

Secondary Hypertension

The prevalence of secondary hypertension is around 5-6% of all hypertensives. Because of low prevalence, routine screening for secondary hypertension is not essential and cost effective. Renal disease constitutes the major group of secondary 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

A. Hypertension in Chronic Kidney Diseases

Hypertension, after diabetes mellitus, is the second leading cause of end-stage renal disease (ESRD) and together these entities account for over 60% of ESRD patients.⁸³ Essential hypertension is an important cause of chronic kidney disease and renal parenchymal disease is a well established cause of secondary hypertension.

There are two forms of kidney diseases causing hypertension namely renal parenchymal and renovascular.

Causes:

Renal parenchymal diseases – (Non-diabetic)^{84,85}

Table 15 : The percentage prevalence of various causes of Hypertension^{81,82}

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	0.50%
Steroids, Cyclosporine	
Miscellaneous	0.50%
Obstructive Sleep apnoea	

- Chronic glomerulonephritis
- Chronic interstitial nephritis
- Analgesic nephropathy
- Polycystic kidney disease
- Gout with renal failure
- Obstructive nephropathy

Stages of Chronic Kidney Diseases and Action Plan

The functional stages are based on estimated GFR in CKD with the relevant action plan as below.⁸⁶

Treatment

Therapy with antihypertensives in CKD has been found to not only control BP but also slows down the progression of chronic kidney diseases. The Ramipril Efficacy in Nephropathy (REIN), ACEI and progressive Renal Insufficiency (AIPRI) and modification of Dietary Protein in Renal Disease (MDRD) trials established the ability of antihypertensives to slow down the progression of non-diabetic chronic kidney disease.⁸⁷⁻⁹⁰

1. Threshold for initiation of AHT²
 - a. BP 140/90 Hg for patient without proteinuria
 - b. BP 130/80 for those with proteinuria
- Target to achieve: BP < 130/80mmHg

In post renal transplant patients, hypertension is an important issue since certain drugs like cyclosporine and erythropoietin used in these patients can aggravate hypertension. At times, combination of multiple drugs

Table 16 : Staging System and Action Plan for Chronic Kidney Disease

Stage	Description	GFR [†] (mL/min per 1.73 m ²)	Action [*]
–	At increased risk for CKD	≥ 90 with risk factors [‡]	Screening CKD risk reduction
1	Kidney damage [‡] with normal or increased GFR	≥ 90	Diagnosis and treatment. Retard progression of CKD. Treat comorbidities. Cardiovascular disease risk reduction.
2	Mild decrease in GFR	60-89	Estimate progression
3	Moderate decrease in GFR	30-59	Evaluate and treat complications
4	Severe decrease in GFR	15-29	Prepare for renal replacement therapy
5	Kidney failure	< 15 or dialysis	Renal Replacement Therapy if uremic

[†]Estimated GFR (eGFR) using Modification of Diet in Renal Disease (MDRD) formula: $GFR (mL/min/1.73 m^2) = 186 \times (Pcr)^{-1.154} \times (age)^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if African American})$

^{*}Includes actions from preceding stages.

[‡]Risk factors : hypertension, dyslipidemia, diabetes mellitus, anemia, systemic lupus erythematosus, chronic analgesic ingestion.

[‡]Kidney damage as manifested by abnormalities noted on renal pathology, blood, urine or imaging tests.

including ACEI, ARB, CCB and diuretics may be required for effective BP control. In patients where BP is still not controlled, clonidine, α methyl dopa or α blockers may be added.

Renovascular:

- The most common cause of renovascular hypertension in India is Takayasu's syndrome (progressive aortoarteritis),⁹¹ though atherosclerotic renovascular disease is also being recognised more often now in early patients.
- The most common cause of renovascular disease in Western population are atherosclerotic disease in 60% of elderly population and fibromuscular dysplasia in 35% of young. Atherosclerotic renal artery stenosis have associated cardiovascular disease.
- 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 which can be unilateral or bilateral.⁹²
- Renovascular disease is much more common than renovascular hypertension (RVH).
- Atherosclerotic disease involves the proximal segment and fibromuscular dysplasia involves the distal segment of renal artery.

Investigations :

- A paraumbilical 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 arteriography is recommended.
- Colour Doppler Ultrasound (CDUS), CT angiography and MRI angiography are other good and non-invasive modalities. MRI angiography has higher sensitivity (90%) and specificity (92%).
- ⁹⁹Tc – DTPA and ¹²³I – Hippuran scan are useful non-invasive investigations. These tests give functional status of CKD.
- 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.

Treatment of renal artery stenosis

Goals are control of BP and preservation of renal function. In general there are three options. :

Medical

Percutaneous transluminal renal angioplasty

Surgery

Patients with fibromuscular dysplasia benefit from angioplasty or surgical revascularisation. Patients with atherosclerotic renovascular disease do not demonstrate any significant benefit from renal artery intervention but medical therapy is equally effective in these patients.⁹²

B. 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.⁹⁴

Investigations

- Screening tests include plasma and 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: α methyl dopa, β blockers, clonidine, 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 specific way of diagnosing adrenal and extra adrenal pheochromocytomas.⁹⁵ Other modalities include PET scan using ¹⁸F-fluorodeoxy glucose.
 - 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 α 1-receptors on vessel wall and leave pre-synaptic α 2- receptors. As a result, tachycardia is less of a problem. B-blockers may be given to these patients to control tachycardia and arrhythmias, only after α -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. Plasma Aldosterone to Plasma Renin Activity (PRA) ratio more than 20 to 25 (normal < 10) is 95% sensitive and 75% specific for Primary Hyper Aldosteronism. It is usually diagnosed by imaging techniques.
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. This can be screened by performing early morning serum cortisol levels. Hypertension remits in most patients after successful treatment.

c. Miscellaneous

Other important secondary causes include:

- Oral contraceptives (see Hypertension in Women pg. no. 29)
- 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. Polysomnography is diagnostic. No specific drugs have proven superior in sleep apnea but use of C-PAP improves the hypertension
- Acute stressful situations cause intense sympathetic discharge and may temporarily induce hypertension. B blockers are preferred.
- 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.