Evaluation of the Differences Between Office and Ambulatory Blood Pressure Values in Children with Structurel Renal Anomaly.

Yapısal Böbrek Anomalisi olan Çocuklarda Ofis ve Ambulatuvar Kan Basıncı Arasındaki Farklılıkların Değerlendirilmesi

Nuran Cetin, Aslı Kavaz Tufan

Department of Pediatric Nephrology, Faculty of Medicine, Eskisehir Osmangazi University, Eskisehir, Turkey

Abstract: Structural renal abnormalities are one of the most common causes of hypertension in children. In this study, it was aimed to compare office blood pressure (OBP) and ambulatory blood pressure monitoring (ABPM) values in children with structural renal abnormalities. The data from patients with structural renal abnormalities who performed ABPM were evaluated in this study. It was investigated whether there were significant differences between OBP and ABPM values. The paired t-test was used to determine the significance of the differences between OBP and ABPM values. The factors affecting the differences between office and ambulatory blood pressure values were investigated using linear regression analysis. The OBP values were significantly higher than nighttime systolic blood pressure (SBP) and diastolic blood pressure (DBP) ($p<0.01$). The OBP values were positively correlated with all differences ($p<0.05$). Age and body mass index were positively associated with OBP–nighttime SBP difference ($p = 0.001$, $p = 0.015$, respectively). Serum blood urea nitrogen level was positively associated with OBP–nighttime DBP and OBP–24h DBP differences ($\beta = 0.220$, $p = 0.033$, $\beta = 0.205$, $p = 0.045$, respectively). There was a negative correlation between glomerul filtration rate and OBP–nighttime SBP difference ($\beta = -0.05$, $p = 0.01$). The performing of ABPM and the evaluation of the differences between office and ambulatory blood pressure is very important in the early recognition of the hypertension in children with structural renal anomaly.
Key Words: office blood pressure, ambulatory blood pressure, structural renal abnormalities, children

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Özet: Yapısal böbrek anomalileri çocukluk döneminde görülen hipertansiyonun en sık nedenlerinden biridir. Bu çalışmada yapısal böbrek anomalisi olan çocuklarda ofis kan basıncı (OKB) ile ambulatuar kan basıncı izlemi (AKBİ) sonuçlarının karşılaştırılması amaçlanmıştır. Bu çalışmada AKBİ yapılan yapısal böbrek anomalili hastaların sonuçları değerlendirildi. Hastaların OKB ile AKBİ değerleri arasında anlamlı farklılık olup olmadığı araştırıldı. OKB ve AKBİ sonuçları arasındaki farklılıkların anlamlılığını belirlemek için t-testi (paired samples t-test) kullanıldı. Farklılıkları etkileyen faktörler lineer regresyon analizi ile araştırıldı.OKB değerleri gece sistolik kan basıncı (SKB) ve diastolik kan basıncı (DKB) değerlerinden anlamlı olarak daha yüksekti ($p<0.01$). OKB değerleri farklılıkların hepsi ile pozitif korele bulundu ($p<0.05$). Gece SKB ile OKB arasındaki farklılıklar yaş ve vücut kitle indeksi ile pozitif yönde koreleydi (sırası ile $p = 0.001$, $p = 0.015$). Kan üre azotu ile OKB - gece DKB ve OKB - 24 saat DKB farklılıkları arasında anlamlı ilişki olduğu belirlendi (sırası ile $\beta = 0.220$, $p = 0.033$, $\beta = 0.205$, $p = 0.045$). Glomerul filtrasyon hızı ve OKB-gece SKB farklılığı arasında anlamlı negatif ilişki olduğu saptandı ($\beta = -0.05$, $p = 0.01$). Yapısal böbrek anomalisi olan çocukların izlemi sırasında AKBİ yapılması ve ofis ile ambulatuvar kan basınçları arasındaki farklılıkların değerlendirilmesi hipertansiyonun erken dönemde tanınmasında oldukça önemlidir.
Anahtar Kelimeler: ofis kan basıncı; ambulatuvar kan basıncı; yapısal böbrek anomalisi; çocukluk çağı

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ORCID ID of the authors: N.C. 0000-0001-5763-9815; A.K.T. 0000-0003-1311-9468

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Yazışma Adresi / Correspondence Address
Nuran ÇETİN
mail: nurancetin17@hotmail.com

1. Introduction

Hypertension is perhaps one of the important modifiable causes of chronic diseases such as coronary heart disease and stroke in the World (1). The prevalence of hypertension has increased significantly in children in recent years (2). Structural renal abnormalities are one of the most common causes of secondary causes of hypertension in children. It was reported that renal diseases was the cause of hypertension in 34% to 79% of children with secondary hypertension (3, 4). The early detection and treatment of hypertension in childhood is important for preventing target organ damage (5).

In daily practice, the diagnosis of hypertension is usually made by repeated clinical measurements. But, clinical measurements of blood pressure (BP) does not provide enough information about the characterization of actual BP (6). Ambulatory blood pressure monitoring (ABPM) is a diagnostic tool that provides a more accurate and comprehensive assessment for BP measurements. Published reports have shown that ABPM gives more accurate information about mean BP level, the diurnal rhythm of BP, and BP variability (7). The ABPM is superior in predicting target organ damage cardiovascular risk in children and adults (8). Chronic kidney diseases or structural renal abnormalities are one of the high-risk conditions for which ABPM may be useful (9).

In this study, we aimed to compare office blood pressure (OBP) and ABPM values measured in children with structural renal abnormalities. In addition, we investigated the the factors affecting the OBP-ABPM differences in this population.

2. Materials and Methods

Study group

In this retrospective study, we evaluated data from children who were performed ABPM between December 1, 2012 and December 1, 2017 in the our Pediatric Nephrology Outpatient Clinic. The results of ABPM of 310 consecutive patients between 5 and 18 years of age were evaluated. The patients with structural renal abnormalities were included in this study. We excluded those patients who had essential hypertension or another underlying cause of their hypertension. In addition, the patients who have eGFR <90 ml/min per 1.73 m^2 were not included in this study. American Academy of Pediatrics criteria were used to classify patients data as hypertensive (9). Ambulatory hypertension was defined by the systolic or diastolic mean BP at daytime and/or nighttime ≥95th percentile that was determined according to the body height and sex of patient (10, 11). The data of 93 patients meeting inclusion criteria were analysed in this study. The OBP values of the patients included in this study were measured by manual auscultation with a mercury sphygmomanometer by trained personnel using methodology recommended by the Fourth Report (12). Clinical information was obtained by electronic medical records. Body mass index (BMI) was calculated as weight (kg)/height $(m)^2$. Serum laboratories including serum creatinine (Cr), blood urea nitrogen (BUN) were determined by standard methods. Estimated glomerular filtration rate [eGFR (ml/min/1.73 m^2) = k x body length (cm)/serum Cr level (mg/dL)] was determined by the old Schwartz Formula (13). Urinary excretion of albumin and creatinine were measured in morning samples. Spot urine albumin/creatinine ratio (ACR) of 30-300 mg/g was defined as microalbuminuria.

Ambulatory Blood Pressure Monitoring

The ABPM was performed over a 24-hour time period using Scanlight II/III long-term blood pressure monitoring system. BP was measured every 20 min during daytime and every 30 min during nighttime (only recordings with a minimum of 40 readings and without breaks longer than 2 h). Mean systolic BP (SBP) and diastolic BP (DBP) at daytime, nighttime, and 24 h were calculated. BP readings were expressed as the BP load (percentage of SBP and DBP readings at daytime and nighttime above the 95th percentile). Non-dipping status was defined as the lower than 10 % reduction in nocturnal

average SBP and/or DBP. Nocturnal hypertension was diagnosed when nighttime BP elevated (14). Children without clinic hypertension but a 24-hour systolic BP or diastolic BP greater than the pediatric 95th percentile and BP load greater than 25% were considered to have masked hypertension (3).

Ethics Committee Approval

This study was approved by the local Ethics Committee and conducted in accordance with Declaration of Helsinki.

Statistical analysis

Statistical analyses were performed by using SPSS 11.5 (SPSS Inc, Chicago, IL). Values are expressed as mean and SD for continuous variables and interquartile range (IQR) for qualitative variables. The Shapiro–Wilk test was used to determine normality of data. Means were compared using independent sample t-test in normally distributed data. The comparison of the non-normally distributed data were done by using the Mann-Whitney U test. Correlations between variables were evaluated using Pearson's or Spearman's test as appropriate. A p value <0.05 was considered significant. Qualitative variables were compared by using the ki-kare test. The paired t-test was used to determine the significance of the differences between OBP and ABPM values. The factors affecting the differences between office and ambulatory blood pressure values were investigated using linear regression analysis.

3. Results

The mean age was 11.6 ± 4.02 years (47 girls and 46 boys). Among the study group, there were 55 (59.1%) patients with hypertension [28 clinical hypertension (30.1%), 27 masked hypertension (29%)]. Other BP categories, demographic and laboratory features of the patients were shown in Table 1. The underlying diseases of study group were as follows: Scarred kidney associated vesicoureteral reflux (VUR) 13.9% (n=13), atrophic kidney without VUR 31.2% (n=29), unilateral multicystic dysplastic kidney 6.5% (n=6), congenital renal agenezi 32.3% (n=30), minimally functioning kidneys with ureteropelvic junction obstruction 16.1% (n=15).

The ABPM values were significantly correlated with OBP values (Table 2). But, significant differences were found between OBP and ABPM values in our study population. The OBP and 24-h ambulatory blood pressure values for different blood pressure categories were shown in Table 3. Office SBP and DBP were significantly higher than nighttime SBP and nighttime DBP in all patients and hypertensive group ($p<0.05$). Daytime SBP and DBP values were significantly different from office SBP and DBP in patients with masked hypertension ($p<0.05$, Table 4). The normotensive patients had a significantly lower office SBP than daytime SBP and 24-h SBP ($p=0.000$, $p=0.043$, respectively). Also, we found a significantly lower office DBP compared with daytime DBP in these patients ($p=0.000$). The other comparisons between OBP and 24-h ambulatory blood pressure values were summerized in Table 4.

Using the linear regression analysis, we investigated the factors that had a significant influence on differences between OBP and ABPM values in patients. The mean age and BMI were only positively associated with OBP–nighttime SBP difference ($p<0.05$). The OBP values were positively correlated with all differences between OBP and ABPM values ($p<0.005$). ABPM values were mostly significant negative effects on the differences of the OBP-ABPM values (Table 5).

Table 1.
The demographic and laboratory features of the patients.

Age (years)	11.6 ± 4.02
Gender (Female %)	50.5
Height (cm)	139.8 ± 21.4
Weight (kg)	38.3 ± 17.90
BMI (kg/m²)	17.2 (15.8-19.8)
Creatinine (mg/dL)	0.55 (0.47-0.69)
BUN (mg/dL)	10.6 (9-13)
Uric acid (mg/dL)	4.4 ± 1.13
GFR	122.2 (92.2-147.6)
ACR	66 (27.3-159.2)
Hypertension (n, %)	55 (59.1)
Clinical hypertension (n, %)	28 (30.1)
Masked hypertension (n, %)	27 (29)
Nocturnal hypertension (n, %)	17 (18.3)
Diurnal hypertension (n, %)	20 (21.5)
Non-dipper status (n, %)	62 (66.7)

Values were expressed as mean ± SD, median (interquartile range) and number (%). BMI; Body mass index, BUN; blood urea nitrogen, GFR; glomerular filtration rate, ACR; albumin/creatinine ratio.

Table 2.
The correlations between office and ambulatory blood pressure values in patients.

	Office SBP		**Office DBP**	
	r	**p**	**r**	**p**
Office SBP	-	-	0.842	0.000
Office DBP	0.842	0.000	-	-
24-h SBP	0.393	0.000	0.338	0.001
24-h DBP	0.475	0.000	0.407	0.000
Daytime SBP	0.329	0.001	0.285	0.006
Daytime DBP	0.478	0.000	0.380	0.000
Nighttime SBP	0.315	0.002	0.271	0.009
Nighttime DBP	0.455	0.000	0.429	0.000

SBP; systolic blood pressure, DBP; diastolic blood pressure, BP; blood pressure. R; Pearson correlation coefficients. A p value <0.05 was considered significant.

Table 3.
Office blood pressure and ambulatory blood pressure values in patients for different blood pressure categories.

	All Patients	**Hypertension**	**Clinical HT**	**Masked HT**	**Normotension**
Office SBP	109.4 ± 12.54	115.7 ± 10.8	123.1 ± 7.54	107.9 ± 7.89	103.6 ± 9.31
Office DBP	67.9 ± 12.42	73.3 ± 11.95	81.3 ± 9.31	65.1 ± 8.22	62.3 ± 8.72
24-h SBP	108.3 ± 10.95	112.1 ± 11.29	112.4 ± 11.55	111.8± 11.24	106.6 ± 10.31
24-h DBP	66.1 ± 10.56	70.4 ± 10.96	70.9 ± 12.01	69.7 ± 9.88	64 ± 9.21

Daytime SBP	111.6 ± 11.7	115.1 ± 13	114.7 ± 12.36	115.5± 13.87	110.3 ± 11.26
Daytime DBP	69.3 ± 10.51	72.9 ± 11.32	74.1 ± 12.76	71.7 ± 9.71	67.3 ± 8.77
Nighttime SBP	103.1 ± 11.98	106.8 ± 12.91	106.1 ± 15.42	107.5 ± 9.92	101.8 ± 10.07
Nighttime DBP	63.1 ± 11.4	68.1 ± 11.69	68.4 ± 13.62	67.8 ± 9.55	60.8 ± 9.59

Values were expressed as mean ± SD. HT; hypertension, SBP; systolic blood pressure, DBP; diastolic blood pressure.

Table 4.
The differences between office and ambulatory blood pressure values in patients.

	Mean ± SD	**95% CI of the Difference**	**p**
All patients (n=93)			
Office SBP x daytime SBP	-2.26 ± 14.06	-5.19 to 0.66	0.128
Office SBP x nighttime SBP	6.28 ± 14.55	3.25 to 9.31	0.000
Office SBP x 24-h SBP	1.02 ± 13.01	-1.68 to 3.73	0.456
Office DBP x daytime DBP	-1.38 ± 12.87	-4.06 to 1.29	0.308
Office DBP x nighttime DBP	4.85 ± 12.76	2.19 to 7.51	0.000
Office DBP x 24-h DBP	1.82 ± 11.61	0.81 to 4.45	0.171
Hypertension (n=55)			
Office SBP x daytime SBP	0.55 ± 15.63	-3.76 to 4.85	0.801
Office SBP x nighttime SBP	8.84 ± 16.56	4.28 to 13.41	0.000
Office SBP x 24-h SBP	3.58 ± 13.77	-0.21 to 7.38	0.064
Office DBP x daytime DBP	0.39 ± 14.6	-3.63 to 4.42	0.844
Office DBP x nighttime DBP	5.22 ± 14.97	1.09 to 9.35	0.014
Office DBP x 24-h DBP	2.94 ± 14.5	-1.05 to 6.94	0.146
Normotensive patients (n=38)			
Office SBP x daytime SBP	-6.75 ± 12.44	-9.85 to -3.64	0.000
Office SBP x nighttime SBP	1.78 ± 11.34	-1.05 to 4.61	0.213
Office SBP x 24-h SBP	-3.06 ± 11.84	-6.02 to -0.11	0.043
Office DBP x daytime DBP	-5.02 ± 10.44	-7.62 to -2.41	0.000
Office DBP x nighttime DBP	1.47 ± 10.99	-1.28 to 4.22	0.289
Office DBP x 24-h DBP	-1.75 ± 10.67	-4.42 to 0.92	0.194

Masked hypertension (n=27)			
Office SBP x daytime SBP	-7.57 ± 15	-13.64 to -1.52	0.016
Office SBP x nighttime SBP	0.42 ± 12.74	-4.72 to 5.56	0.867
Office SBP x 24-h SBP	-3.81 ± 13.07	-9.08 to 1.47	0.151
Office DBP x daytime DBP	-6.69 ± 11.54	-11.35 to -2.03	0.007
Office DBP x nighttime DBP	-2.73 ± 12.43	-7.75 to 2.29	0.274
Office DBP x 24-h DBP	-4.69 ± 11.95	-9.52 to 0.13	0.056

Values were expressed as mean ± SD. CI; confidence interval, SBP; systolic blood pressure, DBP; diastolic blood pressure. A p value <0.05 was considered significant.

Table 5.
Linear regression analyses of the differences between office and ambulatory blood pressure values in patients

	Differences of SBP						**Differences of DBP**					
	OBP–dt ABP		**OBP–nt ABP**		**OBP–24h ABP**		**OBP–dt ABP**		**OBP–nt ABP**		**OBP–24h ABP**	
	β	**p**	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**	**β**	**p**
Age	0.547	0.140	0.091	0.001	0.401	0.244	0.181	0.596	0.560	0.096	0.183	0.584
BMI	0.268	0.077	0.228	0.015	0.197	0.150	0.159	0.238	0.073	0.568	0.105	0.424
BUN	0.195	0.090	0.090	0.260	0.191	0.072	0.182	0.082	0.220	0.033	0.205	0.045
Creatinine	2.165	0.071	0.962	0.254	2.059	0.063	1.567	0.155	1.941	0.075	1.547	0.152
GFR	-0.039	0.174	-0.050	0.010	-0.043	0.104	-0.025	0.329	-0.035	0.177	-0.036	0.162
ACR	0.013	0.361	0.016	0.201	0.013	0.320	0.005	0.725	0.007	0.576	0.007	0.590
OSBP	0.693	0.000	0.642	0.000	0.657	0.000	0.423	0.000	0.410	0.000	0.424	0.000
ODBP	0.602	0.000	0.536	0.000	0.542	0.000	0.679	0.000	0.606	0.000	0.654	0.000
DT-SBP	-0.647	0.000	0.419	0.000	-0.411	0.000	-0.454	0.000	-0.286	0.012	-0.322	0.004
DT-DBP	-0.324	0.021	0.539	0.000	-0.204	0.118	-0.551	0.000	-0.387	0.002	-0.452	0.000
NT-SBP	-0.148	0.234	0.660	0.000	-0.231	0.043	-0.151	0.183	-0.316	0.004	-0.185	0.096
NT-DBP	-0.083	0.528	0.566	0.000	-0.125	0.301	-0.243	0.004	-0.533	0.000	-0.321	0.005
24-h SBP	-0.421	0.001	0.554	0.000	-0.550	0.000	-0.330	0.007	-0.295	0.016	-0.369	0.002
24-h DBP	-0.160	0.257	0.559	0.000	-0.245	0.059	-0.413	0.001	-0.440	0.000	-0.522	0.000

β; beta coefficient, BMI; body mass index, BUN; blood urea nitrogen, GFR; glomerular filtration rate, OSBP; office systolic blood pressure, ODBP; office diastolic blood pressure, DT-SBP; daytime systolic blood pressure, DT-DBP; daytime diastolic blood pressure, NT-SBP; night-time systolic ambulatory blood pressure, NT-DBP; night-time diastolic blood pressure, SBP; systolic blood pressure, DBP; diastolic blood pressure. A p value <0.05 was considered significant.

The median BUN, creatinine levels and eGFR were shown in Table 1. Serum BUN levels were positively associated with OBP–nighttime DBP and OBP–24h DBP differences ($\beta = 0.220$, $p = 0.033$, $\beta = 0.205$, $p = 0.045$, respectively). On the other hand, serum creatinine did not have a significant influence on differences between OBP and ABPM values ($p>0.05$). Pearson's correlation analysis revealed significant negative correlations between eGFR and office SBP with DBP (r=-0.289, p=0.036, r=-0.497, p=0.000, respectively). In addition, there were significant correlations between eGFR and ambulatory DBP values (r=-0.318, p=0.018 for daytime DBP, r=-0.357, p=0.007 for nighttime DBP, r=-0.368, p=0.006 for 24 h DBP).

Sixty-three (67,7%) patients had microalbuminuria. The ACR was weakly correlated with 24- h DBP and daytime DBP ($r = 0.311$, $p = 0. 028$, $r = 0. 280$, $p = 0. 049$, respectively). Unfortunately, we could not demonstrate significant correlations between ACR and the differences of OBP-ABPM values (Data not shown).

4. Discussion

The results of our study revealed that there were significant differences between OBP and ABPM values in the children with structural renal abnormalities. Daytime DBP, daytime and 24-h SBP were higher than office SBP and DBP. Lower eGFR was associated with higher ambulatory and office BP values.

In routine practice, OBP measured by manual auscultation with a mercury sphygmomanometer is used to diagnose hypertension (7). Hypertension according to OBP may lead to misclassification in patients with masked hypertension due to poor measurement techniques, the diurnal rhythm of BP and BP variability (15). ABPM provides more accurate information about mean BP level, the diurnal rhythm of BP, and BP variability (16). Also, it has been reported that ABPM is associated with early detection of target organ damage due to hypertension in children (17). In the literature, there are several studies on differences between OBP and ABPM in children. Previous studies of normotensive and hypertensive children suggested that OBP values were significantly lower than ABPM values. Salice et al. reported OBP was lower than ABPM values in normotensive patients, but higher than ABPM values in untreated hypertensive patients (18). Similarly, Salgado et al. showed the office DBP was lower than daytime ABPM in the patients between 5 and 15 years of age with previous high BP. But, only about one-third of the group (28%) included in the study had kidney disease (19). In another study, it has been reported that normotensive children have higher ABPM values than both office SBP and DBP. There were no significant differences between OBP and ABPM values in children with hypertension. But, the children with a history of hypertension or chronic disease were excluded from study mentioned above (20). Whereas, we mainly evaluated children with structural renal abnormalities in our study. To our knowledge, this study is the first in children with structural renal abnormalities evaluating the differences between OBP and ABPM values. Our results contradicted the findings of earlier studies. This contradictory results may be due to the differences in the study populations. In addition, white-coat effect may have contributed to this contradictory results in children who are predisposed to develop hypertension due to their renal diseases.

We investigated the factors correlated with the OBP-ABPM differences. Several studies reported that age was correlated with the OBP–ABP differences. Salice et al. showed that a weak correlation between age and OBP–ABPM differences in children and adolescents (18). In our study, age was only positively associated with OBP–nighttime SBP in study group. It has been reported that obesity is associated with the higher daytime and nighttime SBP in children and adolescents (21). Conversely, Macumber et al. reported that SBP levels were similar between the obese and lean groups (22). Moreover, Samuel et al. showed that there were no significant relationship between the differences OBP-ABPM values and BMI (23). Similarly, we could not show significant

correlations between BMI and the differences OBP-ABPM values in our patients.

Masked hypertension is a clinical condition in which the OBP is normal but ABPM shows hypertensive values. It has been reported that masked hypertension is an important risk factor for the development of end organ damage (24). The prevalence of masked hypertension is from 7.6% to 22% in children (8, 25). Lurbe et al. reported that nearly half of children with masked hypertension were developed persistent elevated ambulatory BP or progressed to clinical hypertension in their 3-year follow-up study (26). In our study, about one third of patients had masked hypertension. Our results may suggest that ABPM is useful for making a more accurate diagnosis of hypertension in the children with structural renal abnormalities who had normal OPB values during clinical visit. On the other hand, there were only significant differences between OBP and daytime ABPM values in masked hypertension. The physically active during the day than at night might be effective in determining the higher daytime BP values in masked hypertension.

The reduction of renal mass due to unilateral hypoplastic/dysplastic kidneys are associated with hypertension and renal failure. In the literature, there were several studies on the relationship between GFR and ABPM values. Iimuro et al. demonstrated that low GFR was significantly associated with the difference between OBP and ABPM values in the adult CKD population (27). Seeman et al. reported that ABPM values were not associated with GFR in children with normal solitary kidney (28). Harshfield et al. showed a negative association between nighttime BP values and GFR in healthy children and adolescents (29). In a study in children with higher grades of renal scarring, it was reported that GFR were independent of BP values (30). Our results showed that eGFR was related negatively to both ABPM and OBP values in patients with structural renal abnormalities. When the differences between ABPM and OBP values are taken into account, our results may suggest that it is absolutely necessary to perform ABPM in the children with structural renal abnormalities who are at risk of renal function impaired.

There are certain limitations of our study. Firstly, our study is a retrospective analysis of data. Secondly, the data of patients using antihypertensive treatment were not included in this study. Thus, our results could reflect the characteristics of the patients without antihypertensive treatment. Thirdly, our analyses are based on single measurement. Nevertheless, we tested for the first time whether there were significant differences between OBP and ABPM values in children with structural renal abnormalities.

5. Conclusions

The results of this study suggest that ABPM should be considered in the clinical management of the children with structural renal abnormalities. When starting antihypertensive drug treatment or diagnosing of hypertension, the differences between OBP and ABPM values should be considered in this population.

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