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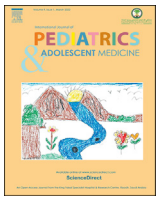

Review article

Pediatric hypertension: Review of the definition, diagnosis, and initial management

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ABSTRACT

Pediatric hypertension (HTN) is a significant and growing health concern. While previously thought to be an uncommon condition in the pediatric population, recent studies have shown an increase in incidence, which is largely due to the obesity epidemic. Accordingly, primary or idiopathic HTN has become more prevalent compared to secondary causes of HTN. The incidence of hypertension is about 3.5%; however, it may be higher as HTN can be missed during routine pediatric well visits. Since childhood HTN frequently tracks into adulthood and is a risk factor for both cardiovascular disease and progression of renal disease; early diagnosis and management of this condition is essential. In this review, we will discuss the approach of a pediatric nephrologist for evaluation and management of pediatric HTN.

CJ is a 10-year-old male who presented to his pediatrician's office for a sports physical. His vitals were as follows: HR 80, RR 18, BP 130/88, Height 134 cm, *Weight* 36 kg. *The rest of his exam was unremarkable. His blood pressure was repeated and found to be 135/82. He was brought back to his pediatrician's office later that week and his blood pressure was 132/85. He denied any symptoms.*

This manuscript describes the clinical approach for evaluation and management of hypertension in children in outpatient settings.

1. Pediatric hypertension definition

Pediatric hypertension (HTN) is defined as having three elevated systolic or diastolic blood pressure (BP) readings for the subject's age, height, and sex. The 2017 Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents provided updated recommendations for the workup and diagnosis of pediatric HTN. In this report, the percentile values for blood pressure staging have been revised, as the previous reference tables included many obese subjects. Because BP measurements can vary across visits, it is recommended that measurements are obtained over the course of multiple visits to classify a patient's blood pressure [1].

Measurements are typically taken by auscultation in the right arm while the child is resting comfortably in the sitting position using the correct size BP cuff. The inflatable cuff should cover 80% of the arm circumference and 40% of the arm length [2]. Oscillometric measurements are widely used in the clinical setting but are known to overestimate the patient's BP [3]. Due to this, elevated BP readings obtained by oscillometric machines should be confirmed by an auscultatory BP measurement. Accurate diagnosis of HTN is essential as studies have shown that it is often missed in children and is a major risk factor for cardiovascular and renal morbidity in children and adults [4] and can be associated with cardiovascular morbidity during childhood.

1.1. General pediatric population

Establishing the diagnosis of HTN requires obtaining three abnormal systolic and/or diastolic BP readings. The updated staging classification parameters are based off age and align with adult guidelines. As shown in Table 1, the classifications are divided into elevated BP and stage 1 and stage 2 HTN.

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Nomenclature

AAP	American academy of pediatrics
ABPM	ambulatory blood pressure monitor
ACEI	angiotensin converting enzyme inhibitor
ARB	angiotensin receptor blocker
CCB	calcium channel blocker
BP	blood pressure
CKD	chronic kidney disease
HTN	hypertension
LVH	left ventricular hypertrophy
UA	urinalysis

HTN can further be classified by etiology:

1. Essential or primary HTN - where an underlying cause cannot be identified [5].
2. Secondary HTN - where an organic cause is established.

Other definitions of HTN include:

1. White coat HTN - elevated BP during health care visits, which then normalizes after relaxation or in nonmedical settings [6]. This is a common phenomenon in primary care settings that accounts for 32–46% of HTN referrals [7,8].
2. Masked HTN - normal BP during health care visits but elevated in the ambulatory setting [9]; it can be often seen in patients with kidney disease and obesity [10].

1.2. Special populations

The updated guidelines from 2017 do not provide recommendations for children under the age of 1 year. However, there are data [11] available for neonates and infants based off gestational age, which are commonly used in practice and summarized in Table 2.

In pediatric patients with chronic kidney disease (CKD), the Kidney Disease Improving Global Outcomes (KDIGO) group defines HTN as a BP value above the 90th percentile for age, height, and sex [12].

2. Etiology

Essential HTN is currently the most common type of HTN in children, especially in adolescents, males, and patients with an abnormal birth history, such as low birth weight or prematurity. Interestingly, essential HTN was less common in the pediatric population in the 1990s. This changed with the obesity epidemic, and essential HTN now accounts for over 50% of the cases of HTN in children [1,13]. Secondary HTN is more often seen in younger patients and those with severe HTN.

There are multiple possible etiologies for secondary HTN (Table 3). About 50–60% of HTN cases are induced by a renal disease or renal artery stenosis. Cardiac disease is the next most common etiology, mainly due to coarctation of the aorta or mid aortic syndrome. Cardiac diseases are commonly diagnosed in the first few months of life, and the frequency then decreases with time. As such, it is rare in adolescents and young adults. Endocrine causes are less common (about 5–10% of cases) and include hyperaldosteronism, hyperthyroidism, or Cushing's syndrome. Medications can be an important cause of HTN especially in adolescents. These medications include oral contraceptive pills, steroids or anabolic steroids, ADHD stimulant medications, and chronic use of non-steroidal anti-inflammatory drugs (NSAIDs). Although most patients with obesity have primary HTN, they should be screened for obstructive sleep apnea as its treatment may alleviate their HTN.

Genetic or monogenic forms of HTN are important to consider, especially in young patients with severe HTN that is difficult to control or with a strong family history of early onset HTN. Despite multiple possible mutations and mechanisms, all forms share a common pathophysiology of sodium retention causing significant suppression of serum renin.

3. Workup

Patients who meet the criteria for HTN require a thorough evaluation aimed at identifying potential underlying causes. Table 4 summarizes evaluation and workup recommendations provided by the 2017 AAP guidelines.

3.1. Medical history

A detailed history should be obtained from all patients as it frequently provides clues for possible etiologies and can help guide further evaluation. Most patients with HTN are asymptomatic; however, some may describe non-specific symptoms such as headaches, fatigue, sleep disturbance, and changes in school performance. A good dietary and activity history is helpful, as well as screening for obstructive sleep apnea. It is common to find a positive family history of HTN in older family members; however, a family history of early onset HTN could suggest a genetic cause.

3.2. Physical examination

The current AAP guidelines state that the BP should be measured annually in children ≥3 years of age and at every visit if they have high-risk comorbidities [1] (Table 5). If elevated, the BP should be measured in all four extremities to screen for coarctation of the aorta or mid-aortic syndrome. An elevated heart rate could be a sign of anxiety, hyperthyroidism, or pheochromocytoma. The neck exam should focus on assessing the thyroid gland. The presence of striae or acanthosis nigricans could indicate metabolic syndrome or Cushing's disease, while edema could point to renal etiologies. All children with stage 2 HTN should have an ophthalmological exam to assess for retinal bleeding or papilledema. While the sensitivity of abdominal bruit is only 40%, if heard, it is over 90%

Table 1
Summary of Pediatric BP Categories and Stages (for more details, please see reference 1).

For Children Aged 1–<13 y	For Children Aged ≥13 y
Elevated BP (previously called prehypertension): ≥90th percentile to <95th percentile or 120/80 mm Hg to <95th percentile (whichever is lower)	Elevated BP: 120/<80 to 129/<80 mm Hg
Stage 1 HTN: ≥95th percentile to <95th percentile + 12 mmHg, or 130/80 to 139/89 mm Hg (whichever is lower)	Stage 1 HTN: 130/80 to 139/89 mm Hg
Stage 2 HTN: ≥95th percentile + 12 mm Hg, or ≥140/90 mm Hg (whichever is lower)	Stage 2 HTN: ≥140/90 mm Hg

Table 2
BP percentiles based off gestational age.

Postmenstrual age	50th percentile	95th percentile	99th percentile
44 weeks			
SBP	88	105	110
MAP	63	80	85
DBP	50	68	73
42 weeks			
SBP	85	98	102
MAP	62	76	81
DBP	50	65	70
40 weeks			
SBP	80	95	100
MAP	60	75	80
DBP	50	65	70
38 weeks			
SBP	77	92	97
MAP	59	74	79
DBP	50	65	70
36 weeks			
SBP	72	87	92
MAP	57	72	77
DBP	50	65	70
34 weeks			
SBP	70	85	90
MAP	50	65	70
DBP	40	55	60
32 weeks			
SBP	68	83	88
MAP	49	64	69
DBP	40	55	60
30 weeks			
SBP	65	80	85
MAP	48	63	68
DBP	40	55	60
28 weeks			
SBP	60	75	80
MAP	45	58	63
DBP	38	50	54
26 weeks			
SBP	55	72	77
MAP	38	57	63
DBP	30	50	56

Reprinted with permission from Dionne JM, Abitbol CL, Flynn JT. Hypertension in infancy: diagnosis, management and outcome. Pediatr Nephrol. 2011; 27:17–32. DBP = diastolic BP; MAP = mean arterial pressure; SBP = systolic BP.

specific for renal artery stenosis [14].

3.3. Ambulatory blood pressure monitoring (ABPM)

Continuous ambulatory blood pressure monitoring (ABPM) is the standard for confirming the diagnosis of HTN in children [1]. This automated cuff measures BP 2–3 times every hour during the day and night and then provides the average BP values during both daytime and nighttime hours. The 2017 guidelines highly encourage the standard use of ABPM when available. ABPMs are usually done by nephrologists and/or cardiologists.

3.4. Diagnostic testing

The initial testing recommended by the AAP was recently updated in 2017 [1] and is largely dependent on level of suspicion. Testing recommended for all patients includes a urinalysis (UA), chemistry panel, and lipid profile. Presence of blood and protein may point toward glomerular disease, while hypokalemia and/or alkalosis can point toward renal artery stenosis or hyperaldosteronism. A renal ultrasound should be performed in those less than 6 years of age, and in older patients with abnormal UA or renal function. In obese patients, liver function and hemoglobin A1c should also be checked. Echocardiogram is helpful for evaluation of coarctation of the aorta and to look for left ventricular hypertrophy (LVH), which is the most common end organ damage in children with HTN. EKG is not a standard recommended test in pediatric HTN patients.

Obtaining a plasma renin activity (PRA) and aldosterone level is not currently recommended as a part of the initial evaluation; however, it can be very helpful in screening for renovascular diseases or if there is concern for a genetic etiology.

Further testing should also be considered based on information collected during history and physical examination, including thyroid studies, serum metanephrines, sleep study, DMSA scan, or voiding cystourethrogram.

4. Treatment options

Management of pediatric HTN is based on the recommendations of the Fourth Report from the National High Blood Pressure Education Program in 2004 [15] and their recent updates in 2017 [1]. It is imperative to grade the patients BP accurately as not all stages of HTN require pharmacologic therapy.

4.1. Non-pharmacologic options

Lifestyle modifications should be offered to all patients, especially in essential HTN patients and obese children. Modifications include implementing the DASH diet, as well as moderate to vigorous activity 3–5 times per week [1]. Adopting a family approach and consulting with an experienced dietician can improve the chance of success. The 2017 guidelines recommend reevaluation every 6 months with a goal BP to be < 90th percentile or <130/80 in children ≥13 years old [1]. Per the AAP, athletes can be permitted to play sports if they have stage 1 HTN in the absence of end organ damage. Aggressive physical activity and weightlifting should be restricted in patients with LVH. Children with stage 2 HTN should be restricted until their blood pressures normalize [16].

4.2. Pharmacologic therapy

A 3-6-month trial of lifestyle modification and weight loss is advised for asymptomatic patients with stage 1 HTN. Antihypertensive therapy is then considered if they fail to improve their BP to below the 90th percentile for age, height, and sex. Patients with stage 2 and/or symptomatic HTN should have their workup done urgently (i.e. within one week), and antihypertensive therapy should then be started promptly.

Once treatment is initiated, the targeted BP value should be below the 90th percentile for the age, height, and sex in children with uncomplicated essential HTN[1]. However, in children with CKD, the target BPshould be below the 50th percentile for age, gender, and height as tolerated [1,12]. Recent data from the Effect of Strict Blood Pressure Control and ACE Inhibition of Chronic Renal Failure in Pediatric Patients (ESCAPE) trial support intensified treatment goals for the CKD population as they found that targeting less than the 50th percentile was associated with slower progression of their renal disease [17].

Antihypertensive medications should be tailored to the underlying etiology. For example, in patients with LVH, diabetes mellitus, or CKD, an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin-receptor blocker (ARB) is recommended as long as the estimated glomerular filtration rate is above 30 mL/min/1.73 m^2 [12,18,19]. Calcium channel blockers (CCB) are frequently used for steroid-induced HTN [20]. Diuretics (with or without CCB) are the first-line therapy in acute post-infectious glomerulonephritis-induced HTN [21]. In primary care settings, either CCB or ACEi are often the first line of treatment for essential HTN and are usually

Table 3
Common conditions associated with hypertension in pediatric population.

Renal disease	Glomerulonephritis
	End-stage renal disease
	Acute renal failure
	Reflux uropathy
	Obstructive uropathy
	Polycystic kidney disease
	Severe hydronephrosis
Cardiac	Coarctation of the aorta
	Mid-aortic syndrome
Vascular	Renal artery stenosis (usually secondary to fibromuscular dysplasia)
	Takayasu arteritis
	Hemolytic uremic syndrome
Malignancy	Wilm's tumor
	Pheochromocytoma
	Neuroblastoma
Medications	Pseudoephedrine
	Cocaine
	Ectasy
	Amphetamines
	NSAID
	Contraception pills
	Corticosteroids
	Anabolic steroids
Endocrine	Congenital adrenal hyperplasia
	Hyperthyroidism
	Hyperaldosteronism
	Cushing's disease
Genetic	Liddle syndrome
	Congenital adrenal hyperplasia
	Glucocorticoid remediable aldosteronism
	Apparent mineralcorticoid excess syndrome
Other	Obesity
	Bronchopulmonary dysplasia
	Obstructive sleep apnea
	Pseudohyperaldosteronism
	Neurofibromatosis
	Tuberous sclerosis
	Prematurity or low birth weight

Table 4
Evaluation and management based on diagnosis.

BP category	BP screening schedule	Lifestyle counseling (weight and nutrition)	Check upper and lower limb BP	ABPM	Diagnostic evaluation	Initiate treatment	Consider subspecialty referral
Elevated BP	Initial check	◊					
	2nd check: repeat in 6 mo	◊	◊				
	3rd check: repeat in 6 mo	◊		◊	◊		◊
Stage 1 HTN	Initial check	◊					
	2nd check: repeat in 1–2 weeks	◊	◊				
	3rd check: repeat in 3 months	◊		◊	◊	◊	◊
Stage 2 HTNd	Initial check	◊	◊				
	2nd check: repeat, refer to specialty care within 1 week	◊		◊	◊	◊	◊

◊: recommended intervention. (for more details, please see reference 1).

Table 5
High risk populations to check blood pressure when <3 years of age.

Prematurity <32 week's gestation
Small for gestational age or low birth weight
History of umbilical artery line
Congenital heart disease
Recurrent urinary tract infections, or abnormal urinalysis
Known renal disease or urologic malformations
Family history of renal disease
History of solid-organ transplant
Malignancy or bone marrow transplant
Treatment with medications known to increase BP
Other systemic illnesses associated with HTN (neurofibromatosis, tuberous sclerosis, sickle cell disease, etc.)
Evidence of elevated intracranial pressure

Indications to check BP in children <3 years of age (for more details, please see reference 1).

Table 6
Summary of commonly used medications in pediatrics.

Drug	Mechanism	Dose	Comments
Enalapril or Lisinopril	Angiotensin-Converting Enzyme Inhibitor (ACEI)	Initial: 0.08 mg/kg/d Max: 0.6 mg/kg/d up to 40 mg/d	Can be used once daily or BID. Contraindicated during pregnancy and not advised in severe renal disease. Monitor serum potassium and creatinine periodically. ARB are unlikely to cause cough in children. Losartan is FDA-approved for children older than 6 years.
Losartan	Angiotensin-Receptor Blocker (ARB)	Initial: 0.7 mg/kg/d Max: 1.4 mg/kg/d up to 100 mg/d	
Amlodipine	Calcium Channel Blocker	Initial: 0.1 mg/kg/d Adolescents: 2.5 mg/d Max: 10 mg/d	Used once daily or BID. May cause gingival hyperplasia, tachycardia, and/or edema.
Extended-release nifedipine	Calcium Channel Blocker	Initial: 0.25–0.5 mg/kg/d Max: 3 mg/kg/d up to 120 mg/d	
Labetalol	Alpha- and Beta- Blocker	Initial: 1–3 mg/kg/d divided BID Max: 10–12 mg/kg/d up to 1200 mg/d divided BID	Avoid in heart failure or asthma. Heart rate is dose-limiting factor. May impair athletic performance. Avoid in insulin-dependent diabetes.
Atenolol	Beta Blocker	Initial: 0.5–1 mg/kg/d Max: 2 mg/kg/d up to 100 mg/d	
Clonidine	Central Alpha Blocker	Initial: 0.2 mg/d divided BID Max: 2.4 mg/d divided BID	May cause dry mouth or sedation. Can be used transdermally. Sudden cessation of therapy can lead to severe rebound hypertension.
Hydrochlorothiazide	Diuretic	Initial: 1 mg/kg/d Max: 3 mg/kg/d up to 50 mg/day	Monitor electrolytes periodically. Can be used once daily or BID. Can cause urinary frequency and affect school.
Furosemide	Diuretic	Initial: 0.5–2 mg/kg/d Max: 6 mg/kg/d	

BID: twice a day, d: day, kg: kilogram, mg: milligram.

very well tolerated.

Regardless of the chosen drug, the practitioner needs to be familiar with the medication dose adjustments, safety profile, side effects, drug interactions, and contraindications. Table 6 provides a brief summary of commonly used antihypertensive medications used in pediatrics.

Initial diagnostic testing revealed normal renal function and lipid profile and an unremarkable UA. An ABPM confirmed the diagnosis of stage 2 hypertension, and treatment with a long acting calcium channel blocker was initiated.

5. Conclusions

Pediatric HTN is often undiagnosed and has a significant effect on long term cardiovascular outcomes. Accurate diagnosis relies on multiple manual measurements and can be confirmed with the use of ABPM. It is important to treat HTN in children to prevent cardiovascular and renal morbidity. Diagnostic workup for an underlying etiology of hypertension should be tailored based on level of suspicion. Physical activity is a crucial portion of lifestyle modification. If pharmacologic therapy is necessary, the medication should be chosen based on etiology with careful consideration of the side effect profiles.

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Conflicts of interest/Competing interests

The authors declare that they have no conflict of interest.

Ethics approval

Approved by the Institutional Review Board at Nationwide Children's Hospital.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and material

All data and materials were stored in accordance with local IRB. The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability

Not applicable.

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