Everyday Practice

Hypertension in a Child: Diagnostic Aspects

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Hypertension is defined as systolic or diastolic blood pressure (BP) above 95th percentile for age on three or more occasions(l). The First Task Force of National Heart Lung and Blood Institute on Blood Pressure Control in Children was organized in 1977, which defined hypertension as blood pressure above 95th percentile for age and sex and set standards for normal blood pressure distribution of 2-15 years old children(2). These standards were set into criticism as they allowed BP of 11-12 years old as normal till 140/90 mm Hg which is abnormal even for adults. These standards were revised by the Second Task Force in 1987 which set standards from newborn to 18 years of age. A new category of high normal blood pressure was established to ensure that children with blood pressure at upper end of distribution have careful longitudinal evaluation. It divided hypertension into significant and severe. Significant hypertension was defined as that between 95th and 99th percentile and severe as that above 99th percentile. Significant hypertension generally requires non-pharmacological regimen of weight reduction, exercise and dietary adjustment. Severe hypertension requires aggressive pharmacological treatment and it is mostly associated with secondary identifiable causes which may be amenable to specific forms of treatment. The Second Task Force has also given data for integration of height and weight for interpretation of blood pressure curves.

Blood pressure is measured in the right arnn-of a relaxed child using proper cuff size which covers two-third of upper arm length and 50-70% of mid arm circumference and the sphygmomanometer at the level of heart. Smaller cuff size and anxiety can cause over-estimation of blood pressure called pseudohypertension. Diastolic blood pressure is recorded at 4th Korotokoff phase, *i.e.,* change in the intensity of sounds below 12 years and 5th phase after that, *i.e.,* disappearance of sounds. Initially at least once blood pressure should be recorded in all the four limbs to diagnose coarctation, Takayasu disease, *etc.*

Measurement of blood pressure in children below three years by auscultation is not accurate as Korotokoff sounds are faint. Palpation measures only systolic blood pressure. Flush method measures only mean blood

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pressure and is affected by anemia, edema and hypothermia. Doppler ultrasound readings correlate well with intra-arterial measurements. This correlation is less strong with diastolic blood pressure. Direct intra-arterial measurement is possible using pressure transducers attached to indwelling catheter passed to aorta through umbilical or peripheral artery. Blood pressure falls during the first 1-2 hours of sleep (slow wave sleep) by 15-20%. It rises immediately on awakening, even without any physical activity. Ambulatory measurement over 24 hours shows diurnal variation, *i.e.,* highest in the morning and decreases as the day passes, with least at night. Average of many ambulatory readings during the day correlates better with patient's correct blood pressure than a single reading at rest. Orthostatic hypertension *(i.e.,* on standing from a supine position) occurs in Certain individuals with normal supine blood pressure due to disinhibition of cardiopulmonary baro reflex and stimulation of carotid sinus. These individuals have low blood volume.

Evaluation of a child with hytpertension is done by history, examination and screening laboratory tests initially and specific investigations later, keeping in mind, the various causes of hypertension(l). As a general rule blood pressure high enough to require treatment is generally secondary in children. Between 43-84% children with hypertension referred to major medical centres have a renal cause(4-6). Thus, detailed examination for renal parenchyma and renovascular system is important in children. Renal parenchymal hypertension is far more frequent than renovascular hypertension(6). By definition, renovascular hypertension is the one which is improved by revascularization and not mere stenosis of renal artery (<25% of diameter)(7,8). Pheochromocytoma and adrenal tumors are rare but important causes as they are surgically curable(9). Between 1-2% of new born infants also are hypertensive, where the commonest cause is umblical artery catheterization leading to renal vein thrombosis or embolism from tip of the cathether(10,11). The important causes of hypertension are listed in *Table I.*

A. History

A history of hypertension, hyperlipidemia or stroke in the family suggests essential hypertension, especially if it is mild(9). History of recent onset, accelerated hypertension, refractory hypertension and young age, *i.e.,* 9-10 years, suggests renovascular hypertension(l,9). A past history of renal disease *e.g.,* oliguria, burning micturition, hematuria and history of abdominal or back trauma or lithotripsy should be asked(ll,12). A history of renal transplantation may be relevent as 60-90% of such children have hypertension due to acute or chronic rejection, renal artery stenosis acquired during transplantation, underlying renal disease or dose of steroids used. History suggestive of SLE or periarteritis nodosa may suggest renal hypertension. A history of umbilical catheterization during neonatal period may be contributory(13-15). Intake of drugs, *e.g.,* amphetamines, corticosteroids and oral contraceptives (in adolescent females) can cause hypertension(9). Transient hypertension can occur due to various causes listed in *Table I.*

TABLE I—*Causes of Hypertension in Children*

Sustained Hypertension	Transient Hypertension
A. Neonates and Infants	
1. Renal artery thrombosis stenosis	1. Abdominal surgery
2. Renal vein thrombosis	2. Bronchopulmonary dysplasia
3. Renal parenchymal or structural diseases	3. Intracranial tension
(a) Infantile polycystic kidney	4. Drugs-steroids, theophylline
(b) Obstructurive uropathy	5. Fluid and electrolyte overload
(c) Renal dysplasia	6. Pneumothorax
(d) Renal failure	7. Hypercalcemia
4. Wilms tumor	8. Extracorporal membrane oxygenation
5. Coarctation of aorta	
6. Endocrineal	
(a) Adrenogenital syndrome	
(b) Cushings syndrome	
(c) Primary aldosteronism	
(d) Hyperthyroidism	
(e) Pheochromocytoma	
B. 1-10 Years	
1. Renin dependent	1. Hypercalcemia
A. Renal parenchymal disease (traction)	2. Immobilization
(a) Chronic pyelonephritis	3. Intracranial tension
(b) Progressive glomerulonephritis	4. Steroids
(c) Obstructive uropathy	5. Acute glomerulonephritis
(d) Polycystic kidneys	6. Acute renal failure
(e) Significant renal hypoplasia	7. Hemolytic uremic syndrome
(f) Chronic renal failure	8. Burns
B. Renal tumors, *e.g.*, Wilm's	9. Gullian Barre syndrome
C. Renal vascular-Renal artery stenosis	10. Acute polio
	11. Salt and water retention
2. Coarctation	
3. Catecholamine excess	
(a) Pheochromocytoma	
(b) Neuroblastoma	
4. Hyperthyroidism	
5. Raised steroid levels	
(a) Congenital adrenal hyperplasia	
(b) Primary hyperaldosteronism	
(c) Cushing's syndrome	
6. Collagen vascular disease, *e.g.*, SLE, polyarteritis	
7. Essential hypertension	
C. >10 Years	
1. Essential hypertension more common	1. Gullian Barre Syndrome
2. All other causes of secondary hypertension mentioned above.	2. Burns
	3. Acute renal failure
	4. Treatment with steroids
	5. Intracranial tension

B. Clinical Examination

Measurement of height and weight for obesity (weight for height above 95th percentile suggests obesity). A positive relationship between blood pressure and body size is established by 6 years. Palpation of femoral and other peripheral pulses (for coarctation and aortoarteritis), cushingoid facies (adrenal hyperplasia or adenoma), signs of hypothyrodism or hyperpituitarism is helpful in etiological diagnosis(l). Bells palsy is an uncommon but unique sign of hypertension in children(9). Neurofibromatosis may be associated with renal artery stenosis. Abdominal bruit (found in renal artery stenosis) is heard with the patient supine and knees flexed. Diaphragm of stethoscope is pressed hard on the abdominal wall just below the xiphoid process and moved along both intercostal margins, one by one. Bruit is heard in systole and diastole. Bruit of intrarenal arterio-venous< fistula is heard at the back. Only systolic component of bruit can be heard in the abdomen in essential hyptertension also. Presence of severe retinopathy suggests renovascular hypertension.

C. Routine Laboratory examination

Urinalysis is done to detect acute glomerulonephritis (75-80% cases have hypertension), nephrotic syndrome (26%), pyelonephritis (14-35%) and other renal parenchymal and vascular causes. Urine culture, blood urea nitrogen, serum creatinine and uric acid abnormalities point towards renal disease. Level of serum cholesterol, triglycerides, HDL and LDL, *etc.* are geared to assess other atherosclerotic risk factors and may be useful in obese adolescents with a family history of hypertension. Baseline serum electrolytes are done if treatment is started and monitored subsequently, as diuretics are often used in the treatment(9,16).

D. Electrocardiography and Echocardiography

Electrocardiography is done to look for left ventricular hypertrophy and echocardiography to quantify left ventricular mass and left atrial size for future monitoring(17,18).

E. Other Special Investigations

Renal ultrasound is a simple and easy test for evaluation of kidney size and anatomy(l). In suspected adrenal cortical tumor/hyperplasia, plasma and urinary steroids are estimated(19). Pheochromocytoma in children does not always present as episodic hypertension but gather as persistent hypertension and should be carefully excluded(9,16). Thus urinary, catechola mines should be evaluated in all cases of moderate to severe hypertension. Kidney biopsy may be done in selected cases of renal parenchymal diseases.

F. Investigations for Renovascular Hypertension

I. Intravenous Pyelograpliy (IVP): Although, it has been done for several years, it is not a very sensitive test (60% sensitivity) and is now almost obsolete. Rapid sequence IVP is also not significantly better *(i.e.,* films taken quickly at 1, 2 and 3 minutes and then at usual 10 and 20 minutes). The finding of disparity of kidney size of >0.5 cm below the age of 15 years and >1 cm above 15 years of age, delayed excretion of contrast material on affected side and

intense though delayed nephrogram have been the criteria used to detect renovascular hypertension by IVP(20). The main value of IVP in children with hypertension is in detection of renal parenchymal disease and collecting system, which can also be now done by ultrasound.

II. Plasma Renin Activity (PRA): Baseline and after captopril load PRA is evaluated.

(a) Basal PRA: Low plasma renin level in untreated patients virtually rules out renovascular hypertension but high renin does not prove it, as volume depletion, salt restriction and upright position, are all stimuli for renin secretion.

(b) Captopril Test: All the following criteria should be met for a positive test for renovascular hypertension: *(i)* Stimulated PRA >12 mg/ml/h; *(ii)* Absolute increase in PRA >3 mg/ml/h; and (*iii)* Per cent increase of >150% of PRA if baseline PRA >3 mg/<ml/h. This is the most sensitive office screening test(21).

III. Renal Angiography: It is better delayed till blood pressure is controlled (diastolic <100 mmHg) by medical therapy. Renal vessel anatomy is visualized by this procedure. Samples of renin activity can also be collected from both renal veins(20). Intra-arterial DSA is better than conventional angiography for better visualization.

IV. *Renal Vein Renin Activity:* A significant difference of renal vein renin of both sides suggests renovascular hypertension. Blood pressure should be carefully monitored during angiography as fall of blood pressure is a stimulus for renin release and if it occurs between sampling from the two kidneys, a false positive high renin activity on one side occurs. Various indices are used to detect renovascular hypertension curable by revascularization. Increase of >50% in renal vein renin on one side, *i.e.,* ratio of 1.5:1 suggests renovascular hypertension but is not 100% correct as patients with lesser ratio have also been cured by surgery. Renal systemic renin index of Fry and Stanlay, *i.e.,* [renal vein PRA (Right + Left) - systemic vein PRA]/ systemic vein PRA, if >0.48 in adults suggest higher renin production than hepatic degradation and documents hyperreninemia. This index is not very well studied in children. Determination of renin levels is a useful adjunct of angiography(7,8,20,21).

V. *Intravenous Digital Subtraction Angiography:* Contrast injected into a peripheral vein is less invasive than conventional angiography but mere is inadequate visualization of segmental peripheral and collateral arteries leading to false negative result. Also a large dose of contrast is required and thus cannot be used in patients of azotemia. A positive DSA study needs to be confirmed by conventional angiography before surgery. DSA has not maintained widespread use(20,21). As a screening test, however, it is better than IVP.

VI. Radionucleide Renography: Scan using 1-131 (OIH) O-iodohippurate without ACE inhibitors is not better than IVP and has been largely abandoned"(20). In this context, Tc99 labelled (DTPA) diethylenetriomine pentacetic acid is a better option. Use of ACE inhibitors has improved both OIH and DTPA scintigraphy and is a useful screening test. With more than 90% stenosis of renal artery, a baseline scan

is abnormal. However, with 60-90% stenosis, abnormality is detected only after ACE inhibitor as compensation of renal function by renin angiotensin system is knocked off by it. With less than 60% stenosis, study is normal with or without ACE inhibitors.

After doing a baseline DTPA or O1H scan, the patient is hydrated orally with 10 ml/kg water and captopril 25-50 mg orally 1 hour before scan or enalaprjl 50 mg/kg intravenously 15 minutes before the scan. In 100% stenosis of renal artery, the kidney shrinks and is non functional and may not be visible on scintigraphy. DTPA renography (with 5-10 mci) is a measure of GFR as it is mostly filtered in glomeruli, while OIH (with 300 mci) is a measure of renal blood flow as it is secreted by the proximal tubule* Criteria used for DTPA and OIH renography with captopril are different due to varying properties of DTPA and OIH.

(A) Criteria for Abnormal OIH *Scan:* These include: (i) Decreased early activ ity at 2-4 minutes; (ii) Prolonged cortical retention of radionucleide at 20 minutes, *i.e.,* RCA upto 30%; (iii) More than 10% increase in RCA with ACE inhibitors; and *(iv)* Renogram shows late plateau or may even show slowly and continuously rising RCA to 100%.

(B) *Criteria for Abnormal DTPA Scan:* These include *(i)* Uptake of DTPA by the affected kidney is less than 4% of total; *(ii)* Time to peak of DTPA >5 minutes longer than contralateral kidney*; (iii)* Prolonged retention of DTPA, *i.e.,* frac tion of peak activity 15 minutes after DTPA administration is atleast 20% greater than contralateral kidney(21).

VII. Doppler Uitrasonography: It requires accurate positioning of transducer for detecting renal artery stenosis. More work is required about it's utility.

VIII. Exercise Renography: It is an experimental modality and so far tried in adults only. Renography is done in prone and sitting positions with ergometric exercise. Ergometric resistance is set at 60 watts for women and 80 watts for men. Renography is begun after pulse rate increases to atleast 20 beats/min and after injection 7 uci (1-131) or 6 µci (1-123), OIH/kg weight. A normal baseline scan may show renovascular stenosis after exercise.

IX. Split Renal Function Study: It is a reliable test which has gone into disfavour as it is invasive requiring cystoscopy and catheterization of both ureters.

As a rute, methods to lateralize renal vein renins are not 100% sensitive for selecting patients for surgery. So with improving results of revascularization procedures (transcutaneous ballon angioplasty/surgery) all patients of hypertension with renal artery stenosis should be offered surgery in the hope of cure or preventing more accelerated hypertension and renal insufficiency.

G. Laboratory Diagnosis of Fheochromocytoma and Other Adrenal Tumors

1. *Biochemical*

Hypertension in pheochromocytoma may be episodic or sustained. Urinary catecholamines and their metabolites, *e.g.,* vinyl mendellic acid (VMA), homovanillic acid (HVA) and metanephrines are excreted in large

amounts in pheochromocytoma. The simplest screening test is metanephrine in single voided urine specimen, which has upto 99% specificity. Plasma catecholamine level is not good for screening, as frequent false positives occur due to non-specific stimulation by numerous activities and 10-30% false normal values can occur. If spot metanephrine is abnormal, confirmation by 24 hours urine metanephrines, HVA, VMA and plasma catecholarriines after supine posture for one hour is done. Urinary catecholamines increase by methyldopa and theophylline and decrease with clonidine and fenfluromine. There is an analytical increase with tetracylines, chloral hydrate and chlorpromazine. Urinary metanephrines show analytical increase with acetaminophen and analytical decrease with propranolol and methyl glucamine (X-ray contrast). VMA shows analytical increase with nalidixic acid and pharmacological decrease with M-dopa, variila, banana, coffee (dietary phenolic acid). Urinary corticosteroids increase in adrenal cortical tumors andcortisol increase with adrenogenital syndrome and cushing syndrome.

2. Imaging Techniques

Preoperative localization of pheochromocytoma is required if biochemistry is suggestive. Ultrasound is not very good as many small tumors are often missed. CT scan has 95% sensitivity if adrenal tumor is more than 1 cm and extra-adrenal pheochromocytoma I >2 cm. I^{131} MIBG (I^{131} labelled metaiodo benzyl guanidine) has 95% predictive accuracy for positive scan and 90% productive accuracy for negative scan. It is selectively taken up by adrenergic vesicles. It is also very useful when identity of any tumor or metastasis is uncertain. Scans are taken few hours after injection of I^{131} MIBG and then 24, 48 and 72 hours later(24,25). MRI is another newer technique for imaging of adrenal masses. MR spectroscopic imaging of adrenal tumors can differentiate between adenoma and carcinomas based on lipid context (13% in adenomas as compared to 3.5% in carcinomas)(26).

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