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Clinical Research

HYPERTENSION IN CHILDREN – A GROWING PROBLEM

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ABSTRACT Primary hypertension is detectable in children and adolescents and, as in adults, is associated with a positive family history of hypertension, obesity and life-style factors. Owing to the well established childhood obesity epidemic, the population prevalence of high blood pressure in the young is increasing. Hypertension in childhood is commonly associated with other cardiovascular risk factors as well as obesity. Although death and cardiovascular disability occur uncommonly in hypertensive children, intermediate markers of target organ damage, such as left ventricular hypertrophy, thickening of the carotid vessel wall, retinal vascular changes and even subtle cognitive changes, are detectable in children and adolescent with high blood pressure. The etiologies of hypertension in children and adolescent are quite different than the adult population but the management strategies remains almost the same. The non-pharmacological methods to control blood pressure also holds true in this subset of population but relatively lesser intensified as compare to their counterparts. As a good number of children having underline hypertension remains undetected, they generally add the substantial burden to cardiovascular disease profile in their later age.

KEYWORDS :

Definition

Rather than a single BP level, the top portion of the distribution of blood pressure (BP) specific to age, gender and height continued to be used to define high BP throughout childhood. The systolic and diastolic BPs are of equal importance; if there is a disparity between the two, the higher value determines the BP category. The age and height-specific blood pressure percentiles may be determined using calculators for boys for girls : Normal BP - Both systolic and diastolic BP $<90^{th}$ percentile.

- Prehypertension - Systolic and/or diastolic BP $>90^{th}$ percentile but $<95^{th}$ percentile or if BP exceeds 120/80 mmHg (even if $<90^{th}$ percentile for age, gender, and height).
- Hypertension - Hypertension (HTN) is defined as either systolic and/or diastolic BP $>95^{th}$ percentile measured on **three** or more separate occasions. The degree of HTN is further delineated by the two following stages.
- **Stage 1 HTN -** Systolic and/or diastolic BP between the 95^{th} percentile and 5 mmHg above the 99^{th} percentile.
- **Stage 2 HTN -** Systolic and/or diastolic BP $>99^{th}$ percentile plus 5 mmHg, [1]

In adults the diagnosis of hypertension is verified by BP $\geq$ 140/90 mmHg on two separate visits. To avoid over-diagnosis of hypertension in a child with a single elevated BP, three separate visits for BP measurement are recommended with an average BP $\geq 95^{th}$ percentile required for diagnosis of hypertension. An exception to the necessity for repeated BP measurement would be stage 2 hypertension or a child with symptomatic hypertension.

Etiology

Childhood HTN is also divided into two categories depending upon whether or not an underlying cause can be identified :

- Primary HTN - No underlying cause is identified.
- Secondary HTN - An identifiable cause is determined. In children with secondary HTN, the underlying disorder may be curable with complete resolution of HTN.

Primary hypertension —

Primary HTN is the most common cause of HTN in older children and is a diagnosis of exclusion. It is more likely in children who are postpubertal, have a family history of HTN, are overweight or obese, or have only mild hypertension (blood pressure [BP] at or just above the 95^{th} percentile). A family history of HTN is present in as many as 70 to 80 percent of all patients with primary HTN (also referred to as essential HTN), which has no identifiable underlying etiology, and in approximately 50 percent of hypertensive children. In patients with primary HTN, elevated BP is thought to result from the interaction of multiple genes and environmental factors. It has been estimated that genetic factors account for approximately 30 percent of the variation in BP in various populations and as much as 60 to 70 percent of HTN in families.

Secondary hypertension —

There are a number of causes of secondary HTN and specific symptoms and findings may point to a particular disorder. The three most common causes are renal disease, endocrinal causes and renovascular diseases. Almost all children younger than 15 years of age have secondary cause, whereas 75 percent of adolescents use to have primary HTN. (Table 1 & 2)

1. Renal parenchymal disease —

A variety of intrinsic renal disorders is associated with HTN and includes the following :

Glomerulonephritis -

TN is a manifestation of both chronic and acute glomerulonephritis (GN). In children, the most common form of acute GN is post-streptococcal GN, which follows after a streptococcal infection. Henoch-Schonlein purpura (IgA vasculitis) can present with renal manifestations including HTN. In children, chronic glomerular disorders associated with elevated BP include IgA nephropathy, membrano-proliferative GN, or lupus nephritis.

In children with glomerulonephritis, the most common mechanisms of HTN are volume expansion due to salt and water retention (as in acute post streptococcal glomerulonephritis) and activation of the renin-angiotensin system. Other common presenting features of glomerular disorders include hematuria, oliguria, peripheral edema, and an elevated serum creatinine or BUN.

- Renal parenchymal scarring can be a sequelae of acute pyelonephritis and may be associated with vesicoureteral reflux. It is also seen in children with congenital anomalies of the kidney and urinary tract, and those with irreversible renal injury from hemolytic uremic syndrome.

Polycystic kidney disease -

Polycystic kidney disease (PKD) is due to two genetic disorders, autosomal dominant and autosomal recessive PKD, that involve the

formation of renal cysts. HTN is a common presenting sign in children with the recessive form of PKD.

Chronic renal failure -
Chronic renal failure (CRF) of any cause can be associated with HTN because of volume expansion. In addition, children who have undergone renal transplantation are at increased risk for HTN due to several different mechanisms including rejection or the administration of drugs that increase BP.

2. Renovascular disease —
HTN due to renovascular disease is due to a decrease in renal blood flow resulting in increased plasma levels of renin, angiotensin, and aldosterone. Children with renovascular disease generally have stage 2 HTN.[2]

Causes of renovascular disease in children include the following :
- Fibromuscular dysplasia - Fibromuscular dysplasia is the most common etiology of renovascular disease. It is characterized by arterial stenosis due to a non-inflammatory, non-atherosclerotic process.
- Umbilical arterial catheterization - During the newborn period, catheterization of the umbilical artery may lead to a clot in the renal artery resulting in renal arterial injury and stenosis.
- Other causes of renovascular disease include neurofibromatosis, arteritis, renal artery hypoplasia, and midaortic syndrome (segmental narrowing of the proximal abdominal aorta).

Renal tubular disease —
Rare Monogenic diseases in which tubular reabsorption of sodium or chloride is increased are associated with increased vascular volume and HTN, such as Liddle's syndrome, Type 1, pseudohypoaldosteronism, Type 2 pseudohypoaldosteronism, or Gordon's syndrome.

3. Endocrinologic disease —
- Endocrinologic conditions associated with HTN include the following Catecholamine excess — Catecholamine excess that results in HTN occurs in patients with pheochromocytoma and neuroblastoma, and those who use sympathomimetic drugs including phenylpropanolamine, cocaine, amphetamines, phencyclidine, epinephrine, phenylephrine, and terbutaline and the combination of a monoamine oxidase (MAO) inhibitor plus ingestion of tyraminecontaining foods.
- Corticosteroid excess — Corticosteroid excess is more commonly due to exogenous administration of glucocorticoids and rarely due to endogenous production of either glucocorticoids or mineralocorticoids. In both settings, corticosteroid excess results in HTN.
- Corticosteroid excess may be seen in patients with Cushing's syndrome due to hypersecretion of adrenocorticotropic hormone (ACTH).
- Mineralocorticoid excess that result in HTN may be seen in patients with congenital adrenal hyperplasia. Other rare causes of HTN due to mineralocorticoid excess include aldosteronesecreting tumors and the monogenic disorder of glucocorticoidremediable aldosteronism.
- Other endocrinologic disorders — Other endocrinologic abnormalities associated with HTN include thyroid disorders (hypothyroidism and hyperthyroidism), and hypercalcemia (e.g. hyperparathyroidism).

4. Cardiac disease —
Coarctation of the aorta is the primary cardiac cause of HTN. The classic findings are HTN in the upper extremities, diminished or delayed femoral pulses, and low or unobtainable arterial blood pressure in the lower extremities. The diagnosis is confirmed by echocardiogram.

5. Prenatal and neonatal factors —
There is increasing evidence that prenatal and neonatal factors contribute to higher BP. There are data demonstrating a role for low birth weight in the development of primary HTN.

In addition, a systematic review reported in utero exposure to preeclampsia was associated with an increase in systolic (mean 2.4 mmHg) and diastolic (mean 1.4 mmHg) BP, as well as an increase in BMI (mean 0.62 kg/m^2)

However, for children with chronic kidney disease, there appears to be no additional effect of an abnormal birth history on BP. This was illustrated in a report from the Chronic Kidney Disease in Children Study that found no difference in BP or the rate of chronic kidney disease (CKD) progression between patients with an abnormal birth history (birth weight <2500 g, gestational age <36 weeks, or small for gestational age) and those with a normal birth history.[3]

Comorbid risk factors and diseases —
HTN is one of several risk factors that increase the risk of premature atherosclerosis in childhood and of cardiovascular disease (CVD) in adults. These risk factors (eg, HTN, overweight/obesity, dyslipidemia, and a family history of premature CVD) do not generally occur in isolation but are usually found concurrently, which further increases the likelihood of premature atherosclerosis and CVD. In addition, several childhood diseases such as type 1 and type 2 diabetes mellitus, and chronic kidney disease are associated with accelerated atherosclerosis and CVD.

Initial Evaluation —
The initial evaluation of the child with hypertension (HTN) includes history, physical examination, and laboratory tests and procedures.

History and physical examination —
Symptoms consistent with hypertensive emergencies include headache, seizures, changes in mental status, vomiting, focal neurologic complaints, visual disturbances, and cardiovascular complaints indicative of heart failure (such as chest pain, palpitations, cough, or shortness of breath). These children require emergent evaluation and treatment.

Secondary versus primary hypertension —
Secondary hypertension should be suspected in children with one or more of the following findings:
- Prepubertal, particularly younger than 10 years of age.
- A thin child with a negative family history for HTN.
- An acute rise in blood pressure (BP) above a previously stable baseline. Severe HTN defined as stage 2 HTN (BP >5 mmHg above the 99th percentile)
- Stage 1 HTN (BP > 95th percentile but less than stage 2) with finding(s) on history or physical examination that suggests systemic disease or a specific secondary etiology of HTN.
- Specific ambulatory blood pressure patterns, such as sustained diastolic hypertension, nocturnal hypertension, and/or blunted nocturnal dipping.
- Past history of urinary tract infection, especially pyelonephritis, or underlying congenital kidney or urologic anomalies raises the possibility of renal scarring.
- Symptoms suggestive of catecholamine excess include headache, sweating, and tachycardia in addition to HTN.
- Ambiguous genitalia may be suggestive of congenital adrenal hyperplasia with excess endogenous secretion of androgens and mineralocorticoids. Children with mineralocorticoid excess may develop hypokalemia.

Edema and hematuria may be indicative of renal parenchymal disease. Initial laboratory testing demonstrating an abnormal urinalysis or elevated serum creatinine add further support for an intrinsic renal disease process.
- Patients with glomerulonephritis due to systemic disorders such as Henoch-Schonlein purpura (IgA vasculitis) or systemic lupus erythematosus have other clinical findings including arthritis, rash, and abdominal pain (the latter especially in Henoch-Schonlein purpura).
- A family history of chronic or congenital renal disease (such as polycystic kidney disease), or other genetic conditions that are associated with HTN, such as neurofibromatosis or tuberous sclerosis.

Perinatal history including :
- Umbilical arterial catheterization (UAC) as a neonate. UAC is a predisposing factor for renovascular disease.
- Oligohydramnios
- Perinatal anoxia

The presence of an abdominal bruit raises the possibility of renovascular disease, but its absence does not exclude the diagnosis.
- The findings of hypertension in the upper extremities and low or

unobtainable blood pressure in the lower extremities, significant difference between right and left arm BP, and diminished or delayed femoral pulses are suggestive of coarctation of the aorta, the primary cardiac cause of hypertension.[4]

Physical findings of end-organ damage —

In addition to obtaining height and weight, and calculating BMI, the physical examination should include a retinal examination to detect any retinal vascular changes due to HTN. Laterally displaced Apex beat may indicate left ventricular hypertrophy (LVH).

Laboratory evaluation and imaging —

Initial laboratory evaluation in all children with persistent HTN is directed at determining the etiology of HTN, identifying other CVD risk factors, and detecting end-organ damage. The following approach is recommended by the 2004 National High Blood Pressure Education Program Working Group (NHBPEP) and the 2016 European Hypertension Society guidelines.

Measurement of serum BUN, creatinine, and electrolytes, and collection of urine for urinalysis. These tests permit quick assessment of renal function and abnormalities in glucose (eg, diabetes mellitus), potassium homeostasis (eg, chronic kidney disease or congenital adrenal hyperplasia), or monogenic disorders (Liddle's syndrome, glucocorticoid remediable hyperaldosteronism etc). An abnormal urinalysis and/or an elevation in serum creatinine are suggestive of underlying renal disease.

- Complete blood count, looking for anemia that may reflect chronic diseases such as vasculitis and chronic kidney disease, or polycythemia.
- Measurement of fasting plasma glucose and lipids to identify children with diabetes mellitus and dyslipidemia. These tests should be performed in prehypertensive children who are obese, have a family history of premature CVD, or have chronic kidney disease.
- An echocardiogram to identify children with left ventricular hypertrophy (LVH) because clinical parameters, such as the severity of HTN, and electrocardiography do not accurately predict LVH. LVH is the most prominent manifestation of end-organ damage from HTN. LVH has been reported in 30 to 40 percent of children and adolescents with HTN and if present, is an indication to initiate or intensify antihypertensive therapy. Echocardiography should also be performed in prehypertensive children with obesity, hyperlipidemia, diabetes mellitus, or chronic kidney disease.
- Renal ultrasonography is used to determine the presence of both kidneys and presence of any other congenital anomaly, or disparate renal size.[5,6]

Therapeutic interventions —

Ambulatory treatment for persistent childhood HTN includes both non-pharmacologic and pharmacologic interventions.

- Non-pharmacologic therapy (i.e, lifestyle changes) includes weight reduction for children who are overweight, a regular aerobic exercise regimen, dietary measures (eg, salt restriction), and avoidance of alcohol consumption, caffeine, energy drinks, and smoking and incorporation of relaxation techniques in daily life.
- Pharmacologic agents used frequently in children that are efficacious and safe include thiazide diuretics, angiotensin converting enzyme (ACE) inhibitors, beta blockers, and calcium channel blockers (CCBs).
- Treatment is directed towards achieving the following blood pressure (BP) target goals recommended by the National High Blood Pressure Education Program Working Group (NHBPEP) and the European Society of Hypertension (ESH).
- In children and adolescents with HTN and with no evidence of end-organ damage or comorbid CVD conditions, the targeted goal for blood pressure (BP) is less than the 95th percentile based upon age, height, and gender. The age and height-specific blood pressure percentiles may be determined using calculators for boys or for girls.
- If there are comorbid CVD risk factors (e.g., obesity or dyslipidemia), or diseases associated with CVD (e.g., diabetes mellitus), or chronic kidney disease, the BP targeted goal is lowered to below the 90th percentile for age, height, and gender and, for adolescents, a target BP <120/80.[7]

Choice of antihypertensive agent —

There are no long-term clinical outcome measures to evaluate the comparative effectiveness of specific antihypertensive drugs in children with HTN. Based upon data from adult studies, the following underlying medical conditions be treated with a specific class of antihypertensive drugs.

- In adolescents with primary HTN without end-organ damage, the choice of medication is dictated by the clinical setting and patient compliance. Low-dose thiazide diuretic therapy is administered to patients who are reliably compliant in taking their medication and adherent to sodium restriction. In other patients, ACE inhibitors/angiotensin-receptor blockers (ARBs) or CCBs are used as the first antihypertensive agent.
- In children with CKD, we suggest that ACE inhibitors be used as the initial antihypertensive agent. In patients who cannot tolerate ACE inhibitors, ARBs are a reasonable alternative.
- In children with either type 1 or type 2 diabetes mellitus, we suggest that ACE inhibitors be used as the initial antihypertensive agent. In patients who cannot tolerate ACE inhibitors, angiotensin-receptor blockers (ARBs) are a reasonable alternative.

Table 1. Causes of secondary hypertension in children and adolescents

Renal disease	Psychologic causes
Pyelonephritis	Mental stress
Renal parenchymal disease	Anxiety
Congenital anomalies	Pharmacologic causes
Reflux nephropathy	Sympathomimetics
Acute glomerulonephritis	Corticosteroids
Henoch-Schonlein purpura	Stimulants
Renal trauma	Oral contraceptives
Hydronephrosis	Anabolic steroids
Hemolytic uremic syndrome	Cocaine
Renal stones	Phencyclidine (PCP)
Nephrotic syndrome	Licorice
Wilm's tumor	Nicotine
Hypoplastic kidney	Caffeine
Polycystic kidney disease	Vascular disease
Endocrine disease	Renal artery abnormalities
Hyperthyroidism	Renal vein thrombosis
Congenital adrenal hyperplasia	Coarctation of the aorta
Cushing syndrome	Patent ductus arteriosus
Primary aldosteronism	Arteriovenous fistula
Primary hyperparathyroidism	Other causes
Diabetes mellitus	Neuroblastoma
Hypercalcemia	Heavy metal poisoning
Pheochromocytoma	Acute pain
Neurologic causes	Collagen vascular diseases
Increased intracranial pressure	Neurofibromatosis
Guillain-Barre syndrome	Tuberous sclerosis

Table 2. Distinguishing clinical features between primary (essential) and secondary pediatric hypertension

Clinical features	Primary HTN	Secondary HTN
Age : Prepubertal	—	HTN in prepubertal children is more likely due to secondary HTN
Adolescents	Adolescents are more likely to have primary HTN	—
Severity	Usually stage 1 HTN	Severe HTN (defined as stage 2) is usually associated with secondary HTN
Diastolic HTN	—	Diastolic HTN is more likely to be associated with secondary HTN
Nocturnal HTN	—	Nocturnal HTN is more likely to be associated with secondary HTN
Overweight/obesity	Overweight or obese children/adolescents are more likely to have primary HTN	—

Family history of HTN	Children with a positive family history of primary HTN are more likely to have primary HTN	Family history may be positive in some cases of secondary HTN due to a monogenic cause (eg, autosomal dominant polycystic kidney disease)
Symptoms of underlying disorder	Patients with primary HTN are typically asymptomatic	Patients with secondary HTN often have other symptoms related to the underlying cause (eg, headache, sweating, and tachycardia due to catecholamine excess in patients with pheochromocytoma)

REFERENCES

1. Gavrilovici C, Boiculese LV, BrumariuO, Dimitriu AG. [Etiology and blood pressure patterns in secondary hypertension in children]. Rev Med Chir Soc Med Nat Iasi. 2007 Jan-Mar. 111 (1):70-81. [Medline].
2. Roulet C, Bovet P, Brauchli T, et al. Secular trends in blood pressure in children: A systematic review. J Clin Hypertens (Greenwich). 2016 Dec 16. [Medline].
3. Hansen ML, Gunn PW, Kaelber DC. Under diagnosis of hypertension in children and adolescents. JAMA. 2007 Aug 22.298(8):874-9. [Medline].
4. Bun SS, Grave GD, Siervogel RM, Pickoff AA, Arslanian SS, Daniels SR. Systolic blood pressure in childhood predicts hypertension and metabolic syndrome later in life. Pediatrics. 2007 Feb. 119(2):237-46. [Medline].
5. Banker A, Gupta-Malhotra M, Rao PS. Childhood hypertension: a review. J Hypertens. 2013 Dec. 2(4):128. [Full Text].
6. YIB, Zhang T, Li S, et al. Can pediatric hypertension criteria be simplified? A prediction analysis of subclinical cardiovascular outcomes from the Bogalusa Heart Study. Hypertension. 2017 Feb 21. [Medline].
7. Dhuper S, Buddhe S, Patel S. Managing cardiovascular risk in overweight children and adolescents. Paediatr Drugs. 2013 Jun. 15(3):181-90. [Medline],