 years, those with raised serum creatinine, or in high risk group need low dose aspirin for primary prevention. All hypertensive patients with coronary, peripheral, or cerebrovascular disease with LDL levels >100 mg/dL should receive statins as secondary prevention strategies. Hypertensive patients without CV diseases but those in high-risk group should also receive statins for primary prevention. The use of vitamin E and other anti-oxidants has not been shown to be of any benefit in these patients. Hence, their use is not recommended.^{67,68}

INDIAN HYPERTENSION GUIDELINES-II

SECONDARY HYPERTENSION

Prevalence

The prevalence of secondary hypertension is approximately 4-5% of all hypertensives. Because of its low prevalence, routine screening for secondary hypertension is not necessary. Renal causes constitute the largest group.

The percentage prevalence of various causes is shown in Table 16.^{69,70}

Table 16: Prevalence of hypertension	
Primary	
Essential hypertension	93-95%
Secondary	
Renal causes	
Parenchymal	2-3%
Renovascular	1-2%
Endocrine causes	
Pheochromocytoma	0.3-1.0%
Primary aldosteronism	
Cushing's syndrome	
Oral contraceptives	0.5%
Miscellaneous	0.5%

Presentation

The presence of following features warrants intensive investigations for secondary hypertension:

- Severe hypertension >180/110 mm Hg with onset at age ≤ 20 years or ≥ 50 years
- Resistant hypertension with significant end organ damage features
- Four P's of pheochromocytoma: pain (headache), palpitation, pallor and perspiration
- Polyuria, nocturia, proteinuria, or haematuria indicating renal disorder
- Absent peripheral pulses, brachiofemoral delay and abdominal or peripheral vessel bruits (coarctation of aorta, Takayasu's and atherosclerotic disease)
- Family history of polycystic renal disease and/or enlarged palpable kidneys
- Cushingoid features, multiple neurofibromas
- Elevation of plasma creatinine with use of ACE inhibitors

INDIAN HYPERTENSION GUIDELINES-II

Important causes

A. Renoparenchymal^{71,72}

- Chronic glomerulonephritis, chronic pyelonephritis, analgesic nephropathy, polycystic kidney disease, gout with renal failure, vasculitis and obstructive nephropathy
- Acute renal insults (acute glomerulonephritis, acute urinary tract obstruction and patients subjected to extra-corporeal shock wave lithotripsy)
- Post-renal transplant patients
- Drug-induced cyclosporine, steroids, and sustained use of erythropoietin

Investigations

Fresh urine examination for sediment and RBCs can be a pointer. Abdominal ultrasound for cyst, kidney size, echogenicity and obstruction may suggest a renal pathology. Renal biopsy in selected cases may be done to confirm the diagnosis.

B. Renovascular

- The most common cause of renovascular hypertension in India is Takayasu's syndrome (progressive aortoarteritis),⁷³ atherosclerotic renovascular disease is also being diagnosed more often now.
- The most common causes of renovascular disease in western population are atherosclerotic disease in 60% and fibromuscular dysplasia in 35%.
- Rare causes include embolic and tumor thrombus and extrinsic reasons.
- Takayasu's disease is a non-specific panarteritis affecting young women. Hypertension is mainly due to renal artery stenosis,⁷⁴ which can be unilateral or bilateral.
- Renovascular disease is much more common than renovascular hypertension (RVH).
- Atherosclerotic disease involves the proximal and fibromuscular dysplasia involves the distal renal artery.

Investigations

- An epigastric bruit is heard in 50-60% of patients with renovascular hypertension and 10% cases of essential hypertension. A diastolic renal bruit is more specific than systolic bruit.
- In patients with moderate degree of suspicion of renovascular hypertension, non-invasive tests are recommended initially.
- Wherever there is a high degree of suspicion, direct selective renal angiography is recommended.
- Captopril augmented renal scan is the non-invasive investigation of choice. It has a 75% sensitivity and specificity. Compounds used are ⁹⁹Tc - DTPA and ¹²³I - Hippuran. The stimulated plasma renin activity after captopril is > 12ng/ml/hour.
- Duplex sonography, CT angiography and MRI angiography are other good and non-invasive modalities. MRI angiography has higher sensitivity and specificity.
- Conventional angiography, though invasive, is the gold standard. Intra-arterial injection with digital subtraction angiography (DSA) may be used. Once the diagnosis is confirmed, renal angioplasty with stenting is the treatment of choice. Physicians should confirm anatomical narrowing versus functional disturbances before embarking upon planning any intervention. When angioplasty is not possible, surgical approach is recommended.

INDIAN HYPERTENSION GUIDELINES-II

C. Endocrine causes

1. Pheochromocytoma

These chromaffin cell tumors are mostly adrenal. These may be extra-adrenal in 15% of the cases and bilateral adrenal in 10% of the cases. 10% of all cases are familial and 10% are malignant.

Episodic hypertension, postural fall, pallor, throbbing headache, palpitations and perspiration are suggestive clinical features.⁷⁵

Investigations

- Screening tests include urinary biochemical assay for free catecholamines, metanephrines and vanillyl-mandelic acid (VMA). These tests have high specificity (99%) and sensitivity (85-90%). Following drugs should be withdrawn for 48 hours before doing these tests: alpha methyl dopa, penicillin and certain vegetables. Patients can be continued on CCBs and ACE inhibitors during evaluation.
- Tumor localisation: Computed Tomography scan and MRI of the abdomen have greatly simplified tumor localisation; MIBG labelled with I¹³¹ is the most accurate way of diagnosing adrenal and extra adrenal pheochromocytomas.⁷⁶
- Once localised, surgery should be offered to all the patients. Mortality from surgery is now less than 5%. For pre-operative preparation, control of blood pressure is important and can be achieved with oral phenoxybenzamine 10 mg once daily, to be increased slowly. Oral prazosin and terazosin preferentially block post-synaptic alpha1-receptors on vessel wall and leave pre-synaptic alpha 2- receptors. As a result, tachycardia is less of a problem. Beta-blockers may be given to these patients to control tachycardia and arrhythmias, only after alpha-blockers have been started.

2. Primary Aldosteronism

Primary aldosteronism is due to excess aldosterone secretion by the adrenal cortex secreted generally by adenomas and occasionally due to bilateral adrenocortical hyperplasia. This is suspected in a case of hypertension showing persistent hyokalaemic metabolic alkalosis in the absence of diuretic therapy. It is usually diagnosed by imaging techniques. Treatment is generally surgical removal of the adenoma.

3. Cushing's Syndrome

Hypertension is present in approximately 80% of patients with Cushing's syndrome. Other clinical features include central obesity, hirsutism, polycythaemia and pink striae on the abdomen. Hypertension remits in most patients after successful treatment.

D. Miscellaneous

Other important secondary causes include:

- Oral contraceptives (see Hypertension in Women Pg. no. 33)
- Coarctation of aorta, a congenital disease needs surgical correction
- Thyroid disorders, both hypothyroidism and hyperthyroidism
- Sleep apnea syndrome is one of the common causes of reversible hypertension
- Acute stressful situations cause intense sympathetic discharge and may temporarily induce hypertension
- Common conditions include acute mental stress, hypoglycaemia, acute intermittent porphyria, exposure to cold, burns, perioperative period and post head injury
- Drugs: Non-steroidal anti-inflammatory drugs, sympathomimetic amines, ephedrine, glucocorticoids, cocaine and amphetamines can all cause significant hypertension

COMPLICATIONS

The complications of hypertension can be considered either hypertensive or atherosclerotic. Although the extent of damage often correlates with the level of blood pressure, it is not always the case. Blood pressure and organ impairment should be evaluated separately. The various complications are as follows:

1. Hypertensive Heart Disease

- Hypertension has the following effects on the heart: left ventricular hypertrophy, increased risk of coronary artery disease, arrhythmias, congestive cardiac failure and sudden death.⁷⁷
- Most episodes of left ventricular failure in hypertensive patients are associated with reduced ejection fraction.
- Treatment of hypertension can reverse ventricular hypertrophy with no impairment of systolic function and improved diastolic function.^{78,79} However, the impact of reduction of LVH on reduction of morbidity and mortality is still debated.

2. Cerebrovascular Disease

- Hypertension is the most important modifiable risk factor for all types of atherothrombotic stroke⁸⁰ and intracerebral haemorrhage due to rupture of Charcot-Bouchard aneurysms.
- The relation between the incidence of stroke and blood pressure is continuous.^{81,82} A 5-6 mm Hg reduction in diastolic blood pressure reduces the risk of stroke by 40%.⁸³
- The SHEP (Systolic Hypertension Elderly Program) study showed substantial benefit following control of systolic blood pressure in the elderly.³⁸

3. Kidney

- About 20-25% of renal failure is attributed to uncontrolled hypertension.⁸⁴
- Development of renal damage is heralded by microalbuminuria, which progresses to overt proteinuria and may further progress to end stage renal disease.⁸⁵
- Reduction of proteinuria can be achieved by effective blood pressure control specially with use of ACE inhibitors and ARBs.^{86,87}

4. Retina

- Hypertensive retinopathy is a condition characterized by a spectrum of retinal vascular signs in people with elevated blood pressure.
- The classification of Keith, Wagener and Barker has been widely used. Grade I retinopathy is characterized by copper wire appearance; Grade II by arteriovenous nicking; Grade III by the presence of haemorrhages and exudates; and Grade IV by papilloedema.
- Grade III and IV retinopathy is seen in long standing uncontrolled hypertension. These changes may regress with effective control of blood pressure.
- Several reviews of hypertensive retinopathy since 1996 have questioned the usefulness of the classification system by Keith, *et al* and its relevance to current clinical practice. Recent studies show that some of the retinal signs (e.g., hemorrhages, microaneurysms and cotton-wool spots) predict stroke and death from stroke independently of elevated blood pressure and other risk factors.⁸⁸

5. Large Vessel Disease

- Hypertension is a risk factor for development of intermittent claudication. It also increases the risk of abdominal aortic aneurysms and aortic dissection. Eighty percent of patients with aortic dissection have hypertension.⁸⁹

HYPERTENSION IN SPECIAL SITUATIONS

Hypertension with diabetes mellitus

- Co-existence of hypertension and diabetes is being increasingly recognised. 30-35% of hypertensives are detected to have diabetes.
- The prevalence of hypertension is 1.5 to 2 times greater in patients with diabetes mellitus compared with matched non-diabetic individuals.⁹⁰
- In India, it is predicted that there is going to be a steep increase in the number of Type II diabetic patients.⁹¹
- Coexistence of diabetes and hypertension increases the risk of macro and microvascular disease.
- Blood pressure should be measured in the supine, sitting and standing positions in a diabetic patient to detect evidence of autonomic neuropathy.
- UKPDS has stressed the importance of effective blood pressure control irrespective of the antihypertensive agent used.³⁰ The study also shows that polypharmacy, i.e. use of two or more drugs is required for optimal control. The HOT study in diabetic patients has shown significantly lower risk of cardiovascular disease in those patients assigned to the lowest target blood pressure (<130/85 mm Hg).²⁹
- In the management of diabetic hypertensives, lifestyle modifications have to be more aggressive.
- Pharmacological treatment of hypertension in diabetic patients differs due to effects of certain drugs on the lipid profile, insulin sensitivity and glucose metabolism.
- ACE inhibitors⁹² have been shown to slow the rate of decline in renal function in diabetic patients. The Heart Outcomes Prevention Evaluation Study (HOPE) emphasized the importance of ACE inhibitors to reduce the risk of complications of diabetes.⁶¹ ACE inhibitors are recommended as first line drugs for management of diabetic hypertensives.
- Beta-blockers potentially mask hypoglycemic symptoms, however at present it is not a major contraindication. Further, there is clear evidence of benefits of beta-blockers in diabetic patients after myocardial infarction.³⁰
- CCBs may be useful in diabetes, alone or in combination to control BP. In ASCOT trial, combination of amlodipine and perindopril was associated with significantly less incidence of new onset diabetes than combination of beta blocker and diuretic.³⁹
- Alpha-blockers are metabolically beneficial in hypertensive diabetic patients.
- Tight metabolic control of diabetes, effective blood pressure control and low protein diet improves overall outcome.

Hypertension with renal disease

- Hypertension results from any form of renal disease that reduces the number of functioning nephrons leading to sodium and water retention.⁹³ Hypertension is widely prevalent in all forms of renal diseases.
- Hypertension is more common in glomerular than in tubulointerstitial disease and chronic pyelonephritis. Microalbuminuria may be a marker of generalized endothelial dysfunction.
- Reducing BP to <125/75 mm Hg may produce additional benefit in patients with chronic renal disease of any aetiology associated with proteinuria of ≥ 1 g per 24 hours. It is emphasised, however, that this concept that 'lower is better' for patients with renal disease and hypertension is based on limited evidence, and is largely extrapolated from retrospective analysis of clinical trial data.⁹

INDIAN HYPERTENSION GUIDELINES-II

- In end stage renal disease of any cause (except diabetes), hypertension is present in more than 75% of the cases.
- It is now documented that all patients with microalbuminuria, irrespective of presence or absence of hypertension, need to be treated with antihypertensive drugs which retard the progression of renal failure.^{94,95}
- Sodium (<4 g/day) and protein restriction (0.6 g/kg/day) form an integral part of the dietary treatment.
- One should be cautious in the use of ACE inhibitors in patients with persistent rising levels of serum potassium and creatinine.
- Low dose diuretics, calcium channel blockers, alpha-blockers, beta-blockers and alpha methyldopa can all be used in these patients.
- Dialysis may control blood pressure due to regulation of fluid volume and electrolytes. However, drug therapy is required in 80-90% of the patients.
- Most patients will require 3 or more drugs to achieve the recommended blood pressure (BP) goal. For patients with chronic kidney disease, ACE inhibitors and ARBs have demonstrated favorable effects on progression of diabetic and non-diabetic renal disease.² As ACE inhibitors and ARBs are increasingly being recommended for the management of hypertension, a note of caution is warranted: Chronic renal failure as opposed to chronic renal disease is a condition where they can have a deleterious effect on GFR and serum creatinine and potassium levels have to be monitored carefully. Diuretics are effective in achieving blood-pressure control in patients with hypertension. The use of low-dose thiazide diuretics in combination with ACE inhibitors usually does not lead to changes in renal function. CCBs exert a vasodilatory effect on the afferent arteriole and are therefore less likely to cause a reduction in the glomerular filtration rate when the blood pressure is lowered. Non-dihydropyridine CCBs are consistently associated with a beneficial effect on renal function; such benefit may be additive when these drugs are combined with an ACE inhibitor. If a dihydropyridine CCB is to be given to patients with established nephropathy, it should be given with either an ACE inhibitor or an angiotensin-receptor blocker.⁹⁶ CCBs represent an important, well-tolerated therapeutic option for those who cannot tolerate ACE inhibitors/ARBs, or when concomitant therapy is required for adequate BP control.⁹⁷ Beta-blockers are effective agents for the treatment of hypertension in both diabetic and nondiabetic chronic renal disease. In general, these drugs have no clinically important effects on renal hemodynamics and the glomerular filtration rate.⁹⁶ The National Kidney Foundation states that alpha-blockers may be a useful adjunct to the control of blood pressure, but have not been shown to have a unique cardio or renoprotective benefit in this patient population. Alpha-blockers are effective in lowering blood pressure and are associated with favorable metabolic profiles in patients with diabetes. However, these agents have not been shown to reduce either albuminuria or CV mortality in people who develop heart failure.^{9,98}

Hypertension with cerebrovascular disease

- The evidence for reduction in incidence of stroke with control of blood pressure has been consistent. In clinical trials, antihypertensive therapy has been associated with reductions in stroke incidence averaging 35% to 40%.^{2,31}
- Immediately after the occurrence of an ischemic cerebral infarction, it is appropriate to withhold treatment in patients who present with high blood pressure, unless blood pressure is very high (>200/120 mm Hg).
- In stroke survivors with hypertension, blood pressure lowering therapy has been shown to result in 43% reduction in stroke recurrence.⁹⁹
- Extensive elevation of blood pressure with slow elevation is more often associated with cerebral haemorrhage than infarction. Moderate reduction in blood pressure is prognostically more rewarding in haemorrhagic stroke than in ischemic stroke.¹³

INDIAN HYPERTENSION GUIDELINES-II

- In clinically evident cerebrovascular disease, the goal is to gradually reduce the blood pressure and carefully monitor it for the first 24 hours in view of the possibility of transient hypertension.
- Hypertensive encephalopathy is an emergency that needs to be identified and aggressively managed.
- BP should not be reduced in ischemic stroke patients who are otherwise not candidates for thrombolysis. In patients for thrombolytic therapy, SBP \geq 185 and DBP \geq 110 mm Hg should be actively treated and maintained below 185/110 mm Hg.¹⁰⁰
- In acute intracerebral hemorrhage, the SBP and DBP should be maintained below 180/105 mm Hg respectively.¹⁰⁰

Hypertension in women

- Some of the side effects of commonly used drugs like ACE inhibitor induced cough, CCB induced pedal edema, and diuretic induced hyponatremia and hypokalemia are seen more often in women than in males.^{2,101}
- Estrogen-progesterone oral contraceptives cause a distinct increase in systolic and to a lesser extent diastolic pressure in virtually all women. Five percent women who use the pill for 5 years develop hypertension. Age, positive family history, history of PIH and obesity are known predisposing factors for pill-induced hypertension.^{2,102} In more than one half, blood pressure returns to normal when the pill is withdrawn.
- The use of hormone replacement therapy in post-menopausal women (low dose estrogen) is not contraindicated in women with hypertension.

Hypertension in pregnancy

- Hypertension occurs in about 5% of all pregnancies. In developed as well as developing countries, hypertensive disorder of pregnancy is one of the leading causes of maternal and perinatal mortality.^{103,104}
- Hypertension in pregnancy is diagnosed by recording phase IV of Korotkoff sounds with the patient lying in a lateral position. DBP $>$ 85 mm Hg should be considered abnormal. The diagnosis requires two consecutive measurements of DBP of 90 mm Hg or more.
- Diastolic blood pressure \geq 110 mm Hg is considered ominous and requires urgent attention.
- If this disorder is diagnosed early and managed appropriately, morbidity and mortality can be largely prevented.
- Chronic hypertension is that which is present before pregnancy or is diagnosed before 20th week of gestation or that which persists beyond six weeks post partum.
- Pre-eclampsia is a pregnancy specific condition characterized by increased blood pressure appearing after 20 weeks of gestation and usually accompanied by oedema and proteinuria. Eclampsia is the occurrence of seizures that cannot be attributed to other causes in a patient with pre-eclampsia.
- Pre-eclampsia superimposed on chronic hypertension is diagnosed when there is a further increase in BP of 30 mm Hg systolic or 15 mm Hg diastolic together with the appearance of proteinuria or oedema.
- Transient hypertension is elevation of BP during pregnancy or during first 24 hrs post partum with no other signs of pre-eclampsia or of pre-existing hypertension.
- Benefits of low-dose aspirin prophylaxis are unproven for most women, including nulliparous women.¹⁰⁵

INDIAN HYPERTENSION GUIDELINES-II

- The antihypertensive agent used should be efficacious and safe to the mother and the foetus. Methylodopa has been evaluated most extensively and is therefore recommended for women whose hypertension is first diagnosed during pregnancy. Calcium channel blockers, beta-blockers, in particular, pindolol, oxprenolol, and labetalol can be used. Drugs like atenolol have been shown to cause foetal retardation. Alpha-blockers may also be used.^{106,107}
- ACE inhibitors and angiotensin II receptor blockers are contraindicated in pregnancy. Use of low dose diuretics is discouraged, since pre-eclampsia is a volume-depleted state.¹⁰⁸
- Intravenous magnesium sulphate is the drug of choice both for prevention and treatment of seizures.^{109,110} Intravenous hydralazine and labetalol are effective agents, but are not currently available in India.
- In some cases, antihypertensive treatment fails to control hypertension and the only means of controlling hypertension would be to induce delivery.

Hypertension in the elderly

The prevalence of hypertension increases with age. The population of India aged 65 years and above is projected to increase from 51 million in 2005 to 65 million in 2015 and 76 million in 2020.¹¹¹ The prevalence of hypertension is age related, being the highest in the age group of 50-59 years in males and 60-64 years in females in urban areas. In rural areas, an age related increase is seen in both the sexes in the age group of 60-64 years. A community based study in Mumbai¹¹² in 1980 showed increase in BP with age, with prevalence in 15% of total population surveyed, 34.5% in those over 55 years, 38.5% in those over 65 years and 44.4% in those over 70 years.

In elderly population, systolic blood pressure is a better predictor of cardio-vascular/cerebrovascular events, end-stage renal disease and all-cause mortality, as compared to diastolic blood pressure.¹¹³

Precautions in measurement

Blood pressure should be measured with care in elderly subjects as some older patients may have falsely high readings due to excessive vascular stiffness. Also as older patients are more likely to have orthostatic hypotension, one should measure BP in supine, sitting and standing positions.

Treatment of hypertension in elderly nowadays is accepted as a highly effective medical intervention. An overview of five randomised trials have shown 34% reduction in stroke, 19% in CHD and 23% in vascular deaths, with a reduction of 12-14 mm Hg SBP and 5-6 mm Hg DBP over a five year period.¹¹⁴

Management

- Lifestyle modification is important in management of hypertension in elderly and should be started in all of these patients. Losing weight and cutting down on salt can lessen and even eliminate the need for blood pressure lowering medications in elderly (Trial of Non-pharmacological Interventions in the Elderly - TONE).¹¹⁵
- Drug treatment: The blood pressure should be lowered gradually in elderly hypertensives with no more than an initial 25% decrease, even in situations requiring rapid reduction in blood pressure with medications.
- Low dose thiazide diuretics are recommended, because they have been shown to be effective in reducing mortality and morbidity. Unless there is a compelling indication to use another class of drugs, low dose hydrochlorothiazide or chlorthalidone 12.5 to 25 mg per day should be the first choice. This could also be combined with potassium sparing diuretic like amiloride 2.5 mg or triamterene 50 mg per day. Long-acting dihydropyridine CCBs such as nitrendipine and amlodipine

INDIAN HYPERTENSION GUIDELINES-II

are considered to be appropriate alternatives in these patients. Depending on the associated conditions, beta-blockers, ACE inhibitors, or alpha-blockers may be the preferred drugs in special situations. Alpha-blockers are the preferred drugs in presence of BPH. In STOP 2, there was some evidence that the risk of myocardial infarction and of heart failure were greater with calcium antagonist based therapy than with ACE inhibitor based therapy. There were no clear differences between either of these regimens and a third based on diuretics and beta-blockers.¹¹⁶

- Bilateral atherosclerotic renovascular disease in the elderly must be kept in mind while treatment with ACE inhibitors or ARBs.

Isolated systolic hypertension

Isolated systolic HT is more often seen in the elderly than in the young. The goal of blood pressure control in older patients should be the same as in younger patients (i.e., 140/90 mm Hg)³; however an interim value of a systolic blood pressure below 160 mm Hg may be necessary in elderly patients with marked systolic hypertension, especially if they develop symptoms of giddiness and light headedness when their blood pressure is reduced to 140/90 mm Hg. Management of isolated systolic hypertension in the elderly is the same as mentioned in the management of hypertension in the elderly.

Isolated systolic hypertension in the young patients, although uncommon, is often successfully treated with life style modification and long-acting beta-blockers.

Hypertension with congestive cardiac failure

Congestive cardiac failure is a common sequel of long standing hypertension and adequate control of BP improves mortality in these patients.

- Several large trials of ACE inhibitors in patients with left ventricular dysfunction due to hypertension, have provided evidence of significant reduction of morbidity, secondary to heart failure.¹¹⁷
- Low dose diuretics are also used in hypertension with heart failure, particularly when associated with fluid retention.
- In patients with congestive heart failure stabilized with ACE inhibitors and diuretics, selective beta-blockers such as metoprolol, bisoprolol and alpha-beta blocker carvedilol may be used wherever indicated. Use of these beta-blockers has been shown to reduce mortality. These agents should be started in low doses and then gradually increased.¹¹⁸⁻¹²⁵
- Amlodipine has been found to be safe in treating hypertensive patients with angina and left ventricular failure, when added to ACE inhibitors, low dose diuretics and digoxin.⁶⁰ Other calcium channel blockers are not recommended in these patients.³
- In patients with severe hypertension and acute left ventricular failure, blood pressure needs to be brought down rapidly to normal or slightly above normal range. This can be done by administration of intravenous drugs such as furosemide, nitroglycerine, enalaprilat or sodium nitroprusside.

Hypertension with chronic obstructive airway disease

- Hypertension in patients with COAD and bronchial asthma is seen. It is often precipitated by the use of systemic steroids, beta-agonists or nasal decongestants. Stress also plays a significant role in the development of hypertension in these patients. It is therefore recommended that the above precipitating factors should be looked for and modified.
- Long acting calcium channel blockers such as amlodipine have been found to be relatively safe drugs in this group of patients.³
- ACE inhibitors have not been found to increase bronchial reactivity in these patients. It is

INDIAN HYPERTENSION GUIDELINES-II

recommended that if cough develops, angiotensin II receptor blockers should be tried as alternative to ACE inhibitors.

- Beta-blockers and alpha-beta blockers are not recommended as they are known to exacerbate asthma. However, alpha-blockers can be used in patients with COAD.¹²⁶
- Inhaled corticosteroids and ipratropium bromide can be used safely in these patients.

Hypertension with coronary artery disease (CAD)

Among all the risk factors documented for pathogenesis of CAD, hypertension is reported to be the major risk factor.¹²³ Blood pressure levels have been shown to be positively and continuously related to the risk of major CAD events.⁸²

- Too rapid lowering of blood pressure, which can cause reflex tachycardia and sympathetic activation, should be avoided in patients with CAD.
- One may have to set the target of BP control even below 130-140/90 mm Hg.
- All other risk factors should be treated appropriately.
- HT in patients with acute coronary syndrome should be treated aggressively.
- Beta-blockers and CCBs are the drugs of first choice in the management of angina in patients with hypertension associated with CAD.
- Beta-blockers have been shown to reduce the risks of re-infarction and cardiovascular death by 25% in patients with MI.¹²⁷
- Amlodipine has been shown to produce subjective and objective improvement in patients with angina.¹²⁸
- Treatment with amlodipine is associated with fewer hospitalisations for unstable angina and revascularisations in patients with angiographically documented CAD.¹²⁹
- Verapamil and diltiazem reduce risk of developing MI following non-Q-wave myocardial infarction.¹³⁰
- After MI, therapy with ACE inhibitors prevents subsequent heart failure and reduces morbidity and mortality.¹³¹ ACE inhibitors in combination with digoxin or low dose diuretics, are effective in reducing morbidity and mortality in patients in heart failure.¹³²
- Statins and aspirin are recommended in patients with hypertension associated with CAD.

Hypertension with dyslipidaemia

Dyslipidaemia often co-exists with hypertension.¹³³

- Lifestyle modification is of particular importance in such patients as it can lower blood pressure and improve lipid levels.
- The choice of antihypertensive agent should be made after considering the effects on the lipid profile that some of these drugs have.
- In high doses, low dose diuretics can induce at least a short-term increase in cholesterol, triglycerides and LDL cholesterol levels. Low dose thiazides do not produce this effect. In spite of these effects on the lipid profile, these drugs when used as monotherapy or in combination, reduce mortality due to CAD and cerebrovascular disease.
- Beta-blockers without intrinsic sympathomimetic activity (ISA) may increase levels of plasma triglycerides and reduce levels of HDL-cholesterol. Despite this, these have been shown to reduce rate of sudden death, overall mortality and recurrent MI in patients with previous MI.
- Alpha-blockers decrease serum cholesterol levels and triglycerides.
- ACE inhibitors and calcium channel blockers are lipid neutral drugs.

INDIAN HYPERTENSION GUIDELINES-II

- Patients with HT and dyslipidaemia warrant lipid lowering therapy (statins) just as for patients with CV disease and diabetes.^{34,35,68,134}

Hypertension with obesity and metabolic syndrome

- Prevalence of obesity and hypertension is increasing. Obesity is almost always accompanied by insulin resistance, hyperinsulinemia, impaired glucose tolerance and dyslipidemia. Truncal obesity is more common in Indian population. Also abdominal obesity is associated with sodium retention, endothelial dysfunction, microalbuminuria, LVH and elevated markers of inflammation.
- The diagnosis of metabolic syndrome is made when 3 or more of the following risk determinants are present.^{135,136}

Table 17: Diagnostic criteria for metabolic syndrome	
Risk Factor	Defining Level
Abdominal obesity (Waist Circumference)	
Men	>90 cm
Women	>80 cm
Triglycerides	≥150 mg/dl
HDL-Cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mm Hg
Fasting glucose	≥110 mg/dL

- Compared with Whites, Indian men and women have a higher prevalence of central obesity.¹³⁷ Anthropometric parameters of Asians are different than those for white Caucasians and blacks. For example, Asian Indians have smaller body size, excess body fat, and truncal and abdominal adiposity than white Caucasians.¹³⁸ In Asians, the BMI cut-offs for overweight (>23.0 kg/m²) and obesity (>25.0 kg/m²) are lower than WHO criteria. These provisional recommendations will need to be revised in the light of further validation of studies and clinical experience.^{136,139}
- Epidemiological studies have consistently shown a tight correlation between body weight and blood pressure, with 70% of hypertension in men and 60% in women being directly attributable to excess adiposity.¹⁴⁰ Essential hypertension is very frequently associated with a decrease in insulin sensitivity. This insulin resistance is very often associated with dyslipidaemia, obesity, hypertension and impaired glucose tolerance, a cluster termed the “metabolic syndrome or the insulin resistance syndrome.”¹⁴¹
- Lifestyle modification (diet, exercise) is the cornerstone in management of hypertension in obese individuals.
- Dyslipidemia in these patients is characterised by high TG levels and low HDL levels. Such patients require fibrates for control of dyslipidemia.
- Overall, the weight loss effects of sibutramine, anti-obesity drugs do not appear to translate into favourable effects on BP. Instead, sibutramine therapy may be associated with small increases in BP and resting heart rate.¹⁴²
- Obstructive sleep apnea (OSA), now considered a cause of secondary hypertension, is closely associated with obesity. The treatment with of OSA with continuous positive airway pressure (CPAP) has been shown to decrease daytime and nocturnal blood pressures.¹⁴³

INDIAN HYPERTENSION GUIDELINES-II

- On the basis of their favourable metabolic profiles, it would appear that ACE inhibitors, ARBs, CCBs and alpha-blockers can decrease blood pressure without worsening the metabolic abnormalities that accompany hypertension in obese patients. ACE inhibitors, low-dose diuretics and non-dihydropyridine CCBs are probably the drugs of first choice in this setting. Alpha-blockers have particular advantages in individuals with dyslipidaemia or glucose intolerance and may be considered as add-on agents. Given that control of hypertension in the majority of hypertensive patients is unlikely to be achieved with any single drug alone, the discussion on choice of drug class may be moot.^{140,142}

Resistant hypertension

- Resistant hypertension is defined as the failure to reach goal BP in patients who are adhering to full doses of an appropriate 3-drug regimen that includes a diuretic. Table 18 gives causes of resistant HT². These causes can be readily identified and treated. Therefore, the prevalence of true resistant hypertension is low.

Table 18: Causes of resistant hypertension²

<ul style="list-style-type: none"> • Volume overload <ul style="list-style-type: none"> - Excess sodium intake - Volume retention from kidney disease - Inadequate diuretic therapy
<ul style="list-style-type: none"> • Drug <ul style="list-style-type: none"> - Induced or other causes - Nonadherence - Inadequate doses - Inappropriate combinations - Nonsteroidal anti-inflammatory drugs and cyclooxygenase 2 inhibitors - Cocaine, amphetamines, other illicit drugs - Sympathomimetics (decongestants, anorectics) - Oral contraceptive hormones - Adrenal steroid hormones - Cyclosporine and tacrolimus - Erythropoietin - Tobacco - Selected over-the-counter dietary supplements and medicines (e.g. licorice and cough syrups)
<ul style="list-style-type: none"> • Associated conditions <ul style="list-style-type: none"> - Obesity - Excess alcohol intake
<ul style="list-style-type: none"> • Identifiable causes of hypertension <ul style="list-style-type: none"> - Chronic kidney disease - Coarctation of the aorta - Non-specific aortoarteritis - Cushing syndrome and other glucocorticoid excess states including chronic steroid therapy - Obstructive uropathy - Pheochromocytoma - Primary aldosteronism and other mineralocorticoid excess states - Renovascular hypertension - Obstructive sleep apnea syndrome - Thyroid or parathyroid disease

INDIAN HYPERTENSION GUIDELINES-II

Management of resistant hypertension:

Most patients with resistant hypertension need to be referred to specialized hypertension clinics after evaluation of level of compliance. More aggressive salt restriction and elimination of drugs interfering with action of anti-hypertensive agents should be looked at. Subsequently, one should look for secondary hypertension and in case, no secondary cause is found these patients need multiple drugs in high dosages.

Hypertensive crises

Hypertensive crises are classified as hypertensive emergencies or urgencies.

Hypertensive emergencies:

- Hypertensive emergencies are characterized by severe elevations in BP (>180/120 mm Hg) complicated by evidence of impending or progressive target organ dysfunction. They require immediate BP reduction (not necessarily to normal) to prevent or limit target organ damage. Examples include hypertensive encephalopathy, intracerebral hemorrhage, acute myocardial infarction, acute left ventricular failure with pulmonary edema, unstable angina pectoris, aortic dissection, or eclampsia.²
- IV nitroprusside is required rarely, in situations like dissection of aorta and subarachnoid haemorrhage with very high blood pressure. It requires intensive care setting and very close monitoring.
- IV nitroglycerine is less effective, but specially useful in patients with ischaemic heart disease and left ventricular failure.¹⁴⁴
- Sublingual captopril, intravenous enalaprilat and/or IV diuretics are useful in hypertensive emergencies, specially in presence of heart failure.

Hypertensive urgencies:

- Hypertensive urgencies are those situations associated with severe elevations in BP without progressive target organ dysfunction. Examples include upper levels of stage II hypertension associated with severe headache, shortness of breath, epistaxis, or severe anxiety. The majority of these patients present as noncompliant or inadequately treated hypertensives, often with little or no evidence of target organ damage.²
- The aim should be safe, prompt and gradual lowering of blood pressure without major side effects.¹⁴⁵
- In most urgencies, blood pressure can be controlled with rapidly acting oral medications like calcium channel blockers and ACE inhibitors.
- IV esmolol has been shown to be specially useful for peri-operative accelerated hypertension.
- Sublingual nifedipine should not be used in hypertensive crises as it can cause precipitous fall in blood pressure, reflex tachycardia and may precipitate renal, cerebral or coronary ischaemia.^{2,146}

INDIAN HYPERTENSION GUIDELINES-II

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