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Original Article

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Hypertension in Children with Unilateral Multicystic Dysplastic Kidney: A Common but Rarely Diagnosed Condition

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ABSTRACT

Objective: In this study, we aimed to determine the frequency of hypertension by performing 24 hours ambulatory blood pressure monitoring in children with unilateral multi-cystic disease of kidney without ipsilateral and/or contralateral kidney and/or urinary system anomalies.

Methods: This study enrolled 24 patients with unilateral multi-cystic disease of kidney and age- and height-matched 20 healthy children. Blood pressure was measured by 2 approaches as follows: manual blood pressure and ambulatory blood pressure monitoring. Day-time, night-time, and 24 hours heart rate, pulse pressure, systolic and diastolic blood pressure, median arterial pressure, and systolic and diastolic blood pressure loads (%) were compared.

Results: Ambulatory blood pressure monitoring measurements showed the presence of masked hypertension in 12 patients (45.8%), although 2 (8.3%) unilateral multi-cystic disease of kidney patients were hypertensive with manual blood pressure measurements. We detected that systolic blood pressure loads (%) (day-time, night-time, and 24 hours) and disatolic blood pressure loads (%) (night-time and 24 hours) were considerably higher than those of healthy children ($P = .030$, $P = .012$, $P = .005$, $P = .012$ and $P = .005$, respectively).

Conclusion: Children with unilateral multi-cystic disease of kidney are more likely to have masked hypertension. Manual blood pressure measurements are not accurate in ruling out hypertension in children with unilateral multi-cystic disease of kidney. Ambulatory blood pressure monitoring contributes to more susceptible outcomes in proportion to manual blood pressure measurement in these patients, and it should be considered in clinical practice instead of manual blood pressure measurements.

Keywords: Ambulatory blood pressure monitoring, children, masked hypertension, multi-cystic kidney disease

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INTRODUCTION

The unilateral multicystic-dysplastic disease of kidney (UMCDK) is disease that is one of the most frequent congenital, non-familial kidney anomaly, and its prevalence has increased in the time of antenatal ultrasonography (US).[1,2] The presence of opposite kidney anomaly or extra-kidney abnormalities and complications are the determinants of the clinical course of UMCDK.[3,4] It has long been believed that the long-term clinical course of UMCDK is completely benign until a recent study suggested that arterial hypertension (HTN) is a likely problem of UMCDK.[5] The frequency of HTN in children with UMCDK was reported as 5.4 per 1000 in a systematic review.[4] Although real prevalence is doubtful, studies revealed quite low ratios of HTN varying from 0.5% to 5.9%.[4,6-11] Recent studies showed that those with an abnormality in the opposite kidney had a higher risk of HTN.[12]

According to the hyperfiltration hypothesis, a functioning single kidney may cause glomerular damage due to HTN and albuminuria, and this process may progress to

end-stage kidney disease.[12,13] However, the information about the effects of UMCDK on blood pressure (BP) and kidney function is still uncertain.

The home or office auscultatory BP method is the most commonly used method to diagnose HTN in normal clinical practice in children with impaired kidney function. However, in recent years, ambulatory blood pressure monitoring (ABPM), an oscillometric method, has been used more widely to control the BP profile in these children.[14,15] It is speculated that the frequency of HTN might have been underestimated in the last few years' studies because BP was not the primary concern, and it was only measured auscultatory in all of those studies.[4,6-11]

There are few studies[16-20] about ABPM in patients with solitary kidney along with UMCDK, and they state that prevalence rates of HTN in these patients were higher than those of the other studies in which BP was measured only auscultatory.[4,6-11] The present study aims to investigate the real prevalence of HTN by measuring BP profile with ABPM in children with UMCDK.

METHODS

Medical reports of 118 patients with UMCDK followed at the Paediatric Nephrology outpatient clinic of İnönü University between 2006 and 2020 were evaluated. Age, age at diagnosis, presence or absence of HTN examined using manual method, follow-up duration, sex, weight, height, body mass index (BMI), type of kidney, parental status, and additional anomalies detected by imaging method were noted. Hypertension was defined as the height-adjusted average systolic BP and/or diastolic BP (SBP and/or DBP) above the 95th percentile according to age and gender.[21] Laboratory parameters, including blood urea nitrogen (BUN), serum creatinine, and uric acid levels, were also recorded. Unilateral multicystic-dysplastic disease of kidney was diagnosed by the presence of non-contagious multidimensional cysts of fluctuating size with no kidney parenchyma on the kidney US. The diagnosis was also made using Tc-99 m dimercaptosuccinic acid scintigraphy, which showed whether there was kidney damage in the contralateral intact kidney and the absence of parenchyma in the kidney with MCDK. Voiding cystourethrogram was performed in patients with additional anomalies in contralateral kidney in US.

MAIN POINTS

- The unilateral multicystic-dysplastic disease of kidney (UMCDK) is disease that is one of the most frequent congenital, non-familial kidney anomalies.
- There are few studies about ambulatory blood pressure monitorization (ABPM) in these patients.
- We found that 1 in every 2 children had hypertension (HTN) monitored based on the ABPM method though the majority of these subjects were not considered as HTN according to auscultatory BP method.

Inclusion and Exclusion Criteria

Children older than 5 years and/or taller than 120 cm diagnosed with UMCDK without ipsilateral and/or contralateral kidney and/or urinary system anomalies such as ectopic ureter, ureterocele, hydronephrosis, ureteropelvic, or ureterovesical junction obstruction, kidney scarring, and VUR; history of previous recurrent urinary tract infection (UTI), HTN, or antihypertensive agent treatment; and who had been regularly followed up were included in this study. Bilateral UMCDK patients, other cystic kidney illnesses like polycystic kidney disease patients, those patients who underwent nephrectomy in the course of the follow-up period (not for HTN), and obese patients were not included in this study.

In conclusion, 24 children with UMCDK and 20 healthy children of similar age, weight, and height with normal kidney US findings were included in this study. Parents of the healthy children had no indication of HTN, and kidney US results of those children were normal. All patients and controls had a normal kidney function (glomerular filtration rate was over 90 mL/min/1.73 m^2 calculated by Schwartz formula).[22]

The procedures were performed according to the Declaration of Helsinki for the ethical standard for human experiments. Our study was approved by the Ethics Committee of our University (approval date and no: November 07, 2017—2017/298), and a written consent form was given by the parents before participating in this study.

Study Design

Auscultatory SBP and DBP were evaluated 3 times after a 15-minute rest at each control, and the average of all 3 measurements was used. Clinical visit BP readings were stable over multiple visits. For the ABPM assessment, Mobil O'Graph NG called oscillometric device (Numed Healthcare^R, Sheffield, UK) was used, and BP measurement was performed over 24 hours. A cuff with a suitable size selected according to the upper arm circumference was placed in the non-leading arm, and BP measurements were performed automatically every 20 minutes throughout the day-time (DT) and every 30 minutes over the night-time (NT). If at least 60% of the measurements were not valid and correct, they were repeated. Ambulatory blood pressure monitoring profile was based on DT, NT, and 24 hours records, such as heart rates (HR) (beats/min), pulse pressures (PP) (beats/min), SBP and DBP (mmHg) (office and ambulatory BP), median arterial pressures (MAP) (mmHg), SBP and DBP loads (%) adapted to sleep patterns, and activities while awake in each child's diary. In addition, standard deviation score (SDS) for 24 hours, DT, and NT SBP and DBP were calculated by using the European reference standards published by Wühl et al.[23] Hypertension determination was made according to European guidelines: this guideline takes into account the average 24 hours awake and sleep BP measurements.[21] Blood pressure load (%) was defined as what percentage of BP values exceeded the values above the 95th percentile for age, gender,

height, and selected day part. Those with a BP load (%) of more than 25% were defined as HTN.[23] The dipping status (systolic and/or diastolic) was evaluated by subtracting DT BP from NT BP and dividing this value by DT BP. Dipping was described as a ≥10% reduction in SBP and DBP figures between DT and NT.[21]

Statistical Analysis

The data were assessed using the Statistical Package for the Social Sciences software 16.0 (IBM Inc, Chicago, IL, USA). The assessment of normality was determined by the Shapiro–Wilk test. The outcomes were stated as mean ± standard deviation or median (with inter-quartile range) for quantitative data. Differences between the groups were evaluated using the unpaired *t* test or Mann–Whitney *U* test. The categorical variables in the proportions were examined using the chi-square test or Fisher's exact test. A *P*-value <.05 was considered statistically significant.

RESULTS

The study group included 24 UMCDK patients (9 boys and 15 girls) and 20 healthy children (9 boys and 11 girls) as controls. There was no significant difference between the UMCDK patients and healthy children regarding gender, age, weight, height, and BMI ($P > .05$ for each). Likewise, there was no difference between BUN, serum creatinine, and uric acid levels of UMCDK patients and the control group ($P > .05$ for each). Two UMCDK patients (8.3%) had HTN detected according to auscultatory BP method; however, ABPM computation revealed HTN in 11 patients (45.8%). Hypertension was detected in 5 of 20 healthy children who had auscultatory BP method, but ABPM outcomes of these children were normal and evaluated as white coat HTN. Two HTN patients detected by auscultatory method were also hypertensive by ABPM. Non-dipping HTN was detected in 7 of 11 hypertensive patients, with systolic non-dipping in 5 patients and both systolic and diastolic non-dipping HTN in 2 patients. We did not find any significant difference between patients and controls for auscultatory BP method ($P = .217$). The characteristics of UMCDK patients and healthy children are summarized in Table 1.

Although DT, NT, and 24 hours HR, PP, MAP, SBP, and DBP values were higher than healthy children, this height was not statistically significant ($P > .05$ for each); however, SBP loads (%)

Table 1. Clinical and Laboratory Data of the Patients with UMCDK and Controls

	UMCDK Patients (n = 24)	Controls (n = 20)	*P*
Gender (M/F)	9/15	9/11	.760
Age (year)	9.7 ± 2.9	10.9 ± 2.2	.146
Weight (kg)	32.1 ± 12.0	36.5 ± 14.1	.278
Height (cm)	134.9 ± 16.9	139.5 ± 17.5	.388
BMI (kg/m^2)	17.2 ± 2.9	17.9 ± 3.5	.510
BUN (mg/dL)	11.2 ± 2.5	11.5 ± 4.5	.828
SCr (mg/dL)	0.55 ± 0.1	0.53 ± 0.1	.619
Uric acid (mg/dL)	3.9 ± 1.2	3.2 ± 1.1	.120
Hypertension			
Auscultatory BP (n, %)	2 (8.3)	5 (25.0)	.217
ABPM (n, %)	11 (45.8)	0 (0)	**.0001**

Values are expressed as mean ± standard deviation or proportion. *P* value is for comparison between control and UMCDK patients. $P < .05$ is significant.
M, male; F, female; UMCDK, unilateral multi-cystic disease of kidney; BMI, body mass index; BUN, blood urea nitrogen; SCr, serum creatinine; BP, blood pressure; ABPM, ambulatory blood pressure monitoring.

Table 2. ABPM Parameters of the Patients with UMCDK and Controls

ABPM Parameters	UMCDK Patients (n = 24)	Controls (n = 20)	*P*
Office SBP (mmHg)	113.0 ± 10.0	115.7 ± 12.9	.438
Office DBP (mmHg)	69.8 ± 8.2	66.1 ± 8.9	.159
24 hours MAP (mmHg)	84.2 ± 6.9	82.7 ± 5.7	.594
24 hours SBP (mmHg)	108.6 ± 9.4	106.7 ± 6.4	.561
24 hours DBP (mmHg)	63.4 ± 5.8	61.6 ± 5.3	.416
24 hours PP (beats/min)	45.2 ± 7.2	44.1 ± 4.5	.577
24 hours HR (beats/min)	84.6 ± 9.6	81.6 ± 7.3	.416
DT MAP (mmHg)	86.0 ± 6.8	84.9 ± 5.9	.669
DT SBP (mmHg)	110.9 ± 9.1	108.7 ± 6.5	.449
DT DBP (mmHg)	65.4 ± 6.3	64.4 ± 6.3	.692
DT PP (beats/min)	45.5 ± 6.9	44.2 ± 4.7	.517
DT HR (beats/min)	88.9 ± 10.2	85.4 ± 7.0	.293
NT MAP (mmHg)	78.9 ± 7.2	75.8 ± 4.4	.112
NT SBP (mmHg)	103.3 ± 10.6	99.5 ± 5.2	.157
NT DBP (mmHg)	58.2 ± 5.6	55.5 ± 4.4	.105
NT PP (beats/min)	44.8 ± 7.9	43.7 ± 4.7	.617
NT HR (beats/min)	74.8 ± 9.4	69.9 ± 8.5	.084
24 hours SBP load (%)	7.0 (18.0-40.0)	5.5 (0.0-16.0)	**.005**
24 hours DBP load (%)	18.0 (7.0-33.2)	3.5 (0.0-18.0)	**.005**
DT SBP load (%)	17.5 (5.75-39.5)	7.0 (0.0-19.5)	**.030**
DT DBP load (%)	10.0 (0.5-19.5)	2.5 (0.0-21.2)	.276
NT SBP load (%)	32.0 (15.0-58.7)	15.5 (0.0-31.5)	**.012**
NT DBP load (%)	20.5 (6.2-31.5)	4.5 (0.0-18.0)	**.012**

Values are expressed as mean ± standard deviation or median (with inter-quartile range). *P* value is for comparison between control and UMCDK patients (unpaired *t* test or Mann–Whitney *U* test), $P < .05$ is significant.
ABPM, ambulatory blood pressure monitoring; UMCDK, unilateral multi-cystic disease of kidney; DT, day-time; NT, night-time; HR, heart rates; PP, pulse pressure; MAP, median arterial pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure.

Table 3. Standard Deviation Score (SDS) Values of the Patients with UMCDK and Controls

Parameters	UMCDK Patients (n = 24)	Controls (n = 20)	*P*
24 hours SBP SDS	0.02 ± 1.2	−0.18 ± 0.8	.535
24 hours DBP SDS	−0.54 ± 1.1	−0.83 ± 0.9	.370
24 hours MAP SDS	0.84 ± 1.3	0.63 ± 1.0	.564
DT SBP SDS	−0.32 ± 1.1	−0.55 ± 0.8	.445
DT DBP SDS	−1.07 ± 0.9	−1.22 ± 1.0	.621
DT MAP SDS	0.15 ± 1.1	0.02 ± 1.0	.701
NT SBP SDS	0.68 ± 1.3	0.18 ± 0.5	.128
NT DBP SDS	0.48 ± 0.9	0.16 ± 0.8	.221
NT MAP SDS	1.39 ± 1.1	1.05 ± 0.5	.253

Values are expressed as mean ± SD. *P* value is for comparison between control and UMCDK patients (unpaired *t* test), $P < .05$ is significant.
DBP, diastolic blood pressure; DT, day-time; MAP, mean arterial pressure; NT, night-time; SDS, standard deviation score; SBP, systolic blood pressure; UMCDK, unilateral multi-cystic disease of kidney.

(DT, NT, and 24 hours) and DBP loads (%) (NT and 24 hours) of the patients were significantly higher than the control group ($P = .030$, $P = .012$, $P = .005$, $P = .012$, and $P = .005$, respectively). Ambulatory blood pressure monitoring parameters of the UMCDK patients and healthy children are listed in Table 2 and the SD of SBP, DBP, and MAP values is given in Table 3.

DISCUSSION

Most of the studies that determined BP figures only auscultatory pointed out that HTN was a rare complication in children who have UMCDK.[4,6-11] However, assessments based on auscultatory BP method did not determine the real prevalence of HTN in these children. Current studies[16-20] which used ABPM to look into the frequency of HTN in children with a solitary kidney, as well as UMCDK, disclosed that HTN was one of the most common health problems in these children. In addition, some studies[24,25] pointed out that the prevalence of HTN in these patients was underestimated, and these children got poor monitoring. Furthermore, it has been shown that ABPM was more sensitive than auscultatory BP method to detect real HTN prevalence.[14,15] It has been illustrated that the ABPM values had a better correlation with cardiovascular morbidity and mortality than auscultatory BP values obtained by auscultatory methods.[26] In our study, in accordance with the previous studies that used ABPM[16-20] showed that the prevalence of actual HTN (45.8%) detected by the ABPM method in UMCDK patients was higher compared to the auscultatory method (8.3%). According to our results, it can be suggested that the children with UMCDK have masked HTN more frequently than we expected. On the other hand, white-coat HTN was more common in the control group. Therefore, we suggest that ABPM should be used instead of auscultatory BP methods for assessing HTN or BP profile as we found that ABPM is a more sensitive method for monitoring BP in UMCDK patients. In this context, ABPM may lead to better management and protection of a solitary kidney in these patients.

The pathogenesis of HTN in UMCDK involves 2 mechanisms: it seems to be mainly related to hyperreninemia due to dysplastic kidney. Indeed, Webb et al[25] pointed out that plasma renin activity was elevated in 2 of their 3 hypertensive children. Besides, hyperfiltration in the opposite solitary kidney may also act upon the pathogenesis of HTN in these patients, although this hypothesis has not yet been confirmed.[12,13] In this context, the findings of the studies investigating the prevalence of HTN in UMCDK patients using auscultatory BP method should be evaluated carefully. While some studies have shown rather a low rate of HTN between 0.5% and 5.9%,[4,6-11] other studies revealed higher rates between 10% and 23.2%.[27,28] This high variability may be related to the BP measurement technique. In our study, we observed that the rate of HTN detected by auscultatory BP method (8.3%) was consistent with the earlier studies.[27-29]

In studies[16-20] assessing HTN in patients with solitary functioning kidney, as well as UMCDK using ABPM, the frequency of HTN was reported in a wide range between 21.1% and 42.5%. Seeman et al[16] used ABPM methods in 25 children with UMCDK and found that HTN prevalence was 5/25 (20%). Similarly, Lubrano et al[20] found that the frequency of pre-HTN and HTN in children with congenital unilateral solitary kidney together with UMCDK was 18% (7/38) at first acceptance and 73.7% (28/38) at the end of 14 years of clinical follow-up.

In our study, in which ABPM method was also used, we found that 45.8% (11/24) of all children with UMCDK were hypertensive. These ratios were higher than those of the other studies.[16-20] This difference may be because our patients had only UMCDK without kidney abnormalities in the opposite kidney.

In conclusion, we found a very high prevalence of HTN, especially masked HTN, in children with UMCDK. Moreover, we found that 1 in every 2 children had HTN based on the ABPM method; though the majority of these subjects were not considered hypertensive according to auscultatory BP method. In clinical practice, these patients are evaluated for HTN with auscultatory BP method, but auscultatory BP method is not accurate in ruling out HTN in children with UMCDK. Thus, we think that ABPM supplies more reliable results compared to auscultatory BP method to detect masked HTN in these patients. Therefore, ABPM should be considered in the monitoring of UMCDK patients and other solitary functioning kidney patients at least once a year.

The restriction of our study is the small sample size, lack of evaluation for end-organ damage (echocardiography, microalbuminuria, carotid intima-media thickness), and kidney size; further prospective studies with larger series and long-term follow-up are needed to support our results.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of İnönü University (Date: November 07, 2017, Decision No: 2017/298).

Informed Consent: A written consent form was given by the parents before participating in this study.

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