

Secondary hypertension in the pediatric group: a review



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ABSTRACT

Secondary systemic arterial hypertension (SAH) is a potentially curable disease. The pediatric population is the most affected. Due to the lack of deep investigation for secondary causes by health care professionals, many children end up living with the pathology without being diagnosed. Since SAH is a disease that evolves with lesions in several organs, treatment is expected to be carried out early, avoiding chronic health damage. The present research aimed to analyze the underdiagnosis of secondary SAH in children and its repercussion; describe the definition of secondary SAH; identify the main causes of secondary hypertension, and analyze forms of diagnosis and treatment. An integrative bibliographic review of secondary hypertension was carried out in children and adolescents between 2013 to 2022. Twenty-seven studies were chosen for this research. Studies have shown a significant degree of underrecognition of high blood pressure (BP) and hypertension, which is related to the steps needed to determine BP percentiles and the lack of SAH screening in pediatric consultations, which must be done through regular manual measurement of the blood pressure. All children with SAH should be investigated for secondary causes. If the diagnosis is confirmed, treatment of the underlying disease should be done by a specialist. Underdiagnosis of secondary hypertension is still very common since screening is not routinely performed in this age group. Therefore, strategies to improve the acceptance of guidelines should be prioritized.

Keywords: Diagnosis, Hypertension, Management, Pediatrics, Underdiagnosis.

1 INTRODUCTION

Secondary arterial hypertension is a form of potentially curable hypertension, having one of the most affected populations in the pediatric age group, which includes from birth to eighteen years old (children up to twelve incomplete and adolescents from twelve to eighteen years age). The forms of diagnosis and treatment depend on what is the base pathology that leads to increased blood pressure (PA), so the diagnosis requires a large number of exams to define such pathology.

The interest in the study of systemic arterial hypertension (has) in children and adolescents is old, but the diagnosis has been made late due to the lack of PA measurement as a routine in the physical examination of the child (Brazilian Society of Pediatrics, 2019). It is extremely important to have a high level of suspicion, as well as early detection, as long-term high blood pressure has to change in the vascular system that culminates in resistant hypertension, renal complications, and severe heart.

HAS in the pediatric age group is associated with increased left ventricular mass and youth atherosclerosis, predicting cardiovascular events in adulthood. An important association was reported between high PA in adolescence and stroke mortality. Hypertension in children is widely unknown and poorly controlled. Identifying pediatric patients with has and treating them has been shown to reduce long-term cardiovascular results (Benenson; Waldron; Frederick, 2020).

In the last 10 years in the US, hypertension has increased to 5% in adolescents and high PA has increased up to 12.6% in girls and 19.2% in boys, and 23% is among healthy 5 to 15 years old (Ashraf; IRSHAD; PARRY, 2020).

Among the 275 hypertensive children, 43% (n = 119; boys = 56%; median age = 12 years; range = 3-17 years) had essential hypertension and 57% (n = 156; boys = 66%; median age = 9 years; interval = 0.08-19 years) had secondary hypertension. When compared to those with secondary hypertension, those with essential hypertension had a significantly higher age to diagnosis (p = 0.0002), a stronger family history of hypertension (94% vs. 68%; p < 0.0001), and lower prevalence of premature delivery (20% vs. 46%; p < 0.001). There was a bimodal distribution of the age of diagnosis in those with secondary hypertension (GUPTA-MALHOTRA; et. AL, 2014 p. 08).

Research, conducted since 1988, indicates that there was an increase in the prevalence of hypertension in childhood. High PA is more prevalent in boys (15%–19%) than in girls (7%–12%), being higher in non-Hispanic African and African American children compared to non-Hispanic white children, with higher rates among adolescents (FLYNN; et. AL, 2017).

The prevalence of hypertension in US children and adolescents ranges from 3% to 4%. Primary cause occurs mainly in children over 13 and has no known cause, but is associated with several risk factors, including family and high IMC history. Secondary hypertension occurs mainly in younger children (under 13) and is caused by genetic, endocrine disorders, kidney disease, or cardiovascular abnormalities (KRIST, et. AL, 2020).

The Blood Pressure Director of the American Academy of Pediatrics (AAP) reinforces the annual screening for HAS in children in preventive and screening consultations for high-risk populations. Existing

PA regulations were reviewed to include data from children with normal weight to represent a healthy population. Already the classification of blood pressure for teenagers follows practically the same expected PA threshold in adults (Dionne, 2017).

“In the investigation of the causes, it is very important to do detailed and complete clinical history and physical examination, in an attempt to identify aspects that can suggest the secondary cause of has” (Brazilian Society of Pediatrics, 2019, p.11). Among the most common causes, we have renal artery thrombosis, renal artery stenosis, renal congenital malformations and aortic coarctation, ranging from position according to the age of the child or adolescent.

Keeping in mind the lack of deepened research by health professionals to rule out a secondary cause, many children and adolescents end up living with a pathology without a diagnosis, and using medications that would not be needed, if the specific diagnosis and treatment for the disease were done if they were done and treatment. Base.

Understanding the severity and importance of this pathology benefits not only patients but the health system as a whole since it would reduce future expenses for avoiding chronic health damage. With the right diagnosis and treatment, the patient does not become a permanent antihypertensive user, avoiding their side effects and improving their quality of life.

Knowing that has is a pathology that can evolve into injuries in various organs, and harm the patient's longevity and quality of life, it is expected that treatment will be performed early, thus avoiding the use of medicines in cases of secondary hypertension. In this way, it is questioned: why is there a secondary hasy in children and what is their repercussion?

The present research aimed to describe the causes and repercussions of the underdiagnosis of secondary arterial hypertension in the pediatric age group, describe the definition of secondary arterial hypertension, identify the main causes of secondary hypertension in the pediatric age group and analyze forms of diagnosis and treatment.

2 MATERIAL AND METHODS

An integrative bibliographic review of studies on secondary arterial hypertension was carried out in children and adolescents in the Medline, Pubmed, Lilacs, Scielo, Canadian Journal of Cardiology, Brazilian Pediatric Society, American Journal of Hypertension and American Academy of Pediatrics. Restrictions of the date of publication were determined between 2013 and 2022 and chosen twenty -seven studies for said research. They were later selected by independent evaluations, following the topics covered: screening, clinical management, diagnosis and treatment in the pediatric age group. They were excluded from the study, works that did not correspond to the pediatric age group and which did not have an objective conclusion on the diagnostic and treatment topics.

3 RESULTS AND DISCUSSIONS

Blood pressure is the pressure that blood exerts on the walls of the arteries, produced by the contraction of the left ventricle against the resistance of the arteries and arterioles that is necessary for the functioning of the organism. Globally, hypertension is the main risk factor responsible for 10.2 million deaths (ASHRAF; IRSHAD; PARRY, 2020). The symptoms of hypertension are irritability, fatigue, dizziness, chest pain, abdominal pain and headache (Dionne, et. Al, 2017).

Some studies have shown that high childhood PA increases the risk of has and metabolic syndrome in adults. Recent studies have found that high PA adolescents have evolved to a (SAH) rate of 7% per year. In addition to these aspects, young patients with hypertension are more likely to have accelerated vascular aging and chronic vascular diseases (FLYNN; et. AL, 2017). The International Childhood Cardiovascular Cohort Consortium showed that the thickness of the intimate-medium layer of the carotid is higher in adults who had high PA during childhood and persisted until adulthood compared to those whose PA normalized later (Dionne, et. 2017).

Secondary Arterial Hypertension is HAS with an identifiable cause (base pathology), being observed mainly in children who are in preschool, therefore younger, where kidney disease is the most common cause of this increase in PA and these children usually have diastolic has (Ashraf; IrShad; Parry, 2020).

HAS in the pediatric age group is associated with increased left ventricular mass and youth atherosclerosis, predicting cardiovascular events in adulthood. An important association was reported between high PA in adolescence and stroke mortality. Hypertension in children is widely unknown and poorly controlled. Identifying pediatric patients with has and treating them has shown long-term cardiovascular damage (Benenson; Waldron; Frederick, 2020).

PA below the 90 percentile by age, sex and height is considered normal blood pressure. Hypertension is defined as systolic and/or diastolic blood pressure greater or equal to the 95 percentile (Gökнар; çalıskan, 2020). For Benenson; Waldron; Frederick (2020) The PA classification occurs as follows:

For children 13 years or older, PA thresholds who meet the definition of hypertension replicate those of adults:

- Normal PA: <120/<80 mmHg
- High PA: Systolic PA between 120 and 129 with diastolic <80 mmHg
- Hypertension Stage 1: PA between 130/80 and 139/89 mmHg
- Hypertension Stage 2: PA \geq 140/90 mmHg.
- In children from 1 to 13 years old, PA levels that define hypertension are determined based on gender, age and height in children with normal weight:
- Normal PA: both systolic and diastolic bread <percentile 90

- High PA: systolic and/or diastolic \geq percentile 90, but $<$ percentile 95 or 120/80 mmHg a $<$ percentile 95
- Hypertension Stage 1: Systolic and/or diastolic \geq Percentile 95 A $<$ percentile 95 + 12 mmHg or 130/80 to 139/89 mmHg
- Hypertension Stage 2: Systolic and/or diastolic PA \geq Percentile 95 + 12 mmHg or \geq 140/90 mmHg

Many studies in the US have demonstrated a significant degree of high PA submission and hypertension that is related to the many steps needed to determine PA percentiles, whether it is a secondary or primary cause and the lack of SHE screening in pediatric consultations (measurement of Pressure) (Brady; Stefani-Glücksberg; SIMONETTI, 2019).

The difference between European and American guidelines occurs according to the value of PA in the first measurement. In the event of PA Normotensa, the European guideline results reassessing in 2 years and the American guideline in 1 year. If in the first measurement, PA is high, the European guideline recommends reevaluation in 1 year and the American in 6 months.

The European Society of Hypertension (ESH) and AAP guidelines adopt the same posture about the PA measurement technique by tracking and diagnosing hypertension. Reinforce that at least three PA measures obtained at rest from manual auscultation, using the first and fifth phase korotkoff sound as a systolic and diastolic measure, are essential in the diagnosis of a child or adolescent with has. If the average PA is changed, repeated measures will be required to confirm the elevation (Brady; Stefani-Glücksberg; Simonetti, 2019).

The AAP guideline recommends annual PA measurement for children ≥ 3 years and specific subgroups (obese, using drugs known for increasing blood pressure, kidney disease, coarctation history, or diabetes) for more frequent checks (each consultation). Children under 3 years should perform regular measurements if they have any of the following conditions: congenital heart disease, urinary tract infection, urological malformation, transplanted organ, bone marrow transplantation, malignancy, neurofibromatosis, tuberous sclerosis, or sickle cell anemia. Small newborns of gestational age, premature (< 32 weeks), or very low-weight newborns, and those with umbilical arterial catheterization also require more frequent PA checks (SINHA; SAHA; SAMUELS, 2019).

Before blood pressure measurement, the child should sit in a comfortable position for 3 to 5 minutes with the feet resting on the floor. The measurement should be performed on the right arm and at the heart level. The height of the expandable part of the cuff should cover 80–100% of the arm circumference and its width should cover at least 40% of the arm circumference. The lower end of the cuff should be placed 2–3 cm above the antecubital fossa and the stethoscope should be placed in the brachial artery (Göknar; çaliskan, 2020).

PAS corresponds to the reappearance of blood flow (phase I of Korotkoff), while the PAD usually corresponds to phase IV of korotkoff (succuting of sounds) that is used in place of phase V (disappearance

of sounds) because most of the time in children Korotkoff sounds are perceived up to 0 mmHg. The auscultatory method produces accurate measures of 2 mm Hg (Bouhanick; ET.AL, 2021).

According to Jin (2020), hypertension screening is performed by reading blood pressure using an inflatable cuff monitor that passes over the arm. 3 readings are indicated in 3 distinct visits. Sometimes additional Home PA monitoring for a period of 12 to 24 hours (outpatient pressure monitoring) is made to confirm the diagnosis.

In the field of the secondary cause, there are many studies, which have shown a strong association between different 24-hour pressure determinants and the basic cause. In addition to the emphasized aspects, in children with secondary hypertension, PA outpatient monitoring parameters offer the advantage of identifying low and high-risk children for target organ injury (Chrysaidou; et. AL, 2020).

The map or MRPA should be used only in situations selected by the doctor who accompanies the child or adolescent. The 24-hour map can be prescribed, preferably in children of at least 5 years measuring 120 cm. This monitoring is indicated to confirm the diagnosis of has, before the beginning of treatment, especially if the cardiovascular risk is high. It can also be indicated when the response to treatment is insufficient. Its reproducibility is greater than the MRPA, but references are lacking for children <120 cm high (Bouhanick; ET.AL, 2021).

Of the 27 studies analyzed, 19 of them concluded that the base disease that generates has altered according to age. The main pathologies causing has of each age are:

- Newborn: renal artery thrombosis, renal vein thrombosis, congenital renal malformation, aortic coarctation, renal artery stenosis and bronchopulmonary dysplasia.
- Infants up to 6 years old: renal parenchyma disease, renal artery stenosis, aortic coarctation and use of medicines (corticosteroids). Dos 6 aos 10 anos de idade: doença do parênquima renal e estenose de artéria renal.
- Adolescence: primary hypertension (mainly by obesity), renal parenchyma disease, substance abuse (cocaine, amphetamines and caffeine) and adolescent pregnancy.

Therefore, all children diagnosed as hypertensive people should be investigated for secondary causes. Renal and renovascular diseases are the main causes of hypertension. Renal parenchyma pathologies and structural abnormalities (such as glomerular, tubular and interstitial abnormalities) constitute 34-79% of secondary causes and renovascular diseases (such as renal artery stenosis) constitute 12-13%. Both renal and renovascular parenchyma disturbances lead to activation of the renin-angiotensin-aldosterone system, causing arterial vasoconstriction and volume expansion with a consequent increase in PA (Benenson; Waldron; Frederick, 2020).

For an early and correct diagnosis to occur, it is of paramount importance a careful history and a complete clinical examination. A detailed history from conception, gestational events, fetal growth patterns,

birth weight, maternal has, perinatal infection and neonatal hospitalization, detailed nutritional history, including breastfeeding, weaning, amount of salt ingested, if the child does physical activity, breathing disorders of sleep, family history of hypertension, kidney disease and psychosocial history are fundamental to guide the doctor to the correct diagnosis (Ashraf; IrShad; Parry, 2020).

Birth histories, such as premature birth and low birth weight, were identified as a risk factors for hypertension and other cardiovascular diseases in adults, but only low birth weight was associated with PA elevation in the pediatric age group. A retrospective cohort study showed that 7.3% of 3-year-olds born preterm have had and a high prevalence of hypertension in older children with premature childbirth history (FLYNN; et. Al, 2017).

When performing the physical examination the doctor should pay attention to general appearance as syndromic facies, along with weight, height, BMI, waist relationship, cephalic perimeter and general growth, and, it is of utmost importance to evaluate vital signs such as heart rate, frequency Respiratory, radio femoral delay, the difference in blood pressure in the upper and lower limbs, dyspnea, breath, abdominal mass, palpable kidneys and joint edema (Ashraf; IRSHAD; Parry, 2020).

Table 1 - Physical Examination and Clinical History Findings suggestive of a secondary cause of arterial hypertension

BODY SYSTEM	HISTORY / PHYSICAL EXAMINATION	POSSIBLE ETIOLOGY
Vital signs	Tachycardia	Hyperthyroidism, feochromocytoma, neuroblastoma
	Decreased pulses in lower limbs; Fall in PA between the measure in upper and lower limbs	Aortic coarctation
Nose, ear, throat	Adenoamigdalial hypertrophy, snoring	Suggests association with a sleep disorder (apnea)
Height / Weight	Growth Delay Obesity (High BMI) Obesity of the trunk	Chronic kidney disease (CDD) Primary has Cushing Syndrome, Insulin Resistance
Head and neck	Full Moon Facies Elf facies Winged neck Thyroid increase	Cushing Syndrome Williams Syndrome Turner Syndrome Hyperthyroidism
Skin	Cushing Syndrome Williams Syndrome Turner Syndrome Hyperthyroidism	Feochromocytoma Cushing Syndrome, Anabolic Abuse
	Sebaceous adenoma	Tuberous sclerosis
Chest	Apical impulse	Left ventricular hypertrophy/ chronic has
Abdomen	Abdominal breath	Renal artery stenosis
	Palpable mass	Feochromocytoma
Abdomen	Palpable kidney	Polycystic kidney disease

Source: Brazilian Society of Pediatrics (2019)

Once the anamnesis and detailed physical examination is performed, and the child has an elevation of PA, is left for laboratory evaluation to confirm secondary has, which occurs by basic exams such as blood count, renal function, serum electrolytes, serum lipids, blood glucose, partial, partial Urine, Uroculture, Protein/Creatinine Relationship, and Chest Radiography. In patients with IMC > Percentile 95 some extra tests should be requested such as glycated hemoglobin, TGO, TGP, TSH, drug sorting and sleep study. In addition to these, echocardiography, renal ultrasound, TC/RM angiography are useful for the proper management of pediatric hypertension (Ashraf; IRSHAD; Parry, 2020).

In case of target organs, exams should be redone and verified at intervals of 6 to 12 months. If the target body injury is not present at the first presentation, the annual verification is sufficient (Göknar; çaliskan, 2020). The diagnosis of secondary HAs related kidney disease showed risk factors that worsen the prognosis, including higher cholesterol values, so the importance of requesting and controlling cholesterol levels for patients with kidney disease (Rasała; et. AL, 2020).

There are precarious data on the long-term sequelae of persistent hypertension in children, but it is known that there is evidence of target organs and risk hypertension in adulthood. In most cases, non-pharmacological measures are recommended as first-rate therapy, but a significant proportion of children will need pharmacological treatment to control SAH, especially those with evidence of target organs, but also for those who fail Lifestyle modifications, which have chronic kidney disease and/or diabetes mellitus with hypertension, symptomatic hypertension and stage 2 hypertension at presentation or during follow - up (Chaturvedi; et. Al, 2014).

Hypertension in children is initially treated with lifestyle changes such as weight loss in case of overweight or obesity, healthy eating and proper and regular exercise. Children with symptomatic hasi or persistent hypertension who need antihypertensive drugs should be evaluated and accompanied by cardiovascular damage with echocardiography (as mainly, left ventricular hypertrophy), background (hypertensive retinopathy) or urine analysis (albuminuria) . Angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers and thiazide diuretics are effective and insurance for pediatric age treatment (Riley; HERNANDEZ; KUZNIA, 2018).

Table 2 - Drug treatment according to base disease

Basic diseases	MEDICINES
Has renewing	IECA, BRA, DIORETIC, VASODILATOR
Aortic coarctation	Beta blocker (especially before correction)
Chronic kidney disease	IECA, BRA
Hypertensive athlete	IECA, BRA, BCC

Source: Brazilian Society of Pediatrics (2019)

Practical guidelines recommend that a single antihypertensive drug with the lowest dose should be started and an increased dose or addition of the second drug should be done, only after 2-4 weeks, until the PA reaches a percentile value or percentile value <50th Percentile in patients with chronic kidney disease. In hypertensive children with chronic kidney disease, proteinuria or diabetes mellitus, initial choice therapy

is the inhibitor of angiotensin converter enzyme or angiotensin receptor blockers (Ashraf; IRSHAD; Parry, 2020).

The patient should be accompanied every 4 to 6 weeks until the PA stands out. If not controlled with a single drug class, a second agent can be started, usually a thiazide diuretic is the second favorite agent (FLYNN; et. Al, 2017). In children with proven secondary hypertension, the treatment of base disease should be initiated by a specialist doctor (Dionne, et. Al, 2017).

4 CONCLUSION

The overall increase in the prevalence of pediatric hypertension, leads to an increased risk of cardiovascular disease. The various existing guidelines for Diagnosis and Clinical Management of HAS, both primary and secondary, aim to facilitate and guide the doctor for the correct diagnosis and treatment of each patient.

The underdiagnosis of secondary arterial hypertension in children and adolescents is still very frequent, since in this age group the screening for this disease is not properly performed. Manual measurement of blood pressure is the best method for both suspicion and has for diagnosis, and yet it goes unnoticed in pediatric consultations, which often only investigate has in obese children, looking for primary HAS diagnosis.

Knowing that secondary has is potentially curable, with the treatment of base pathology, it is expected that every child or adolescent hypertensive is investigated for a secondary cause, regardless of whether or not she has a risk factor for hypertension. Studies show that kidney diseases are the most frequent causes of secondary HAS, and that their diagnosis depends on simple examinations that should be requested by the doctor who follows the child or adolescent.

The repercussion that hypertension causes in the body is related to target organ injury. Adolescents who have not been diagnosed and treated correctly already have cardiovascular disease and greater risk of developing a stroke. Given this, governmental health strategies are necessary to implement continuing health education aiming at the application of clinical practice guidelines to improve screening, diagnosis and treatment of systemic arterial hypertension in the pediatric age group.

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