Journal of
HYPERTENSION RESEARCH
www.hypertens.org/jhr

Review
J Hypertens Res (2021) 7(3):89-95

High blood pressure in children and adolescents - a review of diagnosis and management

Silvia **Deaconu** [1, 2], Gabriela **Marascu** [1], Alexandru **Deaconu** [1, 2], Maria **Dorobantu** [1, 2]

[1] Department of Cardiology, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania
[2] Department of Cardiology, Clinical Emergency Hospital, Bucharest, Romania

Received: July 10, 2021, Accepted: August 26, 2021

Abstract

Hypertension (HTN) is an important risk factor for cardiovascular morbidity and mortality in both adults and children. Previous studies have suggested that elevated blood pressure values in childhood were associated with the development of HTN in adult life. Secondary HTN is seen more often in children and adolescents, but the prevalence of essential HTN is increasing due to the global pediatric obesity epidemic. HTN is frequently underdiagnosed in childhood because blood pressure values vary with age, sex, and height, and guidelines propose different cut-offs to define pediatric HTN. It is mandatory for clinicians to know how to distinguish primary from secondary HTN, identify target organ damage and apply necessary interventions to control blood pressure.

Keywords: hypertension in children, primary hypertension, secondary hypertension.

Introduction

The burden of hypertension (HTN) in children is a real health problem with increasing prevalence and long-term consequences. Similar to adults, HTN in children and adolescents may be primary or essential when the cause is not identified or secondary to another disease. The most common causes of HTN in childhood are secondary and frequently include renal disease, endocrine disease, and coarctation of the aorta [1, 2]. Moreover, studies demonstrated that family history of HTN, low birth weight, and overweight or obesity were associated with pediatric HTN [3–5].

In contrast to adults, there is not a single reference value for HTN, and the definition is based on the concept that blood pressure increases with age and body size [6]. Furthermore, this causes high blood pressure to remain frequently undiagnosed by pediatric clinicians. HTN in children represents blood pressure higher than the 95th percentile for age, sex, and height at three different visits [7, 8]. In 2016, The European Society of Hypertension (ESH) fixed a cut-off value ≥140/90 mmHg for subjects aged ≥16 years independent of age, sex and height, while The Clinical Practice Guidelines released by the American Academy of Pediatrics proposed in 2017 in those aged ≥13 years a fixed cut-off value ≥130/80 mmHg [7, 8].

* Correspondence to: Alexandru DEACONU, Clinical Emergency Hospital, 8 Calea Floreasca 014461, Bucharest, Romania. E-mail: alexandru.deaconu@umfcd.ro

Studies showed that elevated blood pressure in childhood could be considered the strongest predictor of HTN in adult life, and blood pressure values in adolescence can also predict the development of cardiovascular disease other than HTN [1, 7].

Definitions

Definition of HTN in childhood is based on complex tables derived from a database of the National Health and Nutrition Examination Survey, containing both systolic and diastolic blood pressure percentiles, closely linked to age, sex, and height [9]. In 2016, ESH updated the definition of pediatric HTN according to age, as reported in Table 1. As in the previous guidelines, HTN is defined as systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) persistently at least 95th percentile for sex, age and height measured on at least three separate occasions [7]. On the other side, the new Clinical Practice Guidelines issued by The American Academy of Pediatrics in 2017 proposed in subjects aged ≥13 years a cut-off value for blood pressure levels ≥130/80, while ESH fixed for subjects aged ≥16 years a cut-off value ≥140/90 mmHg and appreciated that in these cases, HTN should be graded as for adults [7, 8].

Epidemiology

The prevalence of HTN in children and adolescents is difficult to establish due to the different cut-offs used to define hypertension in children worldwide. European studies report a prevalence between 2.2% in Switzerland [10], 4.9% in Poland [11] to 12% in Greece [12], and 13% in Portugal [13]. Obesity seems to be the most important factor influencing the development of HTN in children. A study by Genovesi et al. indicates that HTN was found in 1.4% of normal weight, 7.1% of overweight, and 25% of obese adolescents [14]. Reports about the incidence of HTN usually refer not to the general population but to the patient who associates diabetes mellitus, operated coarctation of the aorta, obesity [6]. There is enough evidence that HTN is a disease with family aggregation and is considered a polygenic disease with no single gene exerting a predominant effect [6]. Several rare syndromes with classic Mendelian inheritance present with very high or low BP early in life [15].

Causes of HTN

In children, HTN often has an identifiable cause. In infants, HTN is usually related to renal or vascular disease and may be associated with signs and symptoms of congestive heart failure, while after infancy, HTN is frequently silent, and signs and symptoms are evident when the level of blood pressure is particularly high, or hypertension has been present for years [2]. The likelihood of identifying a secondary cause of HTN is directly related to the level of blood pressure and inversely related to the age of the child [2]. The severity of blood pressure elevation does not differ significantly between children with primary and secondary HTN in some studies. However, DBP elevation appears to be more predictive of secondary HTN, whereas SBP elevation appears to be more predictive of primary HTN [8].

Primary HTN

The prevalence of essential pediatric HTN is unknown. Characteristics of children with primary HTN include older age (≥6 years), a positive family history of HTN in a parent and/or grandparent,

Table 1. Definitions of the normal, high-normal blood pressure and hypertension categories according to the 2016 Guidelines of The European Society of Hypertension [7].

	SBP and/or DBP percentile	SBP and/or DBP
Age category	<16 years	≥16 years
Normal	<90th	<130/85 mmHg
High-normal	≥90th <95th	130–139/85–89 mmHg
HTN Stage 1	≥95th <99th + 5 mmHg	140–159/90–99 mmHg
HTN Stage 2	≥99th + 5 mmHg	160–179/100–109 mmHg
ISH	SBP ≥95th and DBP <90th	SBP ≥140 mmHg and DBP <90 mmHg

SBP – systolic blood pressure; DBP – diastolic blood pressure; HTN – hypertension; ISH – isolated systolic hypertension.

and overweight and/or obesity [8]. Several factors related to primary HTN in adults have also been associated with higher blood pressure in children and adolescents [16]. Also, familial studies demonstrated a link between genetic and environmental influences on blood pressure during childhood and the development of essential hypertension [16]. Children from families with HTN tend to have a higher blood pressure than those from normotensive families, and significant correlations in blood pressure and cardiovascular risk factors exist between parents and their children [16].

Secondary HTN

The most common causes for secondary HTN are presented in Table 2.

Secondary HTN should be suspected in the younger patient with very high blood pressure or secondary complications such as hypertensive encephalopathy, cranial nerve palsy, heart failure, or HTN is difficult to treat [7]. Renal diseases are the most frequent cause of secondary HTN in children, and it is appropriate to have a high index of suspicion, particularly in those <6 years of age [8].

Table 2. Seconday causes of hypertension. Adapted from [7, 8].

Etiology	Sings and/or symptoms	Investigations
Renal disease (including chronic renal failure, renal artery stenosis, polycystic kidney disease, multicystic dysplastic kidney, hydronephrosis, reninoma, Wilms tumor)	Renal disease (including chronic renal failure, renal artery stenosis, polycystic kidney disease, multicystic dysplastic kidney, hydronephrosis, reninoma, Wilms tumor)	• Protein, erythrocytes and erythrocyte casts in urine • Serum creatinine concentration and potassium • Plasma renin activity • Abdominal ultrasound • [99Tcm] dimercaptosuccinic acid static scanning • Renal artery Doppler ultrasound • Angiography/MRI angiography
Pheochromocytoma and paraganglioma	tachycardia, pallor, flushing, diaphoresis	• 24-h urine and plasma chatecolamines or metanephrines • MRI • i123 metaiodobenzylguanidine
Primary aldosteronism	muscle weakness	• Plasma renin activity • Plasma aldosterone
Cushing's syndrome	obesity, moon facies, acne, hirsutism, striae	• Plasma cortisol, ACTH • 24-h urinary free cortisol
Hyperthyroidism	tachycardia, proptosis, thyromegaly, goiter	• TSH • FT3 and FT4
Coarctation of aorta	decreased lower extremity pulses, drop in BP from upper to lower extremities, heart murmur	• Rx chest • Echocardiography • MRI angiograpy • Aortography
Congenital adrenal hyperplasia	• ambiguous or virilized genitalia	• Plasma deoxycorticosterone and corticosteron • 18-hydroxycorticosterone, 18-hydroxydeoxycorticosterone and 11 deoxycortisol
Obstructive sleep apneea	type 1: amigdalar hypertrophy, mild overweight, hyperactivity and recurrent infections; type 2: obese patient, diurnal hypersomnia and metabolic disturbance	• Nocturnal pulsioxymetry

ACTH – adrenocorticotropic hormone; MRI – magnetic resonance imaging; FT3 – free triiodothyronine; FT4 – free thyroxine; TSH – thyroid stimulating hormone.

Drug-induced HTN (DIH) is defined as HTN caused by the unintended effect of a drug, and the two major mechanisms involve sodium retention and a sympathomimetic effect [7]. Common prescription medications associated with a rise in blood pressure include oral contraceptives, central nervous system stimulants, and corticosteroids [8]. Medications that contain decongestants (e.g., pseudoephedrine and phenylpropanolamine) may cause a mild increase in blood pressure with the recommended dosing. However, severe HTN has been seen as an idiosyncratic response with appropriate dosing as well as with excessive doses [8]. Another relevant cause of DIH is the use of inhibitors of angiogenesis in cancer treatment [7]. Treatment of DIH involves withdrawal of the drug which caused it; sometimes short-term or chronic antihypertensive treatment may be needed, especially in those where the therapy with a therapeutic agent causing DIH cannot be stopped [7].

Monogenic causes of HTN are uncommon and should be suspected in children with low renin HTN and a family history of early-onset severe HTN, death from cerebral vascular accidents, and heart failure or refractory HTN [7, 8]. Monogenic forms of HTN in children include Liddle syndrome, pseudohypoaldosteronism type II, apparent mineralocorticoid excess, generalized glucocorticoid resistance, familial hyperaldosteronism type I, and congenital adrenal hyperplasia [7, 8]. Treatment of monogenic HTN is directed against main pathophysiological disturbances [7].

Diagnosis

Blood pressure should be measured at the first medical visit in children from 3 years of age and in younger children if they have an underlying condition that increases the risk for HTN: neonatal complications requiring intensive care, congenital heart disease, renal disease, solid-organ transplant, malignancy, treatment with drugs known to raise blood pressure, evidence of elevated intracranial pressure [7, 8].

Blood pressure in childhood may vary between visits and even during the same visit, and it is important to obtain multiple measurements over time before diagnosing HTN [8]. The initial blood pressure measurement may be oscillometric, by using a calibrated and validated machine for use in the pediatric population, or auscultatory, by using a mercury/aneroid sphygmomanometer [8]. Available reference values for defining blood pressure categories have been obtained by the auscultatory method, and because the values obtained with oscillometric methods tend to be higher than the auscultatory ones, the HTN detected by the oscillometric method must be confirmed by the auscultatory measurement [7].

Office blood pressure measurements should be used as a reference, and blood pressure values obtained out-of-office (ambulatory or home blood pressure) may improve the evaluation in untreated and treated patients [7] It is recommended to measure blood pressure after the patient is sitting or relaxed for 3–5 min and using the appropriate cuff size according to bladder width and length to cover 80–100% of the arm circumference [7]. In the auscultatory method, Korotkoff sounds are used to assess SBP (K1) and DBP (K5) while deflating the cuff and blood pressure should be measured 3 times with an interval of 3 min between measurements and use the average of the last two [7]. Also, it is very important to measure blood pressure in both arms at the first visit and consider the arm with the higher value as the reference [7].

Values obtained using 24-h ambulatory blood pressure have some better relationship with the presence of organ damage and a higher reproducibility than those obtained using office blood pressure and should be recommended before starting antihypertensive treatment, to avoid treating with drugs children with "white-coat" HTN [7].

Table 3. Criteria to define HTN-induced organ damage. Adapted from [7].

LVH	LVMI or RWT ≥95th percentile by age and sex
Carotid intima thickness	cIMT ≥95th percentile by age and sex
PWV	PWV ≥95th percentile by age and sex
Kidney	Albuminuria (as measured by urinary albumin/creatinine quotient >30 mg/g creatinine or >3 mg/mmol creatinine) or even proteinuria (as measured by urinary albumin/creatinine quotient (>300 mg/g creatinine or >30 mg/mmol creatinine) or by 24 h urinary protein excretion (>200 mg/m2/day)

LVH – left ventricular hypertrofy; LVMI – left ventricular mass index; RWT – relative wall thickness; cIMT – carotid intima media thickness; PWV – pulse wave velocity.

Home blood pressure correlates closely with daytime ambulatory blood pressure values. It has superior reproducibility to office blood pressure, and it is recommended to measure daily for at least 3–4 days, preferably for 7 days in the mornings and the evenings [7].

Patients evaluation should include appropriate patient and family history (may identify children with essential HTN or determine possible causes or comorbidities associated with HTN), physical examination, laboratory evaluation, and imaging [7, 8]. It is mandatory to identify features of disorders that may be the cause of secondary HTN (Table 2) and to search for target organ damage, using the criteria from Table 3 [7].

Therapeutic management

The goals for the treatment of HTN in children and adolescents include achieving a blood pressure level that reduces the risk for target organ damage and HTN and related cardiovascular disease in adulthood [8]. The antihypertensive treatment should be started according to the values of blood pressure and overall cardiovascular risk (Figure 1) [7]. In children with high normal blood pressure and those with HTN, non-pharmacological therapy should be initiated based on lifestyle changes. Also, it should be continued after starting pharmacological therapy [7].

Lifestyle changes

There are some changes in lifestyle associated with the decrease of blood pressure. In obese children, it has been demonstrated that losing weight is associated with a decrease in blood pressure [6]. The increase in physical activity has also been shown to have cardiovascular benefits [6], and physical activity is recommended for at least 60 minutes, and the intensity should be moderate to vigorous [6]. Regarding diet, it is recommended that mothers limit children's salt intake and avoid excess sugar, soft drinks, and saturated fat. It is recommended to eat fruits, vegetables, and grain products [6]. There are meta-analyses indicating that a reduction of 3 grams per day in salt intake will lead to a decrease in blood pressure [17]. Discouraging maternal smoking and maintaining a smoke-free environment is of great importance as it has been demonstrated to determine cardiovascular risk [6].

Pharmacological therapy

There is a lack of large trials in the pharmacological treatment of HTN. The dosing and choice of treatment are based on hypertensive trials that included adults and expert opinion. There was an increased interest in the last years for conducting trials in children and adolescents with HTN. However, it remains a general lack of high-quality outcome data

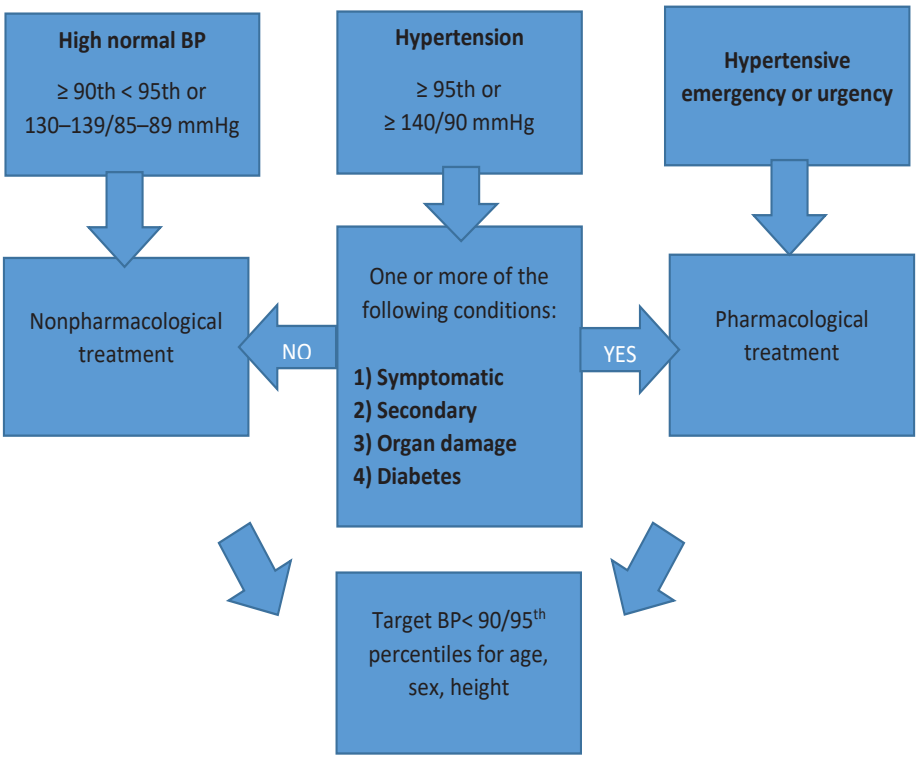

Figure 1. Initiation of antihypertensive treatment. Adapted from [7]. BP – blood pressure.

and a guide to choosing the proper treatment in pediatric patients.

The antihypertensive treatment can be given in monotherapy or combined therapy. The monotherapy includes the five classes for which there is evidence from adult hypertension: Angiotensin-Converting Enzyme inhibitors (ACEi), Angiotensin Receptor Blockers (ARB), beta-blockers, calcium channel blockers, and diuretics. Drug choice should also be targeted by the child's concurrent disorders like diabetes mellitus, kidney disease, migraines, surgical treatment of aortic coarctation. Table 4 summarizes the drug choice considering the underlying diseases. Primary hypertension is also a real problem in pediatric education, and there is evidence that ACEi and ARBs are the first-line agents in obesity-linked hypertension [18]. When these are not tolerated, calcium channel blockers should be given [6]. After choosing one treatment, it should be started with the lowest dose followed by up-titrated doses to decrease the blood pressure at least under the 95th percentile of blood pressure [6]. Periodical monitoring should be performed to avoid side effects. The diagnostic of monogenic hypertension is important because it needs specific treatment. For example, in Liddle syndrome, amiloride and triamterene should be initiated, while thiazide diuretics should be given in Gordon syndrome [6].

Table 4. Clinical conditions and specific antihypertensive drug classes. Adapted from [7].

Disorder	Drug class	Drug	Starting dose (per day)	Maximal dose (per day)
	Thiazide/thiazide-like diuretics	Hydrochlorothiazide	0.5–1 mg/kg	3 mg/kg
		Chlortalidone	0.3 mg/kg	2 mg/kg up to 50 mg
Chronic renal failure	ACEi	Captopril	0.3–0.5 mg/kg	6 mg/kg
		Fosinopril	0.1–0.6 mg/kg	40 mg
		Lisinopril	0.08–0.6 mg/kg	0.6 mg/kg up to 40 mg
	ARB	Lorsartan	0.7 mg/kg up to 50 mg	1.4 mg/kg up to 100 mg
		Valsartan	0.4 mg/kg	40–80 mg
Coarctation of aorta	Beta-adrenergic blockers	Atenolol	0.5–1 mg/kg	2 mg/kg up to 100 mg
		Metoprolol	0.5–1 mg/kg	2 mg/kg
Hyperaldosteronism	Potassium-sparing diuretics	Spironolactone	1 mg/kg	3.3 mg/kg up to 100 mg
		Eplerenone	25 mg	100 mg
		Amiloride	0.4–0.6 mg/kg	20 mg
Obesity-linked primary HTN	ACEi	Captopril	0.3–0.5 mg/kg	6 mg/kg
		Fosinopril	0.1–0.6 mg/kg	40 mg
		Lisinopril	0.08–0.6 mg/kg	0.6 mg/kg up to 40 mg
	ARB	Lorsartan	0.7 mg/kg up to 50 mg	1.4 mg/kg up to 100 mg
		Valsartan	0.4 mg/kg	40–80 mg
	Loop diuretics	Furosemide	0.5–2 mg/kg	6 mg/kg
	Beta-adrenergic blockers	Atenolol	0.5–1 mg/kg	2 mg/kg up to 100 mg
		Metoprolol	0.5–1 mg/kg	2 mg/kg
Congestive heart failure	ACEi	Captopril	0.3–0.5 mg/kg	6 mg/kg
		Fosinopril	0.1–0.6 mg/kg	40 mg
		Lisinopril	0.08–0.6 mg/kg	0.6 mg/kg up to 40 mg
	ARB	Lorsartan	0.7 mg/kg up to 50 mg	1.4 mg/kg up to 100 mg
		Valsartan	0.4 mg/kg	40–80 mg

ACEi – angiotensin-converting enzyme inhibitor; ARB – angiotensin receptor blockers; HTN – hypertension.

When the maximum dose recommended or tolerated by the patient is reached, combination therapy is needed. There is no specific evidence for which combination to use in pediatric patients, and so the combination is based on complementary mechanisms and the experience in adults. For example, an ACEi or ARB can be combined with a diuretic or calcium antagonist [6]. There is extensive data supporting against the combination of ACEi and ARBs or direct renin inhibitors due to the risk of hypotension, hyperkalemia, and impaired kidney function [6]. Few data exist on using fixed combination treatment in children; however, it can be used in adolescents to increase adherence to treatment [19].

Conclusion

In children, HTN remains a real health problem, frequently underdiagnosed, with potential consequences in adult life. Therefore, there is a strong need to implement clear guidelines regarding diagnostic and treatment of HTN in the pediatric population in order to increase diagnostic and improve HTN management.

Conflict of Interest

The authors confirm that there are no conflicts of interest.

References

1. Hansen ML, Gunn PW, Kaelber DC. Underdiagnosis of Hypertension in Children and Adolescents. JAMA. 2007 Aug 22;298(8):874–9.
2. Sinaiko AR. Hypertension in Children. N Engl J Med. 1996 Dec 26;335(26):1968–73.
3. Moore WE, Stephens A, Wilson T, Wilson W, Eichner JE. Body Mass Index and Blood Pressure Screening in a Rural Public School System: the Healthy Kids Project. Prev Chronic Dis. 2006 Sep 15;3(4):A114.
4. Franco MCP, Christofalo DMJ, Sawaya AL, Ajzen SA, Sesso R. Effects of Low Birth Weight in 8- to 13-Year-Old Children. Hypertension. 2006 Jul 1;48(1):45–50.
5. Munger RG, Prineas RJ, Gomez-Marin O. Persistent elevation of blood pressure among children with a family history of hypertension: the Minneapolis children's blood pressure study. J Hypertens. 1988 Aug;6(8):647–53.
6. Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, et al. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. J Hypertens. 2016 Oct;34(10):1887–920.
7. Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, et al. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. J Hypertens. 2016 Oct;34(10):1887–920.
8. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Pediatrics [Internet]. 2017 Sep 1 [cited 2021 Aug 1];140(3). Available from: https://pediatrics.aappublications.org/content/140/3/e20171904
9. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics. 2004 Aug;114(2 Suppl 4th Report):555–76.
10. Chiolero A, Cachat F, Burnier M, Paccaud F, Bovet P. Prevalence of hypertension in schoolchildren based on repeated measurements and association with overweight. J Hypertens. 2007 Nov;25(11):2209–17.
11. Ostrowska-Nawarycz L, Nawarycz T. Prevalence of excessive body weight and high blood pressure in children and adolescents in the city of Lódz. Kardiol Pol. 2007 Sep;65(9):1079–87; discussion 1088-1089.
12. Papandreou D, Stamou M, Malindretos P, Rousso I, Mavromichalis I. Prevalence of Hypertension and Association of Dietary Mineral Intake with Blood Pressure in Healthy Schoolchildren from Northern Greece Aged 7–15 Years. Ann Nutr Metab. 2007;51(5):471–6.
13. Maldonado J, Pereira T, Fernandes R, Santos R, Carvalho M. An approach of hypertension prevalence in a sample of 5381 Portuguese children and adolescents. The AVELEIRA registry. "Hypertension in children." Blood Press. 2011 Jun;20(3):153–7.
14. Genovesi S, Antolini L, Giussani M, Pieruzzi F, Galbiati S, Valsecchi MG, et al. Usefulness of waist circumference for the identification of childhood hypertension. J Hypertens. 2008 Aug;26(8):1563–70.
15. Lifton RP, Gharavi AG, Geller DS. Molecular mechanisms of human hypertension. Cell. 2001 Feb 23;104(4):545–56.
16. Bartosh SM, Aronson AJ. CHILDHOOD HYPERTENSION: An Update on Etiology, Diagnosis, and Treatment. Pediatr Clin North Am. 1999 Apr 1;46(2):235–52.
17. He FJ, MacGregor GA. Importance of salt in determining blood pressure in children: meta-analysis of controlled trials. Hypertens Dallas Tex 1979. 2006 Nov;48(5):861–9.
18. Elliott WJ, Meyer PM. Incident diabetes in clinical trials of antihypertensive drugs: a network meta-analysis. Lancet Lond Engl. 2007 Jan 20;369(9557):201–7.
19. Sorof JM, Cargo P, Graepel J, Humphrey D, King E, Rolf C, et al. Beta-blocker/thiazide combination for treatment of hypertensive children: a randomized double-blind, placebo-controlled trial. Pediatr Nephrol Berl Ger. 2002 May;17(5):345–50.