10.5152/turkjnephrol.2022.21112

Original Article

Turkish Journal of Nephrology

Approaches of Pediatric Nephrologists to Hypertensive Patients in Turkey (Turkish Pediatric Hypertension Working Group Study)

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ABSTRACT

Objective: We aimed to evaluate the approaches of pediatric nephrologists in our country to the management of childhood hypertension.

Methods: The pediatric nephrologists in our country were invited to fill out an online questionnaire including 24 questions. The answers were compared between those working in the field for ≤10 years (Group 1, n =74) and >10 years (Group 2, n = 62).

Results: Of 136 participants (M/F = 101/35), 52% were following a single guideline [31% Fourth Report of 2004, 17% European Society of Hypertension in 2016, and 52% American Academy of Pediatrics in 2017], which is more common in Group 1 (*P* = .035). The most commonly used guideline was American Academy of Pediatrics of 2017 and Group 2 used Fourth Report of 2004 more commonly (*P* = .042). The most common choice to diagnose hypertension was office + home + ambulatory blood pressure monitoring (59%). The frequency of screening for end-organ damage at first evaluation was 96%. The time to wait for the effect of lifestyle modifications was 3 months in 52%. The first choice medication was angiotensin-converting enzyme inhibitors (49%) or calcium-channel blockers (48%) in non-obese and angiotensin-converting enzyme inhibitors (74%) in obese children. Calcium-channel blockers were more commonly prescribed as the first choice in non-obese children in Group 1 (*P* = .035). The most accessible emergency drug was esmolol.

Conclusion: Despite following recent guidelines, the time spent in the proficiency would change the practices.

Keywords: Hypertension, children, adolescents, guidelines, clinical practice patterns

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Received: June 2, 2021 **Accepted:** October 5, 2021

This study has been presented as an oral presentation in the 10th National Pediatric Nephrology Congress, 2019, Antalya.

Cite this article as: Kasap-Demir B, Taşdemir M, Övünç-Hacıhamdioğlu D, et al. Approaches of pediatric nephrologists to hypertensive patients in Turkey (Turkish Pediatric Hypertension Working Group Study). *Turk J Nephrol.* 2022;31(2):110-115.

INTRODUCTION

Until the last few years, the Fourth Report published in 2004 (FR-2004) has been the most popular guide for the diagnosis and management of children and adolescents with hypertension (HT). This guideline was proposed by National High Blood Pressure Education Program (NHBPEP) Children's Working Group of National Heart Lung and Blood Institute (NHLBI) and included 50th, 90th, 95th, and 99th percentile charts for children and adolescents from 1 to 17 years, based on age, gender, and height percentiles.[1]

In 2016, the European Society of Hypertension (ESH-2016) issued a new guideline for use in children and adolescents, in which percentiles revised in FR-2004 were used and adult guidelines for patients ≥16 years were recommended.[2] In addition, they reported systolic and diastolic blood pressure (BP) 50th, 75th, 90th, and 95th percentiles for ambulatory blood pressure monitoring (ABPM) for patients ≥5 years suggested by Wühl et al,[3] and 50th and 95th percentiles for home BP measurements (HBPMs) for children ≥120 cm. They presented recommendations for HBPM monitoring.

In 2017, the American Academy of Pediatrics (AAP-2017) proposed the most recent guideline for children and adolescents, which was endorsed by the American Heart Association (AHA). In this guideline, a new set of BP percentile charts including 50th, 90th, 95th percentile, and 95th + 12 mm Hg were created depending on the measurements of approximately 50 000 non-obese (NO) children. Since overweight children were excluded, these percentile tables have lower limits when compared to those reported in FR-2004. AAP-2017 guideline also suggested evaluating patients ≥13 years concerning adult limits proposed by AHA.[3]

All 3 guidelines offer some different ways to diagnose, evaluate, and treat patients with HT in terms of thresholds and contents. In daily practice, personal experiences and confirmed habits may also play a major role in addition to guidelines. In this study, we aimed to evaluate the approaches of pediatric nephrologists to children and adolescents with HT about considering the contents of the guidelines and how that varies with the time spent in the professional life in our country.

METHODS

The study has been approved by the İzmir Katip Çelebi University Ethics Committee, 17.01.2018/19. All the pediatric nephrologists listed in the Turkish Society of Pediatric Nephrology were invited to fill out the online questionnaire, which was designed by the authors as a web-based electronic survey using Google Forms. Between January 2018 and May 2018, 2 e-mail invitations approximately 4 months apart were sent using the master e-mail list of the society. The pediatric nephrology fellows did not participate. The questionnaire consisted of 24 questions. The first 5 questions were about personal information including gender, age, the time spent in the proficiency as a pediatric nephrologist, the highest academic degree, and the category of the hospital they work. The age categories were ≤35, 36-45, 46-55, and >55 years. The time spent in the proficiency was categorized as 0-5, 6-10, 11-15, 16-20, and ≥20 years. The academic degrees were classified as specialist, assistant professor, associate professor, and professor. The hospitals where the physicians work were categorized as private hospitals, second-line public hospitals, and tertiary referral hospitals including university hospitals and training and research hospitals. Survey results of those who have not fulfilled these 5 questions were not included in the study.

The rest of the questions were about the diagnostic methods and treatment choices for HT in children and adolescents. The participants were informed that they were able to mark more than one item in appropriate questions. They were asked about the guideline and the method they preferred to use while diagnosing HT. If they were using HBPM, they were asked the minimum duration of measurements they considered sufficient, the minimum number of measurements they evaluate, and the criteria they use for deciding HT. The participants were asked whether they evaluate end-organ damage (EOD) at the first visit and the methods they prefer to evaluate. The target BP levels for patients with and without EOD, the time to evaluate the therapeutic effects of non-pharmacologic treatment before medical treatment, and the first and the second choice medication that would be added to the treatment for obese and NO patients were questioned. Whether the clinicians check the biochemical parameters including urea, serum creatinine, sodium, and potassium after prescribing a renin–angiotensin–aldosterone system (RAAS) inhibitor was also questioned.

The first choice medications that the physicians would use in a hypertensive emergency and whether they used to prescribe routine medical anti-hypertensive treatment after a hypertensive emergency were also asked.

After evaluating the answers in the whole group, participants were divided into 2 groups: those working in the field of pediatric nephrology for ≤10 years (Group 1, n = 74) and for >10 years (Group 2, n = 62). All the answers to the above-mentioned questions were compared between the groups.

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences software 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were shown in frequency and were compared using the chi-square test. A *P*-value of <.05 was considered significant in all statistical evaluations.

MAIN POINTS

- The most frequently used guideline by the pediatric nephrologists in our country was American Academy of Pediatrics of 2017 as a single guideline or in combination with others.
- Younger nephrologists more frequently prefer to stick to a single guideline.
- Seniors prefer to follow the earliest guideline (Fourth Report of 2004).
- Younger physicians more frequently prefer calcium-channel blockers as the first choice anti-hypertensive drug than seniors.
- Despite current guidelines, the time spent in the proficiency would change the practices.

RESULTS

A total of 136 volunteer clinicians responded to the questionnaire. Of the participants, 101 (74%) were female, 80 (59%) were ≤45 years, and the mean time spent in proficiency was ≤10 years in 74 (54%). The rate of clinicians working at a tertiary center, including training and research hospitals and/or university hospitals, was 91% (n = 124). The rate of clinicians with the academic degree of at least associated professor was 51% (n = 70). When these personal descriptive findings were compared between the groups, the female gender was significantly more frequent in Group 1, and as expected, clinicians older than 45 years and the rate of clinicians working as an associated professor or professor were significantly higher in Group 2

Table 1. Comparison of Findings Between the Groups

	Group 1 (n = 74), n (%)	Group 2 (n = 62), n (%)	*P*
Gender (F)	64 (86)	37 (60)	<.001
Age (≥45 years)	4 (5)	52 (84)	<.001
Academic degree (associate professor or professor)	25 (34)	55 (89)	<.001
Hospital (tertiary referral hospital)	69 (93)	55 (89)	.532
Following single guideline	45 (62)	26 (42)	.035
FR-2004	32 (44)	39 (63)	.042
ESH-2016	27 (37)	20 (32)	.694
AAP-2017	44 (60)	44 (71)	.263
HBPM use	13 (18)	17(27)	.241
Time required for evaluation of HBPMs (≤1 week)*	24 (40)	16 (36)	.794
Number of HBPMs required for evaluation (≤14)*	32 (52)	24 (53)	1.000
Screening for EOD at first evaluation	70 (95)	60 (97)	.844
Checking biochemical parameters a week after initiation of RAAS blockers	65 (87)	49 (79)	.763
First choice anti-HT agent in non-obese patients			
RAAS blocker	32 (43)	37 (60)	.082
CaCB	42 (57)	23 (37)	.035
First choice anti-HT agent in obese patients			
RAAS blocker	56 (76)	52 (84)	.412
CaCB	13 (18)	6 (1)	.062
First choice ACEI (enapril)	58 (78)	45 (73)	.559
First choice ARB (losartan)	72 (97)	56 (90)	.092
First choice CaCB (amlodipin)	70 (95)	55 (89)	.348
First choice diuretics (thiazide)	25 (34)	26 (42)	.424
Anti-HT use after hypertensive crisis	68 (92)	57 (92)	1.000

Group 1: Clinicians working in the field of pediatric nephrology for ≤10 years.
Group 2: Clinicians working in the field of pediatric nephrology for >10 years.
*The total number of participants using HBPM was 106 including 61 in Group 1 and 45 in Group 2. The ratios were calculated with these numbers.
F, female; FR, Fourth Report, ESH, European Society of Hypertension; AAP, American Academy of Pediatrics; HBPM, home blood pressure measurement; EOD, end-organ damage; RAAS, renin–angiotensin–aldosterone system, HT, hypertension; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CaCB, calcium channel blocker.

(Table 1). The rate of clinicians working at a tertiary center was similar between the groups.

The rate of clinicians following a single guideline was 52% (n = 71). Of those, 31% (n = 22) used FR-2004, 17% (n = 12) used ESH-2016, and 52% (n = 37) used AAP-2017 guidelines. In addition, the rates of participants following guidelines as a single one or in combination with others were 52% (n = 71) for FR-2004, 35% (n = 47) for ESH-2016, and 65% (n = 88) for AAP-2017, respectively. Following a single guideline was more frequent in Group 1 (*P* = .035) and Group 2 was more frequently using FR-2004 (*P* = .042). The usage of the other 2 guidelines was similar between the groups. Thirteen clinicians were not using the most recent guideline, AAP-2017, and the rates were similar between the groups.

Fifty-nine percent (n = 80) of the participants used both office, HBPM, and ABPM for deciding HT in children and adolescents and the others preferred 1 or more methods. Twenty-two percent of the physicians (n = 30) did not prefer HBPM. Of those, 106 who used HBPMs, 38% (n = 40) preferred 7 days, 26% (n = 28) preferred 10 days, 21% (n = 22) preferred 2 weeks, and 15% (n = 16) preferred ≥2 weeks of evaluation. The minimum number of measurements requested by the participants to evaluate for HBPM was ≤14 in 53% (n = 56). While evaluating HBPMs, 30% (n = 32) of the participants defined HT as mean HBPMs being >95 percentile, while 21% (n = 22) defined HT as ≥25% of the measurements being >95 percentile and 49% (n = 52) used both. The rate of HBPM usage, the time required for HBPM evaluation, and the number of HBPMs required for evaluation were similar between groups 1 and 2.

The number of physicians evaluating EOD at first evaluation was 96% (n = 130) in the whole group and rates were similar when compared between the groups. While evaluating EOD in children and adolescents with HT, 10% (n = 14) evaluated both left ventricular mass index (LVMI) and hypertensive retinopathy (HTRP), another 10% (n = 14) evaluated LVH, HTRP, microalbuminuria (MA), and cIMT, 76% (n = 103) evaluated LVMI, HTRP, and MA, and 6% (n = 4) evaluated LVH, HTRP, MA, carotid intima-media thickness (cIMT), and pulse wave velocity (PWV).

The target BP for patients without EOD was described as <95 percentile by 22% (n = 30), <90 percentile by 24% (n = 32), <75 percentile by 2% (n = 3), <95 percentile and <120/80 by 9% (n = 12), <95 percentile and <130/80 by 15% (n = 20), <90 percentile and <120/80 by 16% (n = 22), <90 percentile and <130/80 mm Hg by 7% (n = 9) of the participants and a combination of different limits were used by 5% of the remaining participants. The target BP for patients with EOD was described as <95 percentile by 5% (n = 7), <90 percentile by 25% (n = 34), <75 percentile by 15% (n = 20), <90 percentile and <120/80 mm Hg by 24% (n = 33), and <75 percentile and <120/80 mm Hg by 13% (n = 18) of the participants and a combination of different limits were used by 18% of the remaining participants.

The time to wait before institution of the pharmacological treatment after lifestyle modifications was at least 1 month in 35% (n = 47), 3 months in 52% (n = 70), and ≥6 months in 14% (n = 19) of the participants. The first choice anti-hypertensive treatment in NO hypertensive patients were angiotensin-converting enzyme inhibitors (ACEIs) in 49% (n = 66), angiotensin receptor blockers (ARBs) in 2% (n = 3), and calcium-channel-blockers (CaCBs) in 48% (n = 65). Only 1% of the participants preferred other anti-hypertensive agents including diuretics, beta-blockers, and alpha-agonists. The participants in both groups preferred RAAS-blockers at a similar rate; however, those in Group 1 more frequently preferred CaCBs when compared to Group 2. The second choice anti-hypertensive was ACEI in 44% (n = 59), ARB in 7% (n = 9), CaCB in 44% (n = 60), diuretics in 4% (n = 5), and beta-blockers in 2% (n = 3) in NO patients.

In obese hypertensive youth, the first choice anti-hypertensive agents were ACEIs in 75% (n = 101), ARBs in 5% (n = 7), CaCBs in 17% (n = 23), and others in 3% of the participants. The first choice treatment option in obese patients did not differ between the groups. The second choice anti-hypertensive agent was ACEI in 19% (n = 26), ARB in 16% (n = 22), CaCB in 50% (n = 68), diuretics in 9% (n = 12), beta-blockers in 5% (n = 6), and alpha-agonists in 1% (n = 1) of the participants, and 55% (n = 75) of them used to check biochemical parameters in 10 days after initiation of RAAS blockers. The rates did not differ between the groups.

The first choice ACEI was enalapril in 76% (n = 103), captopril in 6% (n = 9), ramipril in 18% (n = 24); the first choice ARB was losartan in 96% (n = 130) and valsartan in 4% (n = 6); the first choice CaCB was amlodipine in 92% (n = 125) and nifedipine in 8% (n = 11); the first choice diuretic was furosemide in 57% (n = 77), thiazide in 37% (n = 51) and spironolactone in 6% (n = 8) of the participants. The first choice ACEI, ARB, CaCB, or diuretic were similar between the groups.

The first choice medications added were CaCBs to ACEIs in 41% (n = 56), ACEIs to CaCBs in 41% (n = 56), ARBs to CaCBs in 3% (n = 4), and ARBs to ACEIs in 3% (n = 4) for NO patients. The rest of the physicians (12%, n = 16) preferred other groups of drugs. For obese patients, the first choice medications to add were CaCBs to ACEIs in 46% (n = 63); ACEIs to CaCBs in 15% (n = 20), ARBs to ACEIs in 15% (n = 20), diuretics to ACEIs in 8% (n = 11), beta-blockers to ACEIs in 4% (n = 5), and CaCB to ARB in 3% (n = 4). The rest of the physicians (9%, n = 13) preferred other combinations.

In hypertensive emergency cases, 12 (9%) of the participants used esmolol as a sole treatment option, while 55 (40%) of them used any combination of oral enalapril, esmolol, sodium nitroprusside, and oral nifedipine. The rate of the physicians using routine anti-hypertensive treatment after an acute hypertensive crisis was 92% (125/136). The rest of the physicians preferred to use medication only if the case has an EOD. This preference was similar between Groups 1 and 2.

DISCUSSION

In our study, we have found that despite the short time elapse between the electronic publication of the AAP-2017 guideline in August 2017 and the conduct of the questionnaire, the most frequently used guideline by the pediatric nephrologists in our country was AAP-2017 as a single guideline or in combination with others. We also found that younger nephrologists more frequently preferred to stick to a single guideline and seniors followed FR-2004. Besides, younger physicians more frequently preferred CaCBs as the first choice anti-hypertensive drug than seniors.

Office BP measurements are the cornerstones for defining HT. Ambulatory blood pressure monitoring was advised for diagnosis and follow-up in all 3 guidelines. Home BP measurements were taken into consideration specifically in ESH-2016. Most of our participants (59%) preferred to use all 3 methods while evaluating a patient with HT.

European Society of Hypertension in 2016 suggested HBPMs 2 times in a day, in the mornings and the evenings on at least 3-4 days, preferably on 7 consecutive days, which means optimally 14 measurements. Two measurements should be taken 1-2 minutes apart on each occasion. Home BP measurements is the average of these readings with the exclusion of the first monitoring day and values ≥95 percentile may be considered as HT. The guideline advises to use HBPMs for all patients receiving anti-HT medication, in suspicion of white coat hypertension,

in high-risk patients that strict BP control is mandatory and for clinical trials.[2] In AAP-2017, HBPM has been advised as an adjunct to office blood pressure measurements, and ABPM after HTN has been diagnosed, and should not be used to diagnose hypertension (HTN), masked hypertension (MH), or white coat hypertension (WCH). Additionally, AAP-2017 reports that measurements with automated devices may even reduce potential problems including observer bias, inaccurate reporting, and terminal digit preference and HBPM may be more reproducible. However, since only a few devices have been validated for use in children and the number of measurements and the time to monitor is not well defined, the use of HBPMs is limited.[4] Probably due to these concerns, 22% of the participants preferred not to use HBPMs. Of those using HBPMs, 38% performed 7 days of monitoring as suggested in ESH-2016, while the rest of the group preferred to monitor for longer than 7 days and 47% preferred to evaluate >14 measurements probably to increase the reliability.

The three guidelines have different suggestions for EOD. Left ventricular hypertrophy is the most well-known clinical evidence of EOD in children and adolescents.[1] In the FR-2004, echocardiography has been recommended as the primary tool to evaluate EOD for LVH in all patients, and LVH has been defined as values >51 g/m^{2,7}. Only eye examination for retinal changes has been offered as a part of physical examination.[1] European Society of Hypertension in 2016 has suggested searching for LVH and MA once HT is confirmed. Despite publishing limits for cIMT and PWV, routine vascular assessment has not been recommended. The fundoscopic examination has only been recommended for subjects with symptoms, encephalopathy, or malignant HTN.[2] Different from FR-2004, this guideline suggested that LVH should be defined as LVMI or relative wall thickness (RWT) ≥95th percentile by age and sex.[5-7] MA was defined as urinary albumin/creatinine ratio >30 mg/g creatinine or urinary protein excretion >200 mg/m^2/day. For cIMT and PWV, ≥95 percentile by age and sex was defined for HT-induced EOD.[4,8-12] However, AAP-2017 suggested that electrocardiography is not recommended to assess LVH and echocardiography (ECHO) is not offered at the first evaluation until pharmacologic treatment is considered.[4] When a patient is evaluated with ECHO, it is recommended to assess LVM, cardiac geometry with RWT, and function with ejection fraction concerning the American Society of Echocardiography.[4] In addition, AAP-2017 suggested that the routine measurement of vascular structure and function including cIMT and/or PWV as well as MA is not routinely recommended. Fundoscopy was never mentioned in this guideline.[4] However, although AAP-2017 seems to be the most frequently followed guideline, almost all of the physicians (96%) reported that they used to check for EOD at first evaluation. As not suggested together in any of the guidelines, the most preferred combination was LVMI, HTRP, and MA in 76% among our participants. This would be because the physicians worry to miss an evidence for EOD since medical treatment was suggested for cases with EOD in FR-2004 and ESH-2016 without waiting for the results of lifestyle changes.

In FR-2004, the suggested goal for treatment was the reduction of BP to <95th percentile. In ESH-2016, <95th percentile is recommended for non-complicated patients, but <90th percentile was suggested to be considered. In AAP-2017, the goal for non-complicated patients was <90 percentile or <130/80 mm Hg (whichever is lower). Most of our participants reported using the limit <90 percentile for non-complicated limit, and the ratio using the limit reported in the last guideline, <90 percentile or <130/80 mm Hg, was quite low.

The interval between the lifestyle modifications and the pharmacological treatment was not specified in any of the guidelines. The first choice anti-hypertensive medication for NO children and adolescents has not been proposed in any of the guidelines, either and one of those 5 classes may be used: ACEIs, ARBs, beta-blockers, CaCBs, and diuretics. Our participants preferred ACEIs and CaCBs in almost an equal frequency and young nephrologists more frequently preferred CaCBs. This may be related to the dominancy of the clinicians having been educated from the same clinics responding to the questionnaire; however, we did not check. Besides, the need for checking the creatinine and electrolyte levels when prescribing ACEIs or ARBs may have prompted to prefer CaCBs as the first agent. The guidelines have more precise recommendations about the first-choice medications for HT in obese children and adults and they all suggest ACEIs or ARBs, and 80% of the participants reported using these 2 groups of agents.

Once the high recommended dose of 1 drug is reached and if there is still a need for more medication, a second drug from another class was suggested in FR-2004 and ESH-2016.[1,2] These points have not been mentioned in AAP-2017.[4] As a second agent, most of our participants preferred to add CaCBs to ACEIs or vice versa in an equal manner. However, 15% of them used to add ARBs to ACEI although anti-hypertensives from the same class were avoided.[1,2] Monitoring for kidney functions and electrolytes has been recommended when ACEIs are prescribed in FR-2004 and ESH-2016 but not in AAP-2017. Of our participants, only 55% used to check kidney functions and electrolytes. The incidence of hyperkalemia in patients treated with ACEI or ARB is approximately 3.3% and the risk of a reduction in GFR is prominent in cases with bilateral renal artery stenosis, heart failure, or chronic kidney disease.[13] As the number of patients with such restrictive conditions and those on additional risky medications were limited in the pediatric population, the rest of the clinicians might have preferred not to check biochemical tests depending on their experience.

Intravenous anti-hypertensive agents are not accessible worldwide. With the help of the guideline, we have learned that the available agents for hypertensive emergencies were esmolol,

sodium nitroprusside, oral enalapril, and oral nifedipine in our country and 92% of the participants prescribed anti-hypertensive medication following an acute hypertensive crisis.

Our study has some limitations. The number of participants was limited. We questioned the guideline the physicians prefer to lead on; however, the answers were far from showing the set of percentile charts they use since they were able to mark more than one choice.

CONCLUSION

We showed that pediatric nephrologists easily and quickly adopted current guidelines in managing youth with HT. However, the time spent in the profession would change the individual practice patterns. Although young nephrologists prefer to strict to a single guideline, seniors do not have an objection to using multiple guides that they have experienced. In contrast, some clinicians may act beyond guides at some points. At the moment, it is not clear which guideline is the perfect one for hypertensive children and adolescents in our country; however, it will be revealed when collected data of patients are compared in the follow-up.

Ethics Committee Approval: Ethics committee approval for this study was received from the Ethics Committee of İzmir Katip Çelebi University (Approval Date: January 17, 2018; Approval Number: 19).

Informed Consent: N/A.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - B.K.D., M.T.; Design - H.D., M.Ç.; Supervision - N.Ö., F.S.; Resources - N.K.B.; Data Collection and/or Processing - D.Ö.H., İ.G.; Analysis and/or Interpretation - B.K.D., M.B.; Literature Review - M.T.; Writing - B.K.D.; Critical Revision - F.S.

Declaration of Interests: The authors have no conflict of interest to declare.

Funding: The authors declared that this study has received no financial support.

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