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Original Article

The evaluation of arterial stiffness of essential hypertension and white coat hypertension in children: a case-control study

Semiha Terlemez Tokgöz,[1] Dilek Yılmaz,[2] Yavuz Tokgöz,[3] Bülent Çelik,[4] Yasin Bulut[5]

[1]*Pediatric Cardiology Department, Medicine Faculty;* [2]*Department of Pediatric Nephrology;* [3]*Department of Pediatric, Adnan Menderes University, Aydın;* [4]*Faculty Statistics, Gazi University Chemistry, Ankara;* [5]*Department of Pediatric, Adnan Menderes University, Aydın, Turkey*

Abstract *Background:* The aim of this study was to determine and compare cardiovascular risks by assessing arterial stiffness in children with essential hypertension and white coat hypertension. *Methods:* Paediatric patients followed up with essential hypertension and white coat hypertension diagnoses and with no established end organ damage were involved in the study. Arterial stiffness in children included in the study was evaluated and compared by using the oscillometric device (Mobil-O-Graph) method. *Results:* A total of 62 essential hypertension (34 male, 28 female), 38 white coat hypertension (21 male, 17 female), and 60 healthy controls (33 male, 27 female) were assessed in the present study. Pulse wave velocity of the essential hypertension, white coat hypertension, and control group was, respectively, as follows: 5.3 ± 0.6 (m/s), 5.1 ± 0.4 (m/s), 4.3 ± 0.4 (m/s) ($p < 0.001$); augmentation index outcomes were, respectively, determined as follows: 21.3 ± 6.5, 19.3 ± 6.4, 16.0 ± 0.3 ($p < 0.001$). Pulse wave velocity and augmentation index values of children with essential hypertension and white coat hypertension were found to be higher compared with the control group. This level was identified as correlated with the duration of hypertension in both patient groups ($p < 0.01$). *Conclusion:* Arterial stiffness in children with essential hypertension and white coat hypertension was impaired compared with healthy children. This finding has made us think that white coat hypertension is not an innocent clinical situation. This information should be taken into consideration in the follow-up and treatment approaches of the patients.

Keywords: Essential hypertension; white coat hypertension; arterial stiffness

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Background

Hypertension is a health problem more common in adults than in children. Hypertension complaints observed in childhood are mostly seen with secondary reasons until adolescence. Essential hypertension beginning from adolescence is the most common reason of hypertension in children.[1,2] In recent years, there has been a rapid increase in the frequency of essential hypertension at adolescence and young adult age.[3] This increase has been first and foremost linked to life style, dietary habits, and familial factors.[4]

White coat hypertension is defined as tension values to be detected within normal limits in a daily life of patient, though they are high when measured in a hospital setting or by healthcare professionals. The clinical importance and prognosis of white coat hypertension still remains questions of debate. It has been shown in recent studies that white coat hypertension leads to cardiovascular changes[5–7] and they are slightly effective on mortality and morbidity of cardiovascular diseases.[8–10] However, this effect has not been found to be as high and apparent as essential hypertension.[8] It has been discussed whether white coat hypertension is treated or not; nevertheless, it has been considered that there is no adequate data for white coat hypertension to be cured.[11] White coat hypertension has still been

Correspondence to: S. Terlemez Tokgöz, Pediatric Cardiology Department, Medicine Faculty, Adnan Menderes University, 09100 Aydın, Turkey. Tel: +90 532 721 76 89; Fax: +90 2564122573; E-mail: semihaterlemez@yahoo.com

approved to a clinical situation that does not require treatment but follow-up.

Hypertension is one of the most important risk factors that increase cardiovascular disease risk. Its mortality and morbidity emerge with the development of cardiovascular diseases. Arterial stiffness is a reliable method used to identify cardiovascular disease risk. The aim of this study was to identify and compare cardiovascular disease risks in children with essential hypertension and white coat hypertension and compare them with a sample of healthy children by using the oscillometric method.

Methods

Study group

Patients followed up with white coat hypertension and essential hypertension at Adnan Menderes University Pediatric Cardiology and Nephrology policlinics were included in the study. Patients who were referred to the paediatric cardiology polyclinic with various causes (murmur, chest pain, palpitation, etc.) and with no cardiac pathology detected were included as a healthy control group.

Essential hypertension is defined that at least three blood pressure measurements during examination were determined as ⩾95th percentile according to age, sex, and height. White coat hypertension was accepted that ambulatory blood pressure measurements are established as <95th percentile in patients whose blood pressure is identified as ⩾95th during examination. 2016 CHEP Pediatric Hypertension Guidelines are approved in definitions.[12]

Weight, height, and body mass index measurements of patients were carried out along with their physical examination. Of the patients with essential hypertension, those with end organ involvement – hypertensive ophthalmological findings, nephropathy, myocardial hypertrophy, etc. – and those on medication were not involved in the study. Proteinuria was assessed in 24-hour urine of all patients when hypertensive nephropathy was evaluated in patients. In addition, all patients with hypertension were evaluated with renal Doppler USG in order to exclude renal artery stenosis in the aetiology of hypertension, as patients were in the age group. Patients with renal artery stenosis at the site where nephropathy is detected were excluded from the study. The patients with other diseases – hyperlipidemia, obesity, diabetes, etc. – known to form a risk factor for cardiovascular diseases were excluded from the study. Results were evaluated by attaching an oscillometric device (Mobil-O-Graph, I.E.M., Stolberg, Germany) to patients with essential hypertension, white coat hypertension, and healthy children who were similar in number, and matched for age and sex. In both groups, the time interval between the patients' hypertension diagnosis and study evaluations was accepted as hypertension duration.

Pulse wave analysis measurement. In recent years, automated oscillometric device (Mobil-O-Graph) has been accepted as a reliable tool for assessing arterial stiffness.[13–16] Pulse wave analysis estimates the shape and amplitude of aortic pulse wave. Pulse wave velocity obtained from parameters and augmentation index (Alx@75) is associated with aortic systolic blood pressure. Pulse wave velocity shows the speed of advance of the pulse in the aorta. Its unit is meter/second (m/s). When atherosclerosis increases, a raise in Alx@75 values is determined. Mobil-O-Graph device presents these parameters in conjunction with 24-hour ambulatory blood pressure values simultaneously.

Peripheral blood pressure – peripheral systolic/diastolic blood pressure, central blood pressure – central systolic/diastolic, mean arterial pressure – mean aortic pressure, pulse wave velocity, and augmentation index were measured by using an automatic oscillometric device – by measuring brachial wave form with Mobil-O-Graph. The reliability of Mobil-O-Graph with invasive measurements[17] and, in addition, its calibration superiority over other devices were shown.[18] Mobil-O-Graph device was attached to patients in the morning hours and patients continued their daily activities during the 24-hour registration. The records were transferred by removing the device after 24 hours.

Statistical analysis

All statistical analyses were performed using The Statistical Package for Social Sciences, Version 15.0 (SPSS, Inc., Chicago, Illinois, United States of America). Data were presented as number of cases, mean, and standard deviation. Categorical comparisons were performed by using the χ^2 test. Whether the distributions of continuous variables were normal or not was determined by using Kolmogorov–Smirnov or Saphiro–Wilk test. The differences between two independent groups were compared by using independent sample t-test for normal distributions or Mann–Whitney U-test for non-normal distributions. The differences between three independent groups were compared by using one-way ANOVA with Tukey test for normal distributions or Kruskal–Wallis H-test with Bonferroni adjusted Mann–Whitney U-test for non-normal distributions. Correlation coefficients (r) were calculated using the Pearson correlation. Multiple regression analyses were performed to identify variables that affect pulse wave velocity and Alx@75 values. A two-sided p-value < 0.05 was considered statistically significant for all analyses.

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Results

The present study included 62 essential hypertension (34 male, 28 female), 38 white coat hypertension patients (21 male, 17 female), and 60 healthy controls (33 male, 27 female). The age of the patients with essential hypertension was 13.3 ± 3.0 years (9.7–16.8 years), with white coat hypertension was 13.5 ± 2.3 (10.2–17 years), and for the control group was 14.1 ± 2.6 (10.6–16.9 years). The demographical data of patients are presented in Table 1. There was no statistically significant difference between weight, height, age, and body mass index for the three groups (Table 1). Essential hypertension history in family was found significantly higher in the two patient groups with white coat hypertension and essential hypertension compared with the healthy control group ($p = 0.003$). Coronary artery disease history in family was not identified statistically different in the two patient groups and the healthy control group (Table 2).

When oscillometric device results were evaluated, it was observed that peripheral systolic blood pressure value was higher compared with the patients with essential hypertension ($p < 0.001$); mean aortic pressure, pulse wave velocity, and augmentation index values were higher in patients with essential hypertension and white coat hypertension compared with the controls ($p < 0.001$, Table 3).

Table 1. The demographic data of the patients and the control group.

Variables	EHT (n = 62)	WCH (n = 38)	Control (n = 60)	p Value
Age (year)	13.3 ± 3.0	13.5 ± 2.3	14.1 ± 2.6	0.397
Weight (kg)	51.4 ± 16.6	54.1 ± 15.4	53.9 ± 13.4	0.571
Height (cm)	153.4 ± 17.6	154.7 ± 19.4	157.5 ± 13.0	0.636
BMI (kg/m^2)	21.1 ± 3.8	22.7 ± 5.6	21.4 ± 3.8	0.393
HT time (month)	24.3 ± 12.2	22.1 ± 8.6		0.546

BMI = body mass index; EHT = essential hypertension; HT = hypertension; WCH = white coat hypertension

Table 2. Family history for coronary artery disease (CAD) and essential hypertension (EHT).

Variables	EHT (n = 62) (%)	WCH (n = 38) (%)	Control (n = 60) (%)	p Value
Gender				
Male	34 (54.8)	21 (55.3)	27 (45)	0.472
Female	28 (45.2)	17 (44.7)	33 (55)	
EHT in families	25 (40.3)	19 (50.0)	11 (18.3)	0.003*
CAD in families	17 (27.4)	7 (18.4)	7 (11.7)	0.087

WCH = white coat hypertension
*Control versus EHT and WCH

The connection of pulse wave velocity and augmentation index values with other parameters was assessed by using multiple regression analyses. Pulse wave velocity values were found to be linked with central systolic pressure, central diastolic pressure, central diastolic pressure, systolic blood pressure, and hypertension time. Augmentation index value, however, was found to be related to central systolic pressure, central diastolic pressure and mean aortic pressure (Tables 4 and 5). Pulse wave velocity values in patients

Table 3. Ossilometric device analysis.

Variables	EHT	WCH	Control	p Value
pSBP	118.3 ± 10.9	114.2 ± 6.9	110.7 ± 8.8	<0.001*
pDBP	77.7 ± 9.0	68.8 ± 5.9	69.2 ± 6.2	0.341
MAP	91.2 ± 9.8	88.8 ± 5.9	80.0 ± 6.5	0.013**
cSBP	104.4 ± 10.5	103.2 ± 6.2	101.4 ± 7.1	0.144
cDBP	71.3 ± 8.3	70.2 ± 5.8	70.2 ± 5.7	0.583
Pulse	83.4 ± 11.1	81.4 ± 8.1	82.8 ± 9.1	0.588
CO (I/DK)	4.8 ± 0.5	5.0 ± 0.4	4.9 ± 0.5	0.301
PWV (m/s)	5.3 ± 0.6	5.1 ± 0.4	4.3 ± 0.4	<0.001**
Alx@75	21.3 ± 6.5	19.3 ± 6.4	16.0 ± 4.3	<0.001**

Alx@75 = augmentation index; cDBP = central diastolic blood pressure; CO = cardiac output; cSBP = central systolic blood pressure; EHT = essential hypertension; MAP = mean arterial pressure; pDBP = peripheral diastolic blood pressure; pSBP = peripheral systolic blood pressure; PWV = pulse wave velocity; WCH = white coat hypertension
*EHT versus control
**Control versus EHT and WCH

Table 4. Result of multiple regression analysis pulse wave velocity in hypertension and white coat hypertension group.

Variable	B coefficients (95% CI)	p Value
Constant	3.719 (2.632; 4.806)	<0.001
HT time (month)	0.027 (0.019; 0.035)	<0.001
MAP	0.014 (0.0192; 0.0042)	<0.001
cDBP	0.032 (0.019; 0.043)	<0.001
cSBP	0.012 (0.018; 0.036)	<0.001
pSBP	0.020 (0.010; 0.030)	<0.001

cDBP = central diastolic blood pressure; cSBP = central systolic blood pressure; MAP = mean arterial pressure; pSBP = peripheral systolic blood pressure; PWV = pulse wave velocity
Adjusted R^2 for the model: 0.465

Table 5. Result of multiple regression analysis augmentation index (Alx@75) in hypertension and white coat hypertension group.

Variable	B coefficients (95% CI)	p Value
Constant	1.432 (−8.317; 11.181)	0.771
MAP	−6.912 (−8.324; −5.501)	<0.001
cDBP	0.306 (0.209; 0.403)	<0.001
cSBP	0.375 (0.305; 0.444)	<0.001

cDBP = central diastolic blood pressure; cSBP = central systolic blood pressure; MAP = mean arterial pressure
Adjusted R^2 for the model: 0.722

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Table 6. PWV and Augmentation index (Alx@75) values correlations with other parameters.

	EHT		WCH		Control	
	PWV (m/s)	Alx@75	PWV (m/s)	Alx@75	PWV (m/s)	Alx@75
Age (year)	0.091	−0.297*	0.138	−0.246	0.255*	−0.229
BMI (kg/m^2)	0.032	−0.215	0.110	−0.318	0.126	−0.134
HT time (month)	0.608**	0.159	0.653**	−0.059		
pSBP	0.368**	−0.081	0.062	0.199	0.016	0.255*
pDBP	0.293*	0.222	0.149	0.481**	0.207	0.119
MAP	0.442*	0.324*	0.409*	0.459**	0.286*	0.203
cSBP	0.292*	−0.054	0.195	0.086	0.137	0.160
cDBP	0.250	0.228	0.146	0.479**	0.114	0.207

BMI = body mass index; cDBP = central diastolic blood pressure; cSBP = central systolic blood pressure; EHT = essential hypertension; HT = hypertension; MAP = mean arterial pressure; pDBP = peripheral diastolic blood pressure; pSBP = peripheral systolic blood pressure; PWV = pulse wave velocity; WCH = white coat hypertension
*p < 0.05; **p <0.01

with essential hypertension were determined, which had a correlation with hypertension time and many blood pressure value – mostly with systolic blood pressure. Pulse wave velocity values in patients with white coat hypertension were found to be correlated with hypertension time. Augmentation index values were correlated with mean aortic pressure, peripheral diastolic pressure, central diastolic pressure values (Table 6).

Discussion

Essential hypertension prevalence commencing at childhood (2%)[19] is quite low[20] compared with the adult ages (30%). Although essential hypertension is a multifactorial disease, genetic factors are seen to be more apparent in children.[21] The results of our study supported this information as well. Essential hypertension history in families of patients with both essential hypertension and white coat hypertension was found significantly higher compared with the control group.

It is important to note that both white coat hypertension and essential hypertension have been gradually seen with a growing rate during childhood.[2–4] The significance of revealing cardiovascular risk in these patients in an early period has progressively increased. Arterial stiffness is a trustworthy method used in the determination of cardiovascular disease risk. Thanks to the evaluation of arterial stiffness in patients with essential hypertension, much information related to cardiovascular disease risks was revealed.[22–24] Nonetheless, there a large number of studies involving children have been carried out. In once such study conducted by Liu et al, arterial stiffness was assessed in hypertensive children and no significant difference was determined compared with the control group.[25] Stergiou et al, on the other hand, established pulse wave velocity values higher in children with hypertensive compared with the control group.[26] We determined that arterial stiffness was impaired even in the subclinical period in children with essential hypertension but there was no end organ damage compared with healthy children. Automated oscillometric device (Mobil-O-Graph), which has been used in recent years, has been accepted as a reliable method for assessing arterial stiffness.[13–16] We reviewed our patients with this method as distinct from other studies.

One of the most substantial issues of recent years is whether white coat hypertension increases cardiovascular disease risk or not, and thus, is there a need for treatment in these patients or not. End organ involvement in patients with white coat hypertension is not an expected finding, and no medical treatment is usually used in the follow-up of these patients. Therefore, we wanted to compare patients with essential hypertension showing similar clinical findings – namely with no determined end organ damage – and patients with white coat hypertension. There are studies indicating that white coat hypertension leads to cardiovascular changes.[5–7] Tientcheu et al showed that white coat hypertension is associated with arterial stiffness and end organ damage in adult ages.[9] Wojciechowska et al evaluated subclinical end organ involvement and arterial stiffness in patients with constant hypertension and white coat hypertension, and reported that there was a cardiovascular end organ involvement in patients with white coat hypertension.[27] All these studies were performed in adult patients. We determined that white coat hypertension affected arterial stiffness even in childhood. This result shows that white coat hypertension leads to cardiovascular changes from very early periods. Our study made us think that, white coat hypertension is not an innocent

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condition as it is thought, and therefore more attention should be paid in the follow-up of patients. The findings of our study, together with those of other similar studies, may bring forward treatment necessity in the follow-up of patients with white coat hypertension.

Pulse wave velocity, an indicator of arterial stiffness and augmentation index values were identified in approximate values in patients with essential hypertension and white coat hypertension ($p = 0.52$). Nevertheless, pulse wave velocity and augmentation index values were shown to be higher in both patients with essential hypertension and white coat hypertension compared with the healthy control group. The elevations in these values were, as expected, found to be associated with hypertension duration and most central and peripheral blood pressure measurements. However, pulse wave velocity values were seen to have a high correlation with hypertension in both patient groups. Hypertension durations and pulse wave velocity values were similar in both patient groups. This result was perplexing as hypertension is expected to be non-continuous in these patients. Hypertension durations indicated in our study display elapsed period from the diagnoses of patients. However, elapsed duration before diagnosis can also be affecting the results. Another possibility is that the effect of hypertension on vascular changes in patients with white coat hypertension may not be different from that of continuous hypertension.

Conclusion

At an early age when end organ damage has not been detected, arterial stiffness was impaired in children with white coat hypertension and essential hypertension compared with healthy children. This finding has made us think that white coat hypertension is not an innocent clinical situation. This information should be taken into consideration in the follow-up and treatment approaches of patients.

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Authors' Contributions

Study design: S.T.T., D.Y. Data analyses: S.T.T., B.Ç., Y.T., and Y.B. Writing the first draft: S.T.T., D.Y. Data interpretation, discussion, and preparation of the final manuscript: S.T., Y.T. All authors read and approved the final manuscript.

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Conflicts of Interest

None.

Ethical Standard

The study was carried out by obtaining Adnan Menderes University Ethics Committee Approval (approval date/num :2016/942) and all participants gave their informed and written consent to participate.

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