

Ambulatory Blood Pressure Monitoring in Children: Single Center Experience

Mehmet Baha AYTAÇ, Kenan DOĞAN, Şule Ayas ERGÜL, Neslihan Dinçer MALKOÇ, Kenan BEK

Department of Pediatric Nephrology, Kocaeli University, Kocaeli, Türkiye

ABSTRACT

Objective: Ambulatory blood pressure monitoring (ABPM) is the preferred method for diagnosis of hypertension (HT) in children. Here, we aimed to demonstrate the reasons for ABPM application and incidence of HT, white coat and masked HT in our cohort besides the evaluation of dipping status, biochemical and radiological parameters between the patients with normotension, elevated blood pressure (EBP) and HT.

Material and Methods: Twenty-four hour ABPM results of children followed at department of pediatric nephrology and whose office blood pressure measurements revealed HT or EBP and ABPM records of normotensive patients having chronic kidney disease or renal anomalies were evaluated retrospectively. Twenty-four hour ABPM SD score ≥ 1.96 defined HT while the value between 1.64 and 1.95 indicated EBP. In addition to assessment of blood pressure loads and nocturnal dipping; age, gender, body mass index (BMI), proteinuria, kidney function tests and ultrasound of urinary system were also assessed.

Results: Although ABPM was applied to total of 244 patients, 189 of them were included in the study. High casual blood pressure measurements in 108 (57.1%) asymptomatic patients constituted the major group for ABPM application. Total of 57 patients (30.2%) were normotensive, 18 (9.5%) with EBP and 114 (60.3%) were hypertensive. No difference was found in regards of BMI, proteinuria, serum creatinine levels and sonographic results between the groups. Patients with HT and EBP had significantly lower nocturnal dip than normotensive group ($p < 0.001$). However there was no difference in number of patients with inadequate nocturnal fall in all three groups.

Conclusion: ABPM should be preferred for definitive diagnosis of HT in childhood. Patients with inadequate nocturnal fall should be evaluated carefully and followed-up regularly as it had been implicated in the development of cardiovascular disease.

Key Words: Ambulatory blood pressure, Childhood, Hypertension, Nocturnal dipping

INTRODUCTION

Accurate measurement and evaluation of blood pressure (BP) are initial steps for definitive diagnosis of hypertension (HT) in children and adults. After HT has been detected, it should be investigated for underlying pathology and then a management protocol should

be planned promptly to prevent cardiovascular complications. Ambulatory blood pressure monitoring (ABPM) is the preferred method over office BP measurements in children as it's considered to reduce environmental and anxiety-related measurement errors. ABPM parameters have also been shown to have a closer relationship with target organ damage (TOD) such as left ventricular

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Ethics Committee Approval : This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Kocaeli University, Faculty of Medicine Ethics Committee (09.05.2023-2023/111).

Contribution of the Authors : **AYTAÇ MB:** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. **DOĞAN K:** Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in necessary literature review for the study, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. **ERGÜL ŞA:** Constructing the hypothesis or idea of research and/or article, Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in patient follow-up, collection of relevant biological materials, data management and reporting, execution of the experiments, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. **MALKOÇ ND:** Planning methodology to reach the conclusions, Organizing, supervising the course of progress and taking the responsibility of the research/study, Taking responsibility in logical interpretation and conclusion of the results, Taking responsibility in necessary literature review for the study, Taking responsibility in the writing of the whole or important parts of the study, Reviewing the article before submission scientifically besides spelling and grammar. **BEK K:** Organizing, supervising the course of progress and taking the responsibility of the research/study, Reviewing the article before submission scientifically besides spelling and grammar.

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0000-0002-2561-9593 : AYTAÇ MB
0000-0003-2191-1981 : DOĞAN K
0000-0001-9113-5346 : ERGÜL ŞA

0000-0002-8750-3940 : MALKOÇ ND
0000-0002-1005-2379 : BEK K

Correspondence Address :

Mehmet Baha AYTAÇ
Department of Pediatric Nephrology,
Kocaeli University, Kocaeli, Türkiye
E-posta: mbaha_79@hotmail.com

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hypertrophy (LVH), increased carotid intima-media thickness (cIMT) and arterial stiffness (1,2).

So far, ABPM with continuous readings during 24-hour period, has provided significant clinical data about masked hypertension, BP load and isolated nocturnal HT especially in patients with chronic kidney disease, obesity or diabetes (3). ABPM is also a diagnostic tool for identification of white coat hypertension (WCH) defined as high office BP with ambulatory normotension which is considered to be a pre-hypertensive state in adult studies while any risk has not been reported yet to be correlated with TOD in children (4-6).

The aims of the present study are: (a) to investigate the reasons of ABPM application in children, (b) to determine the incidence of HT, elevated BP (EBP), WCH and MH in our cohort, (c) to assess the frequency of nocturnal dipping status, and (d) to compare the anthropometric, biochemical and radiological parameters between children with normotension, EBP and HT.

MATERIALS and METHODS

In this retrospective study, 24-hour ABPM records of the patients between the ages of 5 and 18-years-old with a height of >120 cm who had been followed up by the department of pediatric nephrology at Kocaeli University School of Medicine from February 2020 to October 2022, were investigated. ABPM had been applied to the children with EBP or HT on office measurements; and also it had been used to screen nocturnal HT in children having chronic kidney disease and congenital renal anomalies with normal office BP. The charts of each patient were reviewed for age, gender, anthropometric data and pastmedical history. Presence of proteinuria, kidney function tests and urinary Doppler ultrasound results were also assessed. The study was approved by Kocaeli University, Faculty of Medicine Ethics Committee (09.05.2023-2023/111). The study was performed in accordance with the Declaration of Helsinki.

Reference values were used to calculate SD scores for weight and height (7). Body mass index (BMI) was defined as the weight (kg) divided by height squared (m^2).

Serum creatinine, urea and blood urea nitrogen (BUN) were measured on the same day of ABPM. Protein to creatinine ratio (mg/mg) in spot fresh morning urine was used. Renal lengths were determined with ultrasound performed within 3 months and SD scores of renal lengths were calculated according to previously reported data (8).

Office BP was measured with an automated oscillometric device (Lutech Datalys 808, USA) after 5 minutes of rest using appropriate sized cuff for each patient. EBP was defined as systolic and/or diastolic office BP between 90th and 95th percentile whereas values above the 95th percentile was considered as hypertension based on recently published American Academy of Pediatrics guideline (9).

All subjects with EBP and HT on office measurements underwent 24-h ABPM. It was performed with an oscillometric device (Mobil-O-Graph, IEM GmbH, Stolberg, Germany) and proper sized cuff

on the non-dominant arm. BP was measured every 15 minutes during the daytime and every 30 minutes at night. Subjects were instructed to keep their arm relaxed while it was measuring and were encouraged to maintain their usual activities. They were asked to avoid strenuous exercise and sleeping during the day. Sleep at night and wake times were requested to be noted. Regarding the young age of patients, only recordings with 70% of the expected number of readings were included for the study.

Twenty-four hour ABPM SD scores based on gender and height were calculated for mean systolic, diastolic BP and mean arterial pressure (MAP) using the normative data of healthy children (10). Twenty-four hour ABPM SD score ≥ 1.96 defined hypertension whereas ≥ 1.64 but <1.96 score revealed EBP. Systolic and diastolic BP load (%) indicates the proportion of measurements above the 95th percentile reference adjusted for gender and height. Systolic and diastolic dipping status (%) were calculated as mean daytime BP minus mean sleeping BP divided by mean daytime BP. Inadequate nocturnal dipping was described as a drop of less than 10%.

Office BP above 95th percentile but mean ABPM SDS <1.96 with BP load $<25\%$ was described as WCH. Office BP below 95th percentile but mean ABPM SDS >1.96 with BP load $>25\%$ was diagnosed as MH (11).

Statistical analysis

Continuous variables are expressed as mean and standart deviation in normal distribution and as median and interquartile range in non-normal distributed cases. Student's t test or Mann-Whitney U test were used to analyze the differences between groups; one-way ANOVA or Kruskal-Wallis for the comparison of multiple categories. Qualitative variables were compared using Chi-square test. IBM Statistical Package for the Social Sciences, version 22.0 (SPSS Inc., Armonk, NY, IBM Corp., USA)22 statistical software was used for analysis and p value of 0.05 or lower was considered significant.

RESULTS

A total of 244 patients underwent 24-h ABPM between February 2020 and October 2022. In cases of multiple practices, only the first successful 24-h study was used and the subjects with

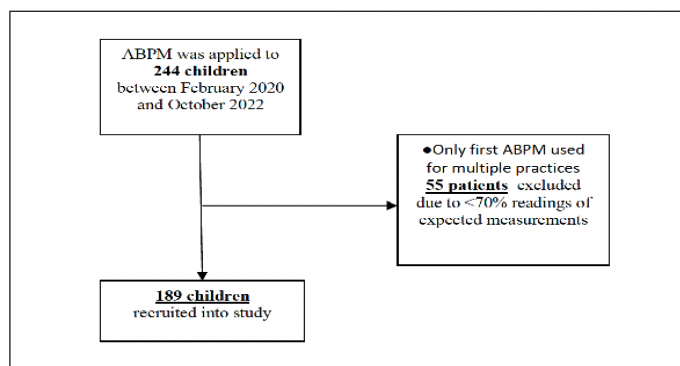


Figure 1: Inclusion criteria for the study. ABPM ambulatory blood pressure monitoring

Table I: Patient characteristics

	Normal (n=57)	EBP (n=18)	HT (n=114)	p
Age(years)*	14.4 (10.33-15.79)	12.78 (9.8-14.97)	14.95 (12.47-16.16)	0.040
Male(%) [†]	31 (54.4)	9 (50)	67 (58.8)	0.710
Height (cm)*	162 (137-173)	153.5 (135-172.2)	165 (151-173)	0.240
Height SD score [‡]	0.31 ± 1.08	0.16 ± 1	0.09 ± 1.14	0.480 [§]
Weight (kg) [‡]	63.05 ± 27.8	55.05 ± 23.63	64.35 ± 22.76	0.320 [§]
Weight SD score*	1.34 (0.3-2.2)	1.14 (0.04-1.53)	1.18 (0.55-1.92)	0.480
BMI [‡]	24.42 ± 6.54	22.15 ± 4.97	24.6 ± 5.52	0.240 [§]
BMI SD score*	1.42 (0.48-1.97)	0.99 (0.11-1.71)	1.34 (0.35-1.98)	0.500
Renal parameters*				
Serum creatinine(mg/dl)	0.59 (0.47-0.68)	0.55 (0.47-0.73)	0.64 (0.53-0.79)	0.430
Urine protein/creatinine(mg/mg)	0.14 (0.1-0.2)	0.14 (0.1-0.23)	0.13 (0.09-0.21)	0.700
Renal lenght(mm)				
Right	95 (86.5-96.5)	91 (81-111.25)	94 (89.75-100)	0.800
Left	98 (88.5-105)	98.5 (85-125.75)	99 (93-104)	0.360
Renal lenght SD score				
Right	-1.16 (-2.11- -0.15)	-1.13 (-1.68-1.24)	-1.12 (-2.1-0.01)	0.620
Left	-0.54 (-0.83-0.33)	-0.17 (-0.93-2.78)	-0.46 (-1.28-0.31)	0.210

*: median (interquartile range), †: n(%), ‡: mean ± standart deviation, §: one-way ANOVA Test, ||: Kruskal-Wallis Test, **EBP**: Elevated blood pressure, **HT**: Hypertension, **SD**: Standard deviation, **BMI**: Body mass index

Table II: Ambulatory BP data

	Normal (n=57)	EBP (n=18)	HT (n=114)	p
24-h values				
24-h systolic BP (mmHg)*	113.54 ± 6.54	115.83 ± 5.38	123.14 ± 8.21	<0.001 [‡]
24-h systolic BP SD score*	0.05 ± 0.54	0.51 ± 0.44	1.2 ± 0.97	<0.001 [‡]
24-h diastolic BP (mmHg)*	61.82 ± 4.85	65.5 ± 3.51	71.56 ± 6.66	<0.001 [‡]
24-h diastolic BP SD score*	-1.03 ± 0.94	-0.29 ± 0.67	0.72 ± 1.17	<0.001 [‡]
24-h MAP (mmHg)*	85 (82-89)	87.5 (86-91)	95 (92-98)	<0.001 [‡]
24-h MAP SD score*	0.62 ± 0.54	1.26 ± 0.37	2.28 ± 1.07	<0.001 [‡]
Day systolic BP (mmHg)*	116.37 ± 7.15	118.06 ± 6.18	125.09 ± 9.21	<0.001 [‡]
Day systolic BP SD score*	-0.21 ± 0.57	0.12 ± 0.4	0.74 ± 0.99	<0.001 [‡]
Day diastolic BP (mmHg)*	64.19 ± 5.04	67.39 ± 4.03	73.11 ± 7.62	<0.001 [‡]
Day diastolic BP SD score*	-1.36 ± 0.78	-0.83 ± 0.71	0.12 ± 1.24	<0.001 [‡]
Day MAP (mmHg)*	88.09 ± 5.21	90.61 ± 4.24	96.86 ± 7.03	<0.001 [‡]
Day MAP SD score*	0.22 ± 0.6	0.66 ± 0.4	1.6 ± 1.11	<0.001 [‡]
Night systolic BP (mmHg) [†]	105 (101-108.5)	109.5 (106.75-111)	116 (112-120)	<0.001 [§]
Night systolic BP SD score [†]	0.49 (-0.05-0.78)	0.95 (0.38-1.46)	1.65 (1.05-2.24)	<0.001 [§]
Night diastolic BP (mmHg) [†]	55 (51.5-57)	59 (58-61)	65 (62-68.25)	<0.001 [§]
Night diastolic BP SD score [†]	-0.13 (-0.79-0.28)	0.55 (0.31-0.76)	1.45 (0.93-1.98)	<0.001 [§]
Night MAP (mmHg) [†]	78 (74-80)	82 (80.75-83)	88 (86-91)	<0.001 [§]
Night MAP SD score [†]	1.14 (0.78-1.34)	1.81 (1.71-1.87)	2.66 (2.23-3.38)	<0.001 [§]
BP load and dipping [†]				
Day systolic BP load (%)	20 (12.5-36)	22.5 (18.75-45)	39 (21-55.5)	<0.001 [§]
Day diastolic BP load (%)	9 (2.5-15.5)	16.5 (10.25-20.25)	23.5 (10-50)	<0.001 [§]
Night systolic BP load (%)	21 (11.5-47)	36 (16.25-69)	57 (32-82.7)	<0.001 [§]
Night diastolic BP load (%)	0 (0.0-7.5)	11 (5.75- 22.25)	22 (8.75-46)	<0.001 [§]
Systolic BP dipping (%)	9.4 (6.8-13.05)	7.7 (5.17-9.5)	5.9 (3.17-11.15)	<0.001 [§]
Diastolic BP dipping (%)	15.9 (9.75-19.05)	13.2 (6.3-16.02)	10.15 (3.25-15.92)	<0.001 [§]

*: mean ± standart deviation, †: median (interquartile range), ‡: one-way ANOVA Test, §: Kruskal-Wallis Test, **EBP**: Elevated blood pressure, **HT**: Hypertension, **SD**: Standard deviation, **BP**: Blood pressure, **MAP**: Mean arterial pressure

available readings of at least 70% of the expected measurements were included in the study. Eventually, the study sample consisted of 189 patients (Figure 1). One hundred and seven (56.60%) of them are male. The mean age was 13.65±3.14 years.

The main indication for ABPM was consisted of 108 (57.10%) asymptomatic patients with high office BP (>90th percentile) according to the recent published guidelines (9). Symptomatic

children having high office BP presented with headache in 62 (32.81%) patients, dizziness in six, chest pain in two, palpitations in two and syncope in one patient.

Of the asymptomatic 108 patients, EBP was found in nine (8.32%) and hypertension in 64 (59.20%) patients. Of the 62 children who underwent ABPM due to headache, five patients (8%) had EBP and 41 (66.11%) had HT.

Table III: BP load and dipping status in patients

	Normal (n=57)	EBP (n=18)	HT (n=114)	p [†]
Day systolic BP load*				
<25%	33 (57.9)	10 (55.6)	37 (32.5)	0.003
≥25%	24 (42.1)	8(44.4)	77 (67.5)	
Day diastolic BP load*				
<25%	52 (91.2)	16 (88.9)	57 (50)	<0.001
≥25%	5 (8.8%)	2 (11.1)	57 (50)	
Night systolic BP load*				
<25%	31 (54.4)	7 (38.9)	17 (14.9)	<0.001
≥25%	26 (45.6)	11 (61.1)	97 (85.1)	
Night diastolic BP load*				
<25%	56 (98.2)	14 (77.8)	59 (51.8)	<0.001
≥25%	1 (1.8)	4 (22.2) ^b	55 (48.2)	
Systolic BP dipping*				
<10%	31 (54.4)	14 (77.8)	80 (70.2)	0.066
≥10%	26 (45.6%)	4 (22.2)	34 (29.8)	
Diastolic BP dipping*				
<10%	15 (26.3)	7 (38.9)	57 (50)	0.011
≥10%	42 (73.7)	11 (61.1)	57 (50)	

*: n (%), †: Chi-square Test, **BP**: Blood pressure, **EBP**: Elevated blood pressure, **HT**: Hypertension, **SD**: Standard deviation

Among 189 subjects, 57 (30.20%) were normotensive, 18 (9.50%) had EBP and 114 (60.30%) were classified as hypertensive based on ABPM SD scores. Gender, height, weight and BMI SD scores were not different between these groups. No statistically significant difference was found among the groups in terms of proteinuria, serum creatinine level, renal length SD scores and findings of doppler ultrasound (Table I).

Systolic and diastolic nocturnal dipping were significantly lower in patients with HT when compared to EBP and normotensive group [(5.90% (3.17-11.15) vs 7.70% (5.17-9.50) and 9.40% (6.80-13.05) p<0.001 for systole, 10.15% (3.25-15.94) vs 13.20% (6.30-16.02) and 15.90% (9.75-19.05) p<0.001 for diastole, respectively)]. ABPM SD scores, BP load and dipping status were presented in Table II. Nevertheless; the incidence of having inadequate systolic nocturnal dip was not statistically different between normotensive, EBP and hypertensive groups (Table III).

Among 57 patients in whom hypertension was not detected according to ABPM measurements, there were three patients with autosomal dominant polycystic kidney disease (ADPKD), one with familial mediterranean fever (FMF), one autosomal recessive polycystic kidney disease (ARPKD), one Williams Syndrome, one Alport Syndrome, one nephrotic syndrome, one ureteropelvic junction (UPJ) obstruction and one patient with double renal artery. Of the remaining 47 healthy children; 11 (23.40%) had both systolic and diastolic nocturnal nondipping, 11 (23.40%) had only systolic nondipping and two patients (4.20%) were found to have nocturnal nondipping only in diastole. Thirteen of these 47 children (27.60%) were asymptomatic and underwent on ABPM due to high office BP measurements.

Of the 114 patients whose diagnosis of hypertension was clarified based on ABPM SD scores; four patients had ADPKD, four had chronic kidney disease (CKD), three had double renal artery, three FMF, two UPJ obstruction, two neurogenic bladder, one coarctation of aorta, one neurofibromatosis, one renal artery stenosis, one

horseshoe kidney, one Williams Syndrome, one systemic lupus erythematosus and one patient had ureterovesical junction obstruction. In the remaining 88 subjects, the ratio of having both systolic and diastolic nocturnal nondipping was 46.60% (41 patients), systolic nondipping was 26.10% (23 patients) and diastolic nondipping was 3.40% (three patients).

In the present study, the incidence of masked and white coat HT was 1.05% (two patients) and 11.11% (21 patients), respectively.

DISCUSSION

Although the effective role of ABPM for predicting cardiovascular complications in adults has been previously demonstrated, comparative studies including pediatric data are scarce due to low incidence of mortality and cardiovascular events in children. There have been limited pediatric reports indicating that high BP and BP load cause LVH and increased cIMT (12-15). In a study of 77 patients aged five to 19 years, 27 of whom were classified as non dippers; Bakhoun et al. (16) reported that they have developed more significant LVH than dippers. Moreover; obesity, obstructive sleep apnea, proteinuria and CKD have been described to be associated with blunted nocturnal dipping.

In a retrospective study including 408 subjects aged 5-21 years; Macumber et al. (17) have reported that both systolic and diastolic dipping were significantly blunted in obese group. Although the patients with CKD, congenital heart disease, prematurity, sleep disorders and medication use were not included in their study, the incidence of nocturnal non dipping was approximately 14% in 22 of 161 non-obese patients (17). In our overall study group, systolic and diastolic non dipping were calculated as 66.10% and 41.71% respectively. Although no statistical significant difference was detected leading to blunted nocturnal dip, the frequency of systolic nondipping was similar between patients with normotension, EBP

and hypertension. Moreover, abnormal nocturnal dip in systolic or diastolic blood pressure was found in 51% of 47 patients, who were classified as normotensive according to ABPM results and who did not have any underlying disease. This rate was also higher when compared to the report by Seeman et al. (18) revealing 30% nocturnal nondipping in 20 normotensive patients.

Some previous studies have revealed that nocturnal dipping status was not found to be significantly associated with LVH (19). Conversely, Szyszka et al. (20) has demonstrated higher LVMI in 50 non dipper patients when compared to 33 dipper patients. In adults, abnormal dipping status was associated with worsening kidney functions, development of CKD and increased cardiovascular morbidity (21-24). Although cardiac assessment could not be performed in the present study due to its retrospective design, it is crucial to evaluate and follow the patients with nocturnal non dipping despite being normotensive on ABPM, considering the previously reported consequences of inadequate nocturnal blood pressure fall on cardiovascular functions.

In spite of the low prevalence of WCH (0.60-1.20%) in the general pediatric population, it has been reported to be higher especially in patients referred for high office BP evaluation. In one study conducted in patients between the ages of 10 and 17 years; 54 of 174 (31%) patients had been diagnosed as having WCH, whereas another cohort with a mean age of 13.3 years has revealed its frequency as 52% (25-27). Inconsistently; we found a lower incidence of WCH in our patient groups. We also detected a lower frequency of masked hypertension; which has been demonstrated to have close relationship with increased cardiovascular morbidity (25-30). The fact that it has been usually associated with chronic kidney disease, obesity or coarctation of aorta; low number of patients having such an underlying disease might have been the reason for low MH ratio in the study sample.

The limitations of our study are the small number of patients with CKD or renal anomalies and the lack of assessments like cIMT and LVMI predicting the development of cardiovascular disease in the study protocol due to its retrospective design.

In conclusion, ABPM is now the most preferred method for correct diagnosis of childhood HT. The increasing frequency of hypertension in pediatric population should not be ignored particularly in healthy adolescents. To prevent the development of cardiovascular and renal diseases especially in non dippers; the diagnosis should be clarified by attaching ABPM for high office BP measurements under optimal environmental conditions and with appropriate cuff size.

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