

HYPERTENSION

Definition and Classification

Hypertension in adults is defined as systolic BP (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. Starting at 115/75mm Hg, cardiovascular disease(CVD) risk doubles with each increment of 20/10 mm Hg throughout the blood pressure range.

Classification

CATEGORY	SYSTOLIC BP(mmHg)	DIASTOLIC BP(mm Hg)
Optimal	<120	<80
Normal	<130	<85
High Normal	130-139	85-89
Hypertension		
Stage1	140-159	90-99
Stage 2	160-179	100-109
Stage3	>180	>110

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.

For persons over age 50, SBP is more important than DBP as a CVD risk factor. SBP is more difficult to control than DBP. SBP needs to be as aggressively controlled as DBP. Therefore, although classification of adult blood pressure is somewhat arbitrary, it is useful for clinicians who make treatment decisions based on a constellation of factors along with the actual level of blood pressure.

The **first** is to rule out any secondary causes. Although about 95% of patients have primary disease (no clearly definable underlying cause), a search for a secondary cause is important because if such a cause is present, it has to be treated to cure hypertension.

When to suspect secondary hypertension clinically?

- Absence of family history of hypertension
- Severe hypertension > 180/110 mm Hg with onset at age <20 years or > 50 years
- Difficult-to-treat or resistant hypertension with significant end-organ damage features
- Combination of pain (headache), palpitation, pallor and perspiration –
4 P's of phaeochromocytoma.
- Polyuria, nocturia, proteinuria or hematuria – indicative of renal diseases
- Absence of peripheral pulses, brachiofemoral delay and abdominal or peripheral vessel bruits
- History of polycystic renal disease or palpable enlarged kidneys

- Cushingoid features, multiple neurofibromatosis
- Significant elevation of plasma creatinine with use of ACE inhibitors
- Hypertension in children
- History of snoring, daytime somnolence, obesity, short and thick neck – Obstructive Sleep Apnoea.

The percentage prevalence of various causes of Hypertension.

A. Primary or Essential	94-95%
B. Secondary	
Renal	
Renal parenchymal	2-3%
Renovascular	1-2%
Endocrinal	0.3-1%
Primary aldosteronism	
Phaeochromocytoma	
Cushing's Syndrome	
Acromegaly	
Vascular – Coarctation of aorta	
Nonspecific aortoarteritis	
Drugs – Oral Contraceptives, NSAIDs	
Steroids, Cyclosporine	0.50%
Miscellaneous	
Obstructive Sleep apnoea	0.50%

The **second** is to assess the severity of disease because risk and type of treatment program derive from degree of pressure elevation and amount of target organ damage.

The **third** is to identify any concurrent cardiovascular risk factors (like diabetes, dyslipidemia) because their presence will affect the threshold for initiating therapy and the nature of the treatment program.

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 chronic kidney disease (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, liquorice (*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 crepitations and rhonchi.
- Examine the abdomen for bruits, enlarged kidneys, masses and abnormal aortic pulsation.
- Examine the optic fundus and do a neurological assessment.

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 as described under “secondary hypertension”.

Management of Hypertension

Initiation of therapy

- In low risk patients(SBP 140-159 or DBP 90-99, no other risk factors), it is suggested to institute life style modifications and observe BP for a period of 2-3 months, before deciding whether to initiate drug therapy.

- In medium risk patients, (SBP 140-159 or DBP 90-99, SBP 160-179 or DBP 100-109, 1-2 risk factors) institute life style modifications and initiate drug therapy after 2-4 weeks, in case BP remains above 140/90.
- In high risk (associated clinical conditions, including clinical cardiovascular disease or renal disease) and very high-risk groups (SBP>180 or DBP>110), initiate immediate drug treatment for hypertension and other risk factors in addition to instituting life-style modification.

Targets of therapy

- Gradual reduction of BP is a prudent therapeutic approach except in stage 3 hypertension.
- 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. (1)

In view of the above studies, it would seem desirable to achieve optimal or normal BP (<140/90 mmHg) in the young and middle aged. In diabetic patients BP lowering to around 140 / 80 mm Hg is recommended. In patients who have survived stroke, a BP of around 130/85 mm Hg is suggested. In elderly patients a high normal BP around 140-145/90mm Hg should be taken as the target BP. (2)

- Initially the J-shaped hypothesis was accepted, and it was felt that lowering BP below a certain level (140/90 mmHg) would increase the risk of coronary events by lowering diastolic perfusion pressure in coronary circulation. Data from the Hypertension Optimal Treatment (HOT) Study and United Kingdom Prospective Diabetes Study (UKPDS) study showed BP reduction to levels of 130/80 specially in high-risk individuals (diabetics, CKD, and CVA) was more beneficial. Hence, at the time of second guidelines it was suggested that the lower the better policy holds true for target BP in hypertension. More recent data (ADVANCE, ACCORD, INVEST) shows lowering of diastolic BP to below 70 mmHg can be deleterious, especially in patients with coronary artery disease. As compared to the previous guidelines of 2007, we now realize that a relatively less aggressive approach towards achieving lower target BP is a reasonable goal, since as suggested above, recent data shows no additional benefit of lowering diastolic BP below certain levels in specific situations. (3-5)

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.
- 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. Alcohol consumption should be

limited to no more than 2 drinks per day (30gm of alcohol, 90 cc of whisky, 300cc of wine, 750cc of beer) for most men and no more than 1 drink per day for women and lighter weight people.

- 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 (amounting to 3-4 gms of sodium), however, in hot summer this may be relaxed (one teaspoon salt is approx. 2.4 gms of sodium). 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.

- 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. Cardiovascular benefits of cessation of smoking can be seen within one year in all age groups.

- Yoga and Meditation: Yoga, meditation and biofeedback have been shown to reduce blood pressure.

- Diet:

- Vegetarians have a lower blood pressure compared to meat eaters. 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.

- Intake of saturated fats is to be reduced since concomitant hyperlipidaemia is often present in hypertensives.

- Adequate potassium intake from fresh fruits and vegetables may improve blood pressure control in hypertensives.

- 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.

- Thus, the diet in hypertensives should be low calorie, low fat, and low sodium, with normal protein intake.

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.

- 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) ACE inhibitors, 2) angiotensin II receptor blockers, 3) calcium channel blockers, 4) diuretics and 5) newer β -blockers.

Direct renin inhibitors: Aliskiren - has been evaluated and found to be effective. In the ALLAY trial, aliskiren was found to be as effective as losartan in regressing LVH.⁽⁶⁾In the more recent ACCELERATE trial,⁽⁷⁾ combination of aliskiren and amlodipine was found to be more effective than monotherapy. It is a useful

agent in resistant hypertension and also reduces the proteinuria in diabetes with hypertension.

- 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.(8)
- Choice of an antihypertensive agent is influenced by age, concomitant risk factors, presence of target organ damage, other co-existing diseases, socioeconomic considerations, and availability of the drug and past experience of the physician.
- Combining low doses of two or more 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.
 - Undesirable combinations
 - B-blocker and ACE inhibitor
 - B-blocker and centrally acting drugs
 - B-blocker and verapamil/diltiazem
 - ACE inhibitors and ARBs
 - Two drugs from the same class
- Use of fixed dose formulations should be considered to improve compliance.
- Drugs with synergistic effects should be combined pertinently to enhance BP lowering effect so as to achieve target BP.
- 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.

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 and alcohol moderations must be promoted vigorously.

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). 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.

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.

2. Cerebrovascular Disease

- Hypertension is the most important modifiable risk factor for all types of atherothrombotic stroke and intracerebral haemorrhage due to rupture of Charcot-Bouchard aneurysms.
- The relation between the incidence of stroke and blood pressure is continuous. A 5-6 mm Hg reduction in diastolic blood pressure reduces the risk of stroke by 40%.

3. Kidney

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

4. Retina

- Hypertensive retinopathy is a condition characterized 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.

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.

6. Hypertensive crises

Hypertensive crises are classified as hypertensive emergencies or urgencies.

Hypertensive emergencies:

Hypertensive emergencies (Malignant Hypertension) 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) often with parenteral agents over a period of 6-8 hours with constant monitoring, 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.

Hypertensive urgencies:

Hypertensive urgencies (Accelerated Hypertension) 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. The aim should be safe, prompt and gradual lowering of blood pressure with oral medication over a period of 1-3 days. In most urgencies, blood pressure can be controlled with rapidly acting oral medications like calcium channel blockers and ACEI/ARB. 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 ischemia.

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Dr Sayed Yasmeen Raunaq
Medical Officer, IITD Hospital.