

## ARTERIAL HYPERTENSION IN CHILDREN AND ADOLESCENTS: STATE OF THE ART

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**Abstract:** Hypertension in childhood and adolescence is a major concern, due to the increasing prevalence and evidence that suggests that adult hypertension has its genesis in childhood. In 2015, high blood pressure was the leading modifiable risk factor for cardiovascular, cerebrovascular, and kidney disease and the largest contributor to global disability-adjusted life years (DALYs) worldwide. Diagnosing high blood pressure in children and adolescents remains challenging due to high rates of false high blood pressure readings at a single visit despite clear guidelines. Our aim is to provide an overview of the state of the art on primary-cause arterial hypertension in children and adolescents, highlighting the definition, prevalence, risk factors, diagnosis and treatment. This is an integrated bibliographic review of the scientific production on arterial hypertension in children and adolescents. The search for articles was carried out with the terms "Hypertension", "Children" and "Adolescents" in English and Portuguese, in the VHL databases, with the following search details: (mh:("Hypertension")) AND children AND adolescents AND (db: ("MEDLINE" OR "BINACIS" OR "LILACS" OR "IBECs" OR "CUMED" OR "MedCarib") AND mj: ("Hypertension") AND type\_of\_study: ("systematic\_reviews" OR "prevalence\_studies" OR "diagnostic\_studies") AND la: ("en" OR "pt")) AND (year\_cluster:[2017 TO 2022]). The Google Academic and Pubmed databases were used in parallel, and 36 articles published from 2017 to 2022 were selected. growth and development, lifestyle changes and results in hypertension in the first two decades of life.

**Keywords:** Arterial hypertension. Children. Teens.

## INTRODUCTION

Arterial hypertension (HTA) is the most prevalent chronic disease in the world and its study in children and adolescents is of old interest (first guideline in 1977), but until today, the diagnosis is made late due to the non-inclusion of the measure of blood pressure as a routine in the physical examination of the child.<sup>(1)</sup>

Although children are more likely to have a secondary cause of hypertension <sup>(2)</sup>, the primary cause is increasingly common, especially in developing countries, due to the increase in obesity, unlike in developed countries where the decline in systolic blood pressure is now documented.<sup>(3,4,5)</sup>

With the epidemiological transition, there is a decrease in infectious diseases and a marked increase in chronic diseases.<sup>(6)</sup> The incorporation of blood pressure measurement as part of the child's physical examination, the publication of standards with definition of reference values and respective percentiles for their early detection, is one of the important factors to be considered, especially in developing countries. where medical attention has been focused on infectious and communicable diseases.<sup>(6,7)</sup>

## DEFINITION

The current definition of arterial hypertension in children and adolescents is based on the normal distribution of blood pressure in apparently healthy children and adolescents, by age, sex and height percentiles, using the auscultatory method.<sup>(8,9)</sup>

According to the American Academy of Pediatrics 2017 Clinical Practice Guideline (Update of the 2004 Fourth Report), normal blood pressure for children aged 1 to 12 years is defined as systolic blood pressure (SBP) and blood pressure values. diastolic blood pressure (DBP) < 90th percentile, based on age, sex, and height percentiles. High blood

pressure is defined as SBP and DBP values  $\geq$  90th percentile, based on age, sex, and height percentiles, or blood pressure (BP) up to 120/80 mmHg, but  $<$  95th percentile (whichever is lower). Arterial hypertension is defined as SBP and DBP values  $\geq$  95th percentile, based on age, sex, and height percentiles. Stage 1 arterial hypertension is defined as SBP and DBP values  $\geq$  95th percentile to  $<$  95 +12 mmHg based on age, sex, and height percentiles, or BP between 130/80 and 139/89 mmHg. Stage 2 arterial hypertension for children aged 1 to 12 years, SBP and DBP values  $\geq$  95 +12 mmHg based on age, sex, and height percentiles, or BP  $\geq$  140/90 mmHg.<sup>(1,8,9,10,11)</sup>

Normal blood pressure for preteens and adolescents ( $\geq$ 13 years) is defined as SBP and DBP values  $<$  120/80 mmHg; high blood pressure, SBP and DBP values from 120 to 129/  $<$  80 mmHg; arterial hypertension SBP and DBP values  $\geq$  130/80 mmHg; stage 1 hypertension, SBP and DBP values  $\geq$  130/80 mmHg up to 139/89 mmHg; stage 2 hypertension, SBP and DBP values  $\geq$  140/90 mmHg.<sup>(1,8,9,10,11)</sup>

The European Society of Hypertension recommends the use of the 140/90 mmHg threshold to define arterial hypertension in adolescents aged  $\geq$  16 years.<sup>(10)</sup>

## PREVALENCE

There is wide variation in estimates of the prevalence of pediatric arterial hypertension worldwide, with an estimated current prevalence of between 3% and 5%.<sup>(9)</sup> In the United States of America (USA) the confirmed prevalence in children ranged from 2% to 4%<sup>(4)</sup> and in Canada 1 to 2% and is associated with obesity and physical inactivity (12). In Europe, the prevalence ranged from 2.2 to 22%.<sup>(15)</sup> Texas, Switzerland<sup>(11)</sup> and Hungary report values of 2.2% – 2.5%.<sup>(8,13,14)</sup> In Brazil, the general prevalence (children and

adolescents) was 9.6%.<sup>(9)</sup> In Afro-descendants it was 21.9%.<sup>(16)</sup>

China reports a prevalence of 17% for boys and 14.1% for girls with normal weight between 7 and 17 years of age.<sup>(17)</sup> A recent study in Guangzhou, China, reported a prevalence of high blood pressure in obese children of 70%.<sup>(18)</sup>

In India the overall prevalence (children and adolescents) of arterial hypertension (systolic, diastolic or both) in a multicenter study in 2018 was 23%. In children it was 5.9%.<sup>(19)</sup> In 25 more recent studies conducted in South and North India, the prevalence of high blood pressure for both sexes combined ranged from 2% in South India to 20.5% in North India.<sup>(20)</sup> In Iran, the estimated prevalence rate of arterial hypertension in children and adolescents was 8.9%.<sup>(21)</sup>

There is wide variation in the estimated prevalence of arterial hypertension in children and adolescents in African countries, ranging from 0.2% to 24.8%, with an aggregate value of 5.5%.<sup>(16)</sup>

To compare the prevalence of arterial hypertension in sub-Saharan Africa is a challenging task due to the scarcity of published data, the heterogeneity of studies<sup>(22)</sup> and the variation according to the locality within the same country, being higher in urban than in rural areas. In Ghana, the prevalence of high blood pressure in urban areas was 33.4% and in rural areas, 27%; Ethiopia in urban areas was 10.1% and in rural areas 9.7%; in The Gambia the prevalence of high blood pressure was 8.2%, in Eritrea and Seychelles it was 15.9% and 39.6% respectively.<sup>(22)</sup>

In developing countries, the prevalence of arterial hypertension in children and adolescents has been established through systematic reviews at between 1 and 5%.<sup>(23)</sup> In a systematic review and meta-analysis of 54 countries in Central and North Africa, the prevalence of high blood pressure in children

and adolescents was 5.5% and high blood pressure was 12.7%<sup>(23)</sup>. In Nigeria, several studies have shown a prevalence of around 3.5% and 6%<sup>(15,24,25)</sup>; in a systematic review and trend analysis of data from the last 4 decades the prevalence of arterial hypertension in Nigerian children and adolescents was 5.1%.<sup>(7)</sup>

In South Africa (KwaZulu-Natal), in a study carried out with twelfth grade students (adolescents), the prevalence of high blood pressure and hypertension was 29.7% and 13.7% respectively.<sup>(26)</sup> In Tanzania, in Dar es Salaam, the proportion of children with high blood pressure (BP) was 15.2% performed 3 times, but measured on a single occasion, with 4.4% high BP and 10.8% hypertension.<sup>(27)</sup> A more recent study (2021) in Cameroon, in children and adolescents aged 3 to 19 years, showed that the prevalence of arterial hypertension was 12% in urban areas and 8.6% in rural areas.<sup>(28)</sup>

In summary, high blood pressure in children and adolescents is a fact; was higher in children and adolescents from urban areas. In Africa, there was a higher prevalence in Cameroon of 12% and South Africa of 13.7% respectively.<sup>(26, 28)</sup> The studies were heterogeneous in the context of a single measurement or 3 measurements in a single day, using different methods (oscillometric or auscultatory) and in different regions of the same location. From the studies carried out in African countries mentioned here, the upward trend is evident, although encouraging data in the US suggest that the prevalence of arterial hypertension in children is decreasing, especially in overweight or obese adolescents.<sup>(4)</sup>

## RISK FACTORS

Risk factors for the development of hypertension in children and adolescents are not clearly defined. Obese children are at increased risk of hypertension, which is consistent with the pathophysiological

relationship between excess adiposity and high blood pressure, in which insulin resistance with compensatory hyperinsulinemia, sympathetic hyperactivity, sodium retention, increased noradrenaline and blood pressure is observed. arterial.<sup>(11)</sup>

There are studies that have not consistently demonstrated the increase in the prevalence of childhood hypertension with the increase in the prevalence of obesity and overweight in childhood, indicating that multiple factors such as prematurity (decreased number of nephrons and excessive weight gain between birth and 36 months of age), low birth weight (due to poor growth of nephrons related to maternal food intake during pregnancy, or congenital deficiency in the number of nephrons with consequent decrease in renal sodium excretion), family history of hypertension (when exposed to environmental factors it results in the activation of the sympathetic nervous systems and renin-angiotensin, whose imbalance culminates in structural and functional alterations of the vessels leading to an increase in systemic vascular resistance), inadequate eating habits (foods with high sodium content, fats, sugars), physical inactivity (by reducing the amount of nitric oxide and increase in arterial vasoconstriction), black race, sex, being the firstborn (due to the incidence of high blood pressure (eclampsia) in the 1st pregnancy which causes a decrease in blood flow to the baby with consequent premature birth, low weight at birth or bronchopulmonary dysplasia), socioeconomic inequalities, poor sleep quality, stress, passive smoking, known kidney or heart disease, diabetes, and transplant patients. may contribute to the development of hypertension.<sup>(11,13,21)</sup>

## DIAGNOSIS

The incorporation of blood pressure (BP) measurement as part of the child's physical

examination, as well as the publication of standards for its evaluation in childhood, makes it possible to detect hypertension in children and adolescents who are usually asymptomatic.<sup>(6)</sup>

Some cases may present with headache, irritability, dizziness, sleep disturbances, or signs and symptoms that may suggest involvement of a specific organ or system, for example, kidneys (macroscopic hematuria, edema, fatigue), or heart (chest pain, dyspnea), exertion, palpitation).<sup>(1)</sup>

One of the most important aspects of monitoring pediatric arterial hypertension is the accurate and adequate measurement of BP. There are 3 types of measurements frequently used in pediatrics: auscultatory, oscillometric and invasive. Invasive BP measurement is obtained using an artery and a fluid-filled transducer connected to a catheter, used primarily in an intensive care unit. Auscultatory and oscillometric measurements are the cornerstones of measurement in the outpatient and inpatient setting.<sup>(1,2)</sup>

The preferred measurement technique is auscultatory, because the normative values on which the pediatric hypertension thresholds are based were obtained using this method. The mercury column sphygmomanometer is the gold standard, however, it is no longer in use, due to its toxicity and risk of contamination by mercury. The aneroid sphygmomanometer has therefore been the most suitable. Oscillometric devices properly validated for the pediatric age group can be used for the initial assessment of blood pressure. The blood pressure measurement altered with the oscillometric method must be confirmed with the auscultatory method (calibrated sphygmomanometer). There are no reliable studies that show safety when measuring wrist cuffs, so they must not be used by health professionals either for diagnosis

or for monitoring hypertensive children and adolescents.<sup>(2,9)</sup>

According to the 2017 American Academy of Pediatrics guidelines, blood pressure must be measured regularly or at least once a year in children 3 years and older by a healthcare professional.<sup>(1,4)</sup> For children under 3 years of age, BP assessment is indicated in special conditions such as prematurity with a gestational age of less than 32 weeks or very low birth weight, umbilical catheterization, admission to an intensive care unit, corrected or uncorrected heart disease, known kidney disease, neoplasms, solid organ or bone marrow transplants, treatment with drugs that increase blood pressure<sup>(1,4)</sup>. In children older than 3 years or adolescents who are obese and who are taking medications that can raise BP, who have kidney disease, who are diabetic, or who have a history of aortic arch obstruction or coarctation of the aorta, blood pressure must be measured at each visit. doctor.<sup>(1,4)</sup>

For BP measurement, the ideal is for the child to be seated, calm, rested for more than 5 minutes, with an empty bladder and without having practiced physical exercises for at least 60 minutes, with legs uncrossed, feet flat on the floor, back leaning in the chair and relaxed; with the arm at heart level, with the right arm being preferred, to be comparable with standard tables<sup>(1,28)</sup>. The arm must be at the height of the heart, supported, with the palm facing up and the clothes must not garrote the limb. It must be 1): measure the distance from the acromion to the olecranon; 2): identified the midpoint of the distance between the acromion and the olecranon; 3): Measure the circumference of the arm at this midpoint. From this measurement, the appropriate cuff for the measurement is selected, which must cover 40% of the width and 80% of the length. In pediatric services, complete availability of cuffs must be available, due to the wide age range and size variation of the population

that is served (from newborns to obese adolescents). After choosing the appropriate cuff, 4): place the cuff without leaving any gaps, 2 to 3 cm above the cubital fossa; 5): center the middle of the compressive part of the cuff over the brachial artery; 6): estimate the level of systolic blood pressure (SBP) by palpating the radial pulse; 7): palpate the brachial artery in the cubital fossa and place the bell or diaphragm of the stethoscope without excessive compression; 8): quickly inflate until it exceeds 20 to 30 mmHg above the estimated SBP level obtained by palpation; 9). deflate slowly (speed of 2 mmHg/second); 10): determine SBP by auscultating the first sound (Korotkoff phase I) and then slightly increasing the deflation rate; 11): determine diastolic blood pressure (DBP) in the disappearance of sounds (Korotkoff phase V); 12): auscultate about 20 to 30 mmHg below the last sound to confirm its disappearance and then proceed with rapid and complete deflation; 13): if the beats persist until the zero level, determine the DBP in the muffled sounds (Korotkoff phase IV) and record the SBP/DBP values. 14): write down exact values without rounding.<sup>(1, 30)</sup>

A cuff size that is too small will overestimate the BP and one that is too large will underestimate the BP. Three measurements are required on the same day, 2-3 minutes apart. If the readings are normal, no further measurements are required. If BP is elevated, remeasurements will be required on two or more occasions to determine the true blood pressure value based on normative tables<sup>(2)</sup> since blood pressure values tend to decrease in subsequent measurements, avoiding false positive cases.<sup>(31)</sup>

The new normative tables were made based on data from the same population and with the same methods used in the fourth report, updated by the new 2017 guidelines of the American Academy of Pediatrics (AAP),

however, overweight and obese children were excluded, due to strong association of these conditions with high BP and hypertension. BP tables include children aged 1 to 17 years. From 13 years of age onwards, BP levels can already be adopted for those of adults as long as the child's pubertal stage is taken into account, and this value must only be used from 13 years of age if the individual is already in puberty (1). European guidelines, unlike American guidelines, include overweight or obese children and adolescents, which may result in a high prevalence of hypertension.<sup>(32, 33)</sup>

Any child who has stage 1 hypertension for 1 year or for 3 or more clinic visits, or any child with suspected white coat hypertension, the AAP recommends having an ambulatory blood pressure measurement (ABPM) as long as they are older than 5 years. years of age and  $\geq 120$  cm in height (for which normative data exist).<sup>(34)</sup> This recommendation includes children with chronic kidney disease, known secondary hypertension, type I or II diabetes, obstructive sleep apnea, history of prematurity, solid organ transplantation or aortic coarctation repair.<sup>(34)</sup>

Routine tests to be performed on all children with high blood pressure include blood chemistry: (sodium, potassium, chloride, total CO<sub>2</sub> and creatinine), urine summary, renal ultrasound. For cardiovascular risk assessment, fasting glucose, total serum cholesterol, high-density lipoproteins (HDL), low-density lipoproteins (LDL) and triglyceride levels are recommended. Echocardiography, retinal examination and albumin/creatinine ratio are performed to evaluate target organ damage.<sup>(4, 35)</sup>

## TREATMENT

The 2017 clinical practice guidelines recommend that the treatment of hypertension in children and adolescents begins with

a non-pharmacological intervention (lifestyle changes)<sup>(11)</sup> which include dietary modifications with reduced sodium intake of 2 to 3 grams per day, potassium and calcium supplementation, reduced cholesterol intake and sugary drinks. The DASH (Dietary Approaches to Stop Hypertension) diet is recommended, with an emphasis on plant-based foods and reduced sugars and sweets.<sup>(9,35)</sup>

The increase in physical activity, the decrease in sedentary lifestyle and (passive) smoking must be taken into account. Sodium restriction is difficult in children. Families must be advised to avoid processed foods, not to add salt to prepared foods, and to pay attention to the sodium content on food labels. Currently, 60 minutes of daily physical activity is recommended and a reduction in sedentary behavior to 2 hours a day.<sup>(35)</sup>

The decision to initiate pharmacological treatment of pediatric hypertension depends on many factors, such as the presence of symptoms of arterial hypertension, level of blood pressure elevation, presence of target organ damage (left ventricular hypertrophy, hypertensive retinopathy and albuminuria), response to non-pharmacological treatment, secondary hypertension or the presence of comorbidities (chronic kidney disease and diabetes) that confer increased cardiovascular risks. The goals of treatment are to achieve a blood pressure level that reduces the risk of end-organ damage in childhood and the risk of hypertension and cardiovascular disease in adulthood.<sup>(11, 35)</sup>

Pharmacological treatment must be initiated with the lowest dose of a single drug until blood pressure is controlled or until the maximum recommended dose is reached. When target blood pressure is not achieved with one drug, a second drug must be added.<sup>(36)</sup>

Recommended options for pharmacological treatment include angiotensin-converting enzyme inhibitors, angiotensin receptor

blockers, calcium channel blockers, and thiazide diuretics as short-term first-line drugs.<sup>(9,11)</sup> They are well tolerated by children, but their long-term effects are unknown. They have been approved by the Food and Drug Administration (FDA) in patients  $\geq$  6 years of age. Captopril has been widely used in neonates and is effective in short-term and long-term blood pressure control. Its short half-life limits its use. Enalapril has few adverse effects, is effective, and has formulations available for young children. The combination of lisinapril and ramipril is also effective in children and adolescents.<sup>(11, 36)</sup> Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers represent the best choice for antihypertensive treatment for pediatric patients.<sup>(36)</sup>

## LIMITATIONS

Scarcity of published articles on arterial hypertension in children and adolescents in the last 3 years, mainly in African countries and difficulty in obtaining articles published recently (2022).

## FINAL CONSIDERATIONS

Despite the scarcity of articles on arterial hypertension in children and adolescents in the last 3 years, especially in African countries, the data presented indicate that childhood hypertension is not rare and has different prevalence in different districts of the same province or locality. Representing an imminent risk to the health of children, adolescents and future adults, altered blood pressure levels must be identified early, because arterial hypertension at this stage of life is not benign. More studies are needed to assess blood pressure in childhood, especially in developing countries, in order to encourage subsidies for prevention programs and government actions aimed at preventable risk factors.

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