

# “MANAGING HYPERTENSION: A COMPREHENSIVE REVIEW OF RISK FACTORS, DIAGNOSIS, AND MANAGEMENT STRATEGIES”

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## INTRODUCTION

Approximately 1-5% of youngsters are currently believed to have hypertension, with rates among ethnic adolescents being higher<sup>1-3</sup>. Primary hypertension (PH), also known as essential hypertension, was once thought to be an adult condition but is now more prevalent in the juvenile population, partly because of the obesity pandemic<sup>4,5</sup>. Children who are obese are three times more likely than non-obese children to develop hypertension<sup>6, 7</sup>. Therefore, the emphasis of this review is adolescent hypertension caused by obesity. When relevant data are available, we also examine hypertension in teenagers who are not obese.

Numerous research in various racial and gender groups<sup>1,7-12</sup> have clearly shown the link between obesity and hypertension. Insulin resistance, sympathetic hyperactivity, and alterations in vascular anatomy have all been implicated as the aetiologies of obesity-related hypertension<sup>13,14</sup>. Increased heart rate and blood pressure variability were found in obese school-age children, demonstrating the presence of sympathetic nervous system hyperactivity that contributed to the aetiology of isolated systolic hypertension in this cohort. Through activation of the renin-angiotensin-aldosterone pathway in the brain, it has been demonstrated that increased sodium content of the cerebrospinal fluid increases sympathetic nervous system activity<sup>13,14</sup>. Selective insulin resistance in obese people causes increased sympathetic activity, altered vascular responsiveness, and salt retention, which is shown by decreased urine sodium excretion<sup>15</sup>. The heterogeneous group of hypertension children can greatly benefit from the lessons learnt from the research of the obese hypertensive persons.

## DEFINITION AND CLASSIFICATION OF PEDIATRIC HYPERTENSION

Healthcare workers frequently ignore paediatric hypertension since it is typically asymptomatic. The Task Force on Blood Pressure Control in Children was hired by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) to create normative blood pressure standards. These requirements came from a study of more than 83,000 visits by newborns and kids. The distributions of systolic and diastolic blood pressure in newborns and children, adjusted for height<sup>16</sup>, are described by the percentile curves, which have

undergone repeated updates. Children and teenagers with hypertension are diagnosed using age-, gender-, and height-specific criteria. Systolic and/or diastolic blood pressure that exceeds the 95th percentile for age, gender, and height on three or more independent occasions is referred to as hypertension. "Pre-hypertension" is defined as blood pressure that is higher than the 90th percentile but lower than the 95th percentile for a patient's age, sex, and height 2,3,17-19. This group of people is at a high risk of developing hypertension. It is imperative that healthcare professionals are aware that an older child's blood pressure frequently surpasses the adult prehypertension cutoff of 120/80mmHg. As a result, every blood pressure reading above 120/80 mmHg, even if it is below the 90th percentile, qualifies as pre-hypertension starting at the age of 12 16. Pre-hypertension may no longer be entirely benign, and over a two-year period, it was revealed that hypertension progressed at a rate of 7% each year 18. Systolic and/or diastolic blood pressure that is greater than the 95th percentile but less than or equal to the 99th percentile + 5 mm Hg is referred to as stage I hypertension. There is no information on how children with stage I hypertension advance to stage II hypertension. Systolic and/or diastolic blood pressure that is higher than the 99th percentile + 5 mm Hg is referred to as stage II hypertension. This type of hypertension is more severe and is frequently linked to organ damage. A study by the National High Blood Pressure Education Programme Working Group on High Blood Pressure in Children and Adolescents found that participants with stage II hypertension had a higher risk of left ventricular hypertrophy (LVH) 20. Surprisingly, compared to their normotensive peers, children and adolescents with pre-hypertension have been reported to have a significantly greater left ventricular mass index and a two-fold higher prevalence of LVH 21–23.

### Primary and Secondary Hypertension

Based on the aetiology, hypertension can be divided into two categories: primary or essential hypertension (PH), which has no known cause, and secondary hypertension (SH), which has a known cause. In today's youth, PH is the most prevalent cause of hypertension. Normal characteristics include stage I (mild) hypertension and a positive family history of the condition<sup>24</sup>. Very young children, those with stage II hypertension, and kids with clinical signs of systemic disorders linked to hypertension should all be given SH a chance. SH could result from:

- an underlying renal parenchymal disease,
- endocrine disease,
- vascular or
- neurological condition.

### RISK FACTORS FOR ESSENTIAL HYPERTENSION

A twofold increase in risk is associated with a history of hypertension in the parent's family. Numerous corticosteroidogenic gene mutations, such as CYP11B1 and HSD11B2 mutations, epithelial sodium channel mutations (SCNN1B and SCNN1G), WNK serine/threonine kinase mutations, epithelial sodium channel polymorphisms, and renin-angiotensin-aldosterone system (RAAS) mutations have all been identified as monogenic causes of PH. Purely monogenic causes of PH are still uncommon. After correcting for height, body mass index, and socioeconomic status, it was discovered in a 10-year longitudinal study<sup>35–38</sup> that African American children had a considerably higher systolic blood pressure spike from childhood to adulthood than white children. Recent research suggests that the increased prevalence of hypertension-related nephropathy in the African American population may be due to mutations in the apolipoprotein-L1 gene on chromosome 22<sup>39,40</sup>. Patients who are homozygous for the mutations are more likely to develop focal segmental glomerulosclerosis, HIV-associated nephropathy, and hypertension-associated nephropathy, according to theories on the autosomal recessive pattern of inheritance for these mutations<sup>40–43</sup>.

Age and body mass index (BMI) have also been strongly linked to the development of hypertension 44, with African Americans and Asians having a higher prevalence of the condition. A increasing body of research has shown that hypertension in children and adolescents is inversely correlated with birth weight. Patients with a history of intrauterine growth retardation and low birth weight have been found to be strongly associated, and this correlation becomes even stronger when current body weight is taken into account. 46-50. Children were found to ingest a mean of 3,387 mg of salt per day (ranging from 1,300 mg to 8,100 mg)51 in a recent study by Yang et al. It was discovered that people who consumed the most sodium had a twice as high risk of having high blood pressure as those who consumed the least sodium. In children who were overweight or obese, this effect was more severe. Children who were overweight or obese and consumed the most salt were more than three times as likely to have raised or high blood pressure as those who consumed the least sodium51.

## DIAGNOSIS OF HYPERTENSION

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### Blood Pressure Measurement

Patients should be permitted to sit for at least five minutes with their backs supported and both feet on the ground in order to achieve an appropriate resting blood pressure reading16. According to a study by Podoll et al. on 390 children evaluated over the course of 580 visits, 74% of blood pressure readings were significantly higher at the vital sign station using oscillometric devices than they were in the examination room by auscultation by staff members trained in accordance with the Fourth Task Force recommendations.16,53 Mean variations in systolic and diastolic blood pressure were 13.2 and 9.6 millimetres of mercury, respectively. This demonstrates the value of using the right procedures and the necessity of carefully reviewing initial abnormal BP readings53. An appropriate-sized cuff should be placed on an upper extremity to take your blood pressure. Auscultation is the preferable method of assessment, particularly because the normative blood pressure tables for kids are based on similar measurements. The inflatable bladder width of an appropriate-sized cuff should cover at least 40% of the patient's arm circumference when measured at the point halfway between the olecranon (elbow) and the acromion (shoulder). 80 to 100 percent of the arm circumference should be covered by the bladder length16. Unlike earlier standards, which also included cuff length for determining cuff adequacy, current recommendations exclusively consider cuff width. The Working Group of the Task Force on high blood pressure in children and adolescents had previously recommended that the BP cuff's width should extend at least three-quarters of the arm's length (measured from the acromion to the olecranon) 54. However, it was discovered that this led to a disproportionate preference for paediatric cuffs. The suitability of this advice was examined by Arafat et al, who concluded that choosing a paediatric cuff size based on three-quarters of the arm length would be excessive 55. With no mention of cuff length or the rationale behind the change in guideline 54, the 1996 update to the Task Force recommendations recommended a cuff width of 40% of the mid upper arm circumference. The revised advice is believed to be in response to studies showing that the ideal bladder width to arm circumference ratio is 0.455 and that it should be between 40% and 50% of the mid-upper arm circumference. When the cuff size is too tiny, blood pressure readings are overestimated, which increases the chance that hypertension will be incorrectly diagnosed. Auscultation should be used to validate elevated BP values that are over the 90th percentile on oscillometric instruments.

In the outpatient context, three separate documented blood pressure increases that are at least one week apart are required to support the diagnosis. Alternative methods for diagnosing hypertension include ambulatory blood pressure monitoring (ABPM)56–58.

### Ambulatory Blood Pressure Monitoring (ABPM)

When there is a discrepancy in the BP readings between daytime ambulatory BP measurements and office BP readings, ABPM serves as the foundation for the diagnosis. Patients with white coat hypertension, isolated clinic hypertension, and masked hypertension benefit the most from it. Office hypertension and ambulatory normotension are referred to as white coat hypertension, whereas ambulatory normotension and office hypertension are referred to as masked hypertension. Oscillometric readings are used by ABPM to measure blood pressure. Over the course of a 24-hour period, blood pressure is checked in the patient's home every 20 to 30 minutes. During this monitoring phase, patients are urged to carry on with their regular activities but to refrain from strenuous ones. To assess nocturnal dipping patterns and nocturnal hypertension, patients keep a diary of their actual sleep and wake times. We take blood pressure readings every 30 minutes during the day and

every hour at night in our office. At least 40 to 50 BP readings, with at least one reading every hour, including at night, should be included in an adequate ABPM report<sup>59</sup>. The percentage of BP above the 95th percentile for age, gender, and height over a 24-hour period is known as the BP load. According to the ABPM, hypertension is characterised as an elevated mean systolic blood pressure that is higher than the 95th percentile and/or an elevated BP load that is higher than 25%. For ambulatory blood pressure readings, normative norms have been created and are available<sup>60</sup>. The use of 24-hour ABPM in paediatric nephrology clinics for the diagnosis of white coat hypertension and masked hypertension is becoming more and more supported by the available data.<sup>57,58,60-64</sup>. ABPM is owned and carried out by nephrology units; cardiologists and endocrinologists rarely carry it out. In order to improve the accuracy of the diagnosis of hypertension and prevent unnecessary therapy, Davis et al. have suggested implementing ABPM in the primary care environment<sup>65</sup>. Because of this, it's critical for primary care doctors to understand how ABPM can help their patients who have inconsistent blood pressure readings or other diagnostic difficulties. White coat hypertension and masked hypertension are both found to be 1% and 10% more common in the general population, respectively<sup>66</sup>. Despite having a higher probability of subsequently acquiring sustained hypertension, patients with white coat hypertension have a lower risk of cardiovascular death than those with disguised or sustained hypertension. Contrary to PH, which has been connected to microalbuminuria<sup>70-72</sup>, white coat hypertension in children is not associated with the onset of LVH or hypertension-related kidney injury. However, it has been linked to a modest rise in left ventricular mass index that falls between people with normotension and those with hypertension. In a research by Lande et al., 81 patients were divided into three groups and matched for age and BMI, which highlighted this finding. They were examined, and mean left ventricular mass indices of normotensive, white coat hypertensive, and sustained hypertension groups were determined to be 29.2, 32.3, and 25.1 g/m<sup>2</sup>, respectively<sup>73</sup>. Increased pulse wave velocity, an indication of increased arterial stiffness, has been linked to white coat hypertension and may indicate a higher cardiovascular risk than previously assumed<sup>74</sup>.

Adults with masked hypertension have also been linked to higher cardiovascular mortality and harm to other target organs<sup>75</sup>. Lurbe et al. found that individuals with masked hypertension were more likely to be obese, had a family history of hypertension, and were at an increased risk of developing persistent hypertension in a study of 592 children aged between 5 and 18 years. In young infants and adolescents, masked hypertension has been demonstrated to be a precursor to chronic hypertension and LVH<sup>66</sup>. Participants with stage 1 hypertension and those with masked hypertension were shown to have comparable risks of LVH<sup>72</sup>. It has been shown that ABPM is more directly linked to target organ damage and elevated left ventricular mass index, increasing the risk of cerebrovascular events and cardiovascular death as a result.<sup>73,76,77</sup> According to Verdicchia et al., who reported a hazard ratio for stroke of 1.15 and 2.01 in individuals with white coat hypertension and persistent hypertension, respectively,<sup>78</sup> white coat hypertension is associated with a low risk for stroke. Ambulatory arterial stiffness index has been presented as a potential measure of cardiovascular mortality by researchers from the Dublin outcome project.<sup>79-81</sup>

## **INVESTIGATIONS IN A HYPERTENSIVE ADOLESCENT**

### **I. Initial Investigations**

Urinalysis, serum creatinine, and echocardiography for LVH evaluation should be part of the first assessment. With a normal physical examination and normal urine results, an obese adolescent does not require routine renal sonography. This was supported by a retrospective analysis by Tuli et al. in which routine renal imaging in 50 children did not add any new diagnostic data to the original examination<sup>82</sup>. These suggestions mirror the assessment of an adult hypertension patient.

### **II. Subsequent Investigations**

In order to rule out co-morbid disorders, fasting blood sugar and lipid profile are taken in the case of the obese adolescent.

### **III. Selected Tests in Unusual Cases**

## MANAGEMENT OF A HYPERTENSIVE TEEN

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Once hypertension has been diagnosed, each patient should receive personalised care 52. A severity-based management approach for teen hypertension.

### I. Therapeutic Lifestyle Modification

This is the first line of management of pediatric hypertension and can be the sole modality of therapy in patients diagnosed with pre-hypertension and stage I hypertension. It focuses on dietary management, increased physical activity, stress reduction and avoidance of illicit drug and tobacco use<sup>83-85</sup>. Dietary management should include an age appropriate, salt-restricted diet with emphasis on weight loss in the overweight or obese children. To have a better chance of success, the entire family should adopt these lifestyle modifications and a primary provider can be instrumental in this endeavor.

### II. Pharmacological Therapy

When there is a dearth of such evidence, the existing evidence on the therapeutic management of paediatric hypertension is based on consensus expert opinion. The following indications for pharmaceutical therapy are listed in the Fourth Task Force report on high blood pressure in children and adolescents<sup>16</sup>:

- Symptomatic hypertension
- Persistent hypertension despite lifestyle modification
- Secondary hypertension
- Presence of hypertensive target organ damage such as LVH, hypertensive retinopathy, microalbuminuria
- Presence of co-morbid conditions that increase cardiovascular risk like diabetes mellitus<sup>16</sup>

For patients with uncomplicated PH, the target BP is less than the 95th percentile for age, gender, and height; while it is less than the 90th percentile for patients with co-morbid conditions like diabetes, chronic kidney disease and in those with evidence of target organ damage<sup>16</sup>.

#### Choice of antihypertensive medications

Regarding the best first-line medication to treat paediatric hypertension, no particular recommendations have been made<sup>52</sup>. The following kinds of antihypertensive drugs can be administered to children with hypertension:

- calcium channel blockers (CCB),
- angiotensin converting enzyme inhibitors (ACEI),

- angiotensin receptor blocker (ARB),
- diuretics, beta-blockers (BB),
- alpha-blockers,
- central acting agents, vasodilators,
- combined alpha and beta-adrenergic antagonists,
- renin inhibitors and
- aldosterone receptor blockers.

The standard procedure is to pick an agent from one of these classes, titrate the dose to achieve the desired therapeutic effect, and keep an eye out for any negative side effects.<sup>52</sup> If blood pressure control is not accomplished with a single medication, combination therapy is advised.<sup>16</sup> To track the patient's reaction to treatment, home blood pressure readings can be taken.

The FDA only approves less than 25% of medications for use in children. Despite this, paediatric patients have utilised practically all of the antihypertensive medications that are available in the US. The Food and Drug Administration Modernization Act (FDAMA), passed in 1997, encouraged businesses to perform paediatric clinical studies and made paediatric anti-hypertensive medications and dosage guidelines more widely available.

A pathophysiologic approach to directing therapy can be provided by knowledge of the underlying etiology<sup>85</sup>. For instance, given that sodium and water retention is the underlying cause for hypertension in this situation, patients with hypertension brought on by steroid use would benefit from diuretic therapy with hydrochlorothiazide.

A patient with diabetes should receive treatment with either an ACEI or an ARB to assist stop the progression of diabetic nephropathy. BB are helpful for treating hypertension brought by hyperthyroidism. In the preoperative management of pheochromocytoma, BB are recommended after effective alpha blockade to moderate the tachycardia brought on by high circulating catecholamine levels and alpha blocking. To prevent unopposed alpha-adrenergic action, they should only be taken after appropriate alpha-blockade. In people with diabetes and asthma, BB should be avoided. They should be used with caution in patients who are obese because they are linked to weight gain.

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