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Determining Cardiovascular Complications in Children with Chronic Kidney Disease by Measuring Blood Pressure Using Ambulatory Blood Pressure Measurement and Traditional Auscultation Method

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Abstract

Background: It is now hypothesized that the Ambulatory Blood Pressure Measurement (ABPM) method in determining and controlling blood pressure and renal disease-related cardiac defects in children with renal impairment can be more applicable. We aimed to compare the mean blood pressure measured by the ABPM method with blood pressure measured by the auscultation method in determining cardiovascular complications by measuring left ventricular mass index (LVMI) in children with chronic kidney disease.

Methods: This cross-sectional study was performed on 40 children suffering from chronic kidney disease referred to Mofid Children Hospital in Tehran between 2019 and 2021. Each child was evaluated during the first 24 hours, every 20 minutes during the day, and every 30 minutes during the night, and blood pressure was assessed by the ABPM method and every 3 hours by the auscultation method. Patients also underwent echocardiography to determine LVMI.

Results: Based on the assessment by auscultation method, 47.0% of children suffered from systolic hypertension, and 40.0% had diastolic hypertension. In total, 50% were hypertensive. According to ABPM blood pressure data, 23 patients (57%) had systolic hypertension and 24 patients (60%) had diastolic hypertension. In total, 16 patients (40%) had normal blood pressure and 24 patients (60%) had hypertension by the ABPM method. Also, according to ABPM measurement, 10 patients (25%) suffered from masked hypertension, and 6 patients (15%) from white-coat hypertension. There was a significant association between LVMI and the blood pressures assessed by the ABPM method.

Conclusion: Auscultation blood pressure measurement alone may not be sufficient to diagnose hypertension in patients with chronic kidney disease. It should be used in conjunction with the ABPM method.

Key Words: Blood Pressure, Echocardiography, Cardiovascular, Kidney Disease.

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INTRODUCTION

Hypertension and chronic kidney disease are so interrelated and have a causal relationship that 70% of people with elevated serum creatinine also have high blood pressure at the same time (1). Most patients with chronic renal failure die from hypertension-related heart disease, while renal dysfunction is also considered as an important predictor of cardiovascular events (2, 3). Thus, the importance of hypertension as a factor in the progression of chronic kidney disease has been discussed in several guidelines. Accordingly, immediate and timely blood pressure control is recommended in almost all guidelines so that the ultimate goal of blood pressure control is to maintain it within the normal percentile based on the sex and age of the child (4-6). However, blood pressure remains uncontrolled in many patients with renal insufficiency (7).

Over the past 30 years, the introduction, determination and monitoring of Ambulatory Blood Pressure Measurement (ABPM) has led to 24-hour control of blood pressure and its changes with high accuracy. Some prospective studies have shown that this method is much better at predicting cardiovascular events than the traditional blood pressure reading in clinics, and on the other hand it is more efficient than classical methods in determining vital organ damages (8). Especially in patients with frequent fluctuations in blood pressure such as patients with chronic renal failure, diabetic patients and even patients with obstructive sleep apnea, determining the amount and changes of blood pressure is very important and it seems that blood pressure assessment and daily control with ABPM method is much more effective than auscultation method (9). In particular, in patients with renal dysfunction, a large difference has been observed between blood pressure assessed in the clinic and the amount manually determined at home; and therefore, determining the accurate evaluation method for this indicator is very important and vital. By using traditional and auscultation methods, it is possible to ignore the cases of hypertension and failure to diagnose the consequences of invasive hypertension in a timely manner, will lead to untimely treatment of many patients (10).

In patients with renal impairment, differences between ABPM-determined blood pressure and the auscultation method have been reported. In one study, it was found that in men with renal impairment, in approximately 30% of cases, blood pressure levels in the traditional method were reported to be higher than the ABPM method, while in 28% of them the opposite was reported (11). Due to the importance of the above issue, especially in children with renal dysfunction and the greater vulnerability of children's vital systems to changes in blood pressure, accurate determination and control of blood pressure in these patients is of particular importance. It is now hypothesized that the use of ABPM method in determining and controlling blood pressure in children with renal impairment can more effectively reduce the adverse consequences of the disease. In this regard, the present study was designed to compare the mean blood pressure measured by ABPM method and blood pressure measured by auscultation method which applies Android sphygmomanometer in determining cardiovascular complications through measuring left ventricular mass index (LVMI) in children with chronic kidney disease.

2- MATERIALS AND METHODS

2-1. Design and Population

This cross-sectional study was performed on children suffering from chronic kidney disease referred to Mofid

children's hospital in Tehran between 2019 and 2021.

2-1-1. Inclusion and Exclusion Criteria

Age<18 years, and GFR <75 ml per minute and the parents' informed consent for their children's participation in the study were considered as the inclusion criteria. In this regard, those with congenital, structural or primary cardiac abnormalities at the time of admission were excluded from the study.

2-2. Study Measurements

Demographic and initial information of patients were extracted from patients' medical records and entered in checklists for each patient. Each child was evaluated during the first 24 hours; blood pressure was assessed by ABPM method every 20 minutes during the day and every 30 minutes during the night, and it was assessed every 3 hours by auscultation method. Systolic and diastolic blood pressures were recorded for each patient in order to obtain a mean 24-hour blood pressure. Blood pressure was measured by ABPM method using oscillometric monitoring by Microlife Watch BP. Blood pressure measurement was also performed by an auscultation method using Honsun Android sphygmomanometer (made in Germany) and by trained personnel. Determining hypertension by auscultation method and ABPM, cases of white coat and masked hypertension were determined as the following: 1) hypertension by auscultation method (according to the fourth NHBPEP report, cases of BP≥95TH Percentile were reported as cases of auscultation hypertension); 2) hypertension by ABPM method (mean systolic or diastolic blood pressure during sleep or awake ≥ 95th percentile or systolic or diastolic blood pressure load ≥ 25%), 3) Normotensive (the patient's blood pressure is normal by both auscultation and ABPM methods), 4) Sustained hypertension (the patient's hypertension has been confirmed by both auditory and ABPM methods), 5) White-coat hypertension (the patient was hypertensive by auscultation method and has normal blood pressure by ABPM method); and 6) masked hypertension (the patient has normal blood pressure by auscultation method but is hypertensive by ABPM method). Also, the patients underwent echocardiography using my lab imagic maestro device by an expert pediatric cardiologist to determine left ventricular mass (LVM) and LVMI. According to the criteria presented by Khoury et al. (30), for LVMI in children, LVMI level> 40 gr/m^2 in girls over 9 years old and LVMI level> 45 gr/m^2 in boys over 9 years old were considered to be abnormal. In order to determine the status of LVMI in patients less than 9 years old, the curve presented by this study was used (30). According to this LVMI curve, the patients who were in the range above 95th percentile by age and sex were considered to be abnormal. Kidney function in patients was based on GFR calculation and according to the Schwart's formula: GFR=0.55× Height (cm) / Creatinine (mg/dl measured by Jaffeei method) and was categorized in five stages including stage I (GFR>90 associated with persistent proteinuria or structural abnormalities), stage II (GFR range 60≤GFR≤89), stage III (GFR ranged 30≤GFR≤59), stage IV (GFR ranged 15≤GFR≤29) and stage IV or ESKD (GFR<15).

2-3. Data Analysis

Results of the analyses were presented as mean ± standard deviation (SD) for quantitative variables and were summarized by frequency (percentage) for categorical variables. Continuous variables were compared using t-test or Mann-Whitney U test whenever the data did not appear to have normal distribution or when the assumption of equal variances was violated across the study groups. The categorical variables were compared using

the Chi-Square test. P values of ≤ 0.05 were considered statistically significant. For the statistical analysis, the statistical software SPSS version 23.0 for windows (IBM, Armonk, New York) was used.

3- RESULTS

Overall, 40 children less than 18 years (23 males and 17 females) were included into the study (**Fig. 1**). The mean age of the participants was 10.75±4.21 (ranged between 1 and 17 years), the mean weight was 29.61±12.30kg, the mean height was 126.37±26.07cm and the mean body mass index was 16.80±3.13 (ranged between 12.80 and 25.90). Thus, 9 children (22.0%) had normal weight and 31 (78.0%) were underweight.

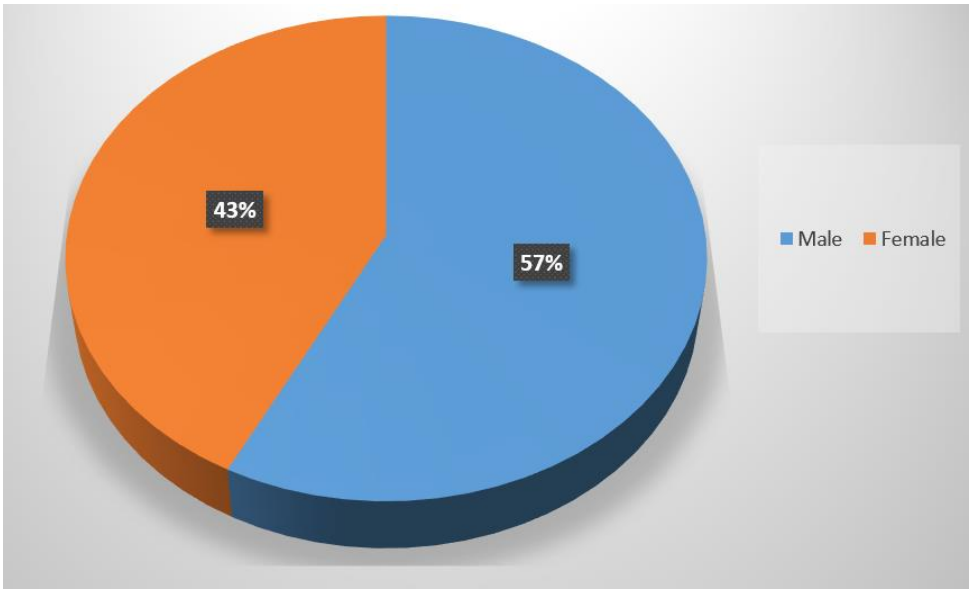

Fig. 1: Gender differentiation in the study group

The findings related to blood pressure assessed by the two methods are summarized in **Table 1**. Based on the assessment by auscultation method, 47.0% of children suffered from systolic hypertension and 40.0% had diastolic hypertension. In total, 50% had normal blood pressure and thus 50% were hypertensive. According to ABPM blood pressure data, 23 patients (57%) had systolic hypertension and 24 patients (60%) had diastolic hypertension. In total, 16 patients (40%) had normal blood pressure and 24 patients (60%) had hypertension by ABPM method. Based on the ABPM method, at the time of awakening, respectively, 53% and 55% of children had systolic and diastolic hypertension and during sleep, 49% and 46% had systolic and diastolic hypertension. Also, according to dipping (defined as the percentage drop from mean daytime to mean nighttime levels) less than 10%, 80% had systolic hypertension and 70% had diastolic hypertension. Also, according to ABPM measurement, 25% suffered from masked hypertension, 15% from white-coat hypertension and 35% from sustained hypertension.

The mean serum creatinine level in children studied was 4.94±2.88 mg/dl, the mean GFR was 19.08±9.80 ml/min and the mean LV mass according to echocardiography assessment was 118.30±94.93 gr/m^2. In this regard, the mean LVMI was 66.86±69.47 gr/m$^{2.7}$ or 114.47±103.70 gr/m^2 indicating abnormal LVMI in 50% of children. Also, GFR

stage I to IV was found in 0%, 5.0%, 17.5%, 10.0% and 67.5%, respectively. Thus, 5% in stage II, 17.5% in stage III, 10.0% in stage IV and 67.5% in stage IV were under-dialysis. Based on the findings, in 9 patients (22.5%) the productivity level of calcium and phosphorus was higher than 65 mg/dl. Moreover, serum phosphorus levels were normal in 15 patients (10.8%), hyperphosphatemia was reported in 18 patients (48.6%) and hypophosphatemia was reported in 4 patients (10.8%).

Table-1: The values of blood pressure assessed by the two study methods

Blood pressure		mean±SD	Ranged
Auditory method	Overall systolic blood pressure, mmHg	114.44±13.22	87 to 138
	Overall diastolic blood pressure, mmHg	73.42±1.45	50 to 99.40
ABPM method	24-hour systolic blood pressure, mmHg	119.52±20.59	88 to 173
	24-hour diastolic blood pressure, mmHg	79.72±18.36	53 to 132
	Awake systolic blood pressure, mmHg	121.62±20.69	97 to 175
	Awake diastolic blood pressure, mmHg	81.20±18.70	52 to 133
	Sleep systolic blood pressure, mmHg	111.83±21.14	78 to 172
	Sleep diastolic blood pressure, mmHg	73.81±20.65	39 to 131
	Load blood * pressure (daily)	35.22±40.61	0 to 100
	Load blood pressure (at night)	53.15±42.84	0 to 100

* The proportion of readings above a threshold (usually the pediatric 95th percentile)

As shown in **Table 2**, there was no association between patients' age and their systolic and diastolic blood pressures assessed by auditory and ABPM methods. In this regard, the mean ages of normotensive and hypertensive patients were 11.20±3.86 years and 10.30±4.60 years, respectively (p=0.50) when assessed by auditory method; and were, respectively, 11.93±3.47 years and 9.95±4.54 years (p=0.14) when assessed by ABPM method.

Table-2: The values of blood pressure assessed by the two methods adjusted for baseline parameters

Item		SBP (auditory)	DBP (auditory)	SBP (ABPM)	DBP (ABPM)
Age	<5 years	105.87±12.74	71.87±14.59	125.25±12.81	89.00±8.86
	5 to 10 years	112.61±13.14	73.24±10.90	112.80±19.47	74.86±15.52
	11 to 15 years	116.65±13.15	73.50±10.18	122.31±24.25	81.18±21.89
	> 15 years	119.75±13.78	74.95±9.79	126.20±13.70	82.20±19.95
	P value	0.37	0.98	0.45	0.53
Gender	Male	111.79±13.39	70.82±10.45	124.21±23.46	83.30±21.62
	Female	118.04±12.48	76.93±9.66	113.17±14.20	74.88±11.66
	P-value	0.14	0.06	0.09	0.12
GFR class	II	118.75±19.44	77.37±12.55	111.50±21.92	7.50±17.67
	III	108.46±16.07	69.10±14.04	118.14±30.40	79.00±24.37
	IV	118.68±17.09	72.00±10.59	112.75±17.17	71.75±16.52
	V	115.05±11.84	74.45±9.58	121.48±18.80	81.77±17.45
	P value	0.56	0.62	0.81	0.67

Similarly, gender was not associated with systolic and diastolic blood pressures assessed by the two methods (**Table 2**).

In this respect, in the auditory method, 25% of males and 25% of female patients were hypertensive (p = 0.33), while in ABPM method, 37% of males and 23% of females were hypertensive (p = 0.43). Moreover, we found no association between blood pressures assessed by the two methods and patients' BMI so that in auditory method, the mean BMI in normotensive and hypertensive groups were 17.55±3.21 and 16.06±2.94, respectively (p = 0.13); and in ABPM method, they were 17.07±3.63 and 16.62±2.82, respectively (p = 0.66). As indicated in **Table 2**, we also showed no association between blood pressures assessed by auditory and ABPM methods and renal functional state based on the GFR classification. We also showed no association between baseline laboratory parameters and blood pressures assessed by the two methods (**Table 3**).

Table-3: The association between blood pressure and laboratory markers

Marker		Normotensive state	Hypertensive state	P-value
SBP (auditory)	Sodium	134.55±4.18	129.17±29.87	0.43
	Potassium	6.54±7.56	4.59±0.94	0.30
	Phosphorus	6.47±2.30	5.44±2.15	0.17
	Calcium	8.72±1.88	9.22±0.85	0.31
DBP (auditory)	Sodium	135.21±4.37	126.92±32.64	0.23
	Potassium	6.29±7.07	4.57±0.93	0.37
	Phosphorus	6.25±2.16	5.56±2.41	0.36
	Calcium	8.90±1.79	9.05±0.87	0.77
Overall (auditory)	Sodium	134.42±4.25	129.61±29.03	0.48
	Potassium	6.57±7.77	4.66±0.96	0.30
	Phosphorus	6.33±2.28	5.63±2.24	0.35
	Calcium	8.76±1.93	9.16±0.86	0.41
SBP (ABPM)	Sodium	136.18±3.78	128.95±26.63	0.29
	Potassium	6.48±8.44	5.00±1.52	0.43
	Phosphorus	5.23±1.73	6.60±2.50	0.06
	Calcium	9.38±1.60	8.61±1.29	0.11
DBP (ABPM)	Sodium	136.40±3.81	129.13±26.00	0.29
	Potassium	6.62±8.72	4.97±1.49	0.38
	Phosphorus	5.25±1.78	6.52±2.46	0.09
	Calcium	9.12±1.24	8.84±1.65	0.57
Overall (ABPM)	Sodium	136.40±3.81	129.13±26.00	-
	Potassium	6.62±8.72	4.97±1.49	-
	Phosphorus	5.25±1.78	6.52±2.46	-
	Calcium	9.12±1.24	8.84±1.65	-

As indicated in **Table 4**, there was a significant association between LVMI and the blood pressures assessed by auditory and ABPM methods. In this regard, both systolic and diastolic hypertension were significantly more prevalent in children with abnormal LVMI as compared to those with normal LVMI. Overall, in auditory assessment methods, 23.5% of normal LVMI group and 76.5% of abnormal

LVMI group were hypertensive (p = 0.002), while in ABPM method, these rates were 41.2% and 70.6%, respectively (p = 0.03).

Table-4: The associations between blood pressures and LVMI status

Blood pressure	Normal LVMI	Abnormal LVMI
Systolic BP (auditory)	-	<0.001
Normotensive	13 (76.5)	5 (29.4)
Hypertensive	4 (23.5)	12 (70.6)
Diastolic BP (auditory)	-	<0.001
Normotensive	15 (88.2)	6 (35.3)
Hypertensive	2 (11.8)	11 (64.7)
Systolic BP (auditory)	-	0.03
Normotensive	11 (64.7)	5 (29.4)
Hypertensive	6 (35.3)	12 (70.6)
Diastolic BP (auditory)	-	0.03
Normotensive	10 (58.8)	5 (29.4)
Hypertensive	7 (41.2)	12 (70.6)

Our study found no relationship between LVMI status and renal function so that the rates of GFR classes of II to IV were shown to be 3%, 12%, 6%, and 30% in normal LVMI and 0%, 3%, 6%, and 40% in abnormal LVMI group (p = 0.32).

Also, no association was found between blood pressure and dipping states; so that in auditory method, the rates of dipping<10% on normotensive and hypertensive groups were 40% and 40% and the rates of dipping >10% were 5% and 15%, respectively (p = 0.36). Also, in the ABPM group, the rates of dipping<10% on normotensive and hypertensive groups were 20% and 60% and the rates of dipping >10% were 60% and 10%, respectively (p = 0.32).

4- DISCUSSION

Hypertension is seen in at least 70% of patients with chronic kidney disease (12). Chronic renal disease is associated with increased risk of heart disease-related death (13). Additionally, increased LVMI and hypertension are both important risk factors for heart disease (14,15). Thus, the accurate assessment of blood pressure along with hypertension in patients with renal failure can facilitate management of disease-related sequels and also prevent adverse clinical consequences, especially heart defects. However, which method of assessing blood pressure will work best remains a challenge. Our study aimed to assess the values of both blood pressure measuring methods including traditional auditory and ABPM methods in determining blood pressure in children suffering chronic renal failure. Such measuring was adjusted for baseline characteristics, renal functional state, and cardiovascular functional index of LVMI.

First, we showed significantly high rates of both systolic and diastolic blood pressures in children with chronic renal failure in both measuring methods without any difference between the two methods. In other words, based on auditory and ABPM methods, 47% and 57% suffered from systolic hypertension and 40% and 60% from diastolic hypertension. However, the values of blood pressures assessed by the two pointed methods were shown to be statistically different in some other studies (27). It was also revealed that by applying auditory and ABPM methods, 25% of

children were normotensives, while the rate of sustained hypertension was also similarly 35%. In a study by Ramaswamy et al. (16), the rate of sustained hypertension was similar to that reported in our study, but this rate was partially lower in the studies by Mitnefes et al. (17) (18%) and Gupta et al. (18) (21.7%). Also, regarding the rate of white-coat hypertension, although our rate was found to be 15%, the rate of white-coat hypertension in various studies varied widely between 1.5% to 46% (23, 25). Therefore, it seems that the values of blood pressure obtained based on both methods of measurement in children are very different in different studies, and even in some studies, a significant discrepancy has been observed between the values obtained from the two methods. This difference can be due to various reasons such as differences in the experience of individuals in measuring blood pressure in the auditory method, differences in the status and clinical severity of kidney disease in children under study and also the time periods of blood pressure assessment in these patients. However, based on our study, indicators such as demographic characteristics, laboratory markers or anthropometric indicators and even renal function status do not seem to be very effective in these assessments. However, as demonstrated in our study, there was a direct relationship between blood pressure status and ventricular function status based on the left ventricular mass index. Based on our findings, the LVMI levels were normal in 17 patients (50%) and abnormal in 17 patients (50%). Also, there was a statistically significant relationship between systolic and diastolic hypertension (both auditory and ABPM methods) with abnormal LVMI status that abnormal levels of LVMI were more common in hypertensive individuals. Unlike the present study, the study by Ramaswamy et al. (16), found no significant relationship between LVMI levels and any of the indicators of blood pressure. However, the participants in Ramaswamy et al.'s (16) study were children with occasional hypertension, while those in the present study all had chronic kidney disease and often had level 5 kidney function, and were on dialysis. Finally, we believe that there is a causal relationship between blood pressure and ventricular function in the field of kidney disease in children and that the method of assessing blood pressure is not an effective factor in assessing such a relationship.

Another point to note was the high rate of latent hypertension among the children surveyed, with 25 percent of these children experiencing the problem. In fact, the traditional method of assessing blood pressure may not be a viable option for assessing and detecting such children. In other words, in detecting occult hypertension, the new method may be more effective. Little research has been done in this regard and more evaluations are needed in future studies.

5- CONCLUSION

Several studies have shown the relationship between chronic kidney disease and heart problems. This study also showed a statistically significant relationship between systolic and diastolic blood pressure with LVMI status in patients with chronic kidney disease. Therefore, it seems that accurate and timely diagnosis of hypertension in patients with chronic kidney disease and the necessary control measures can reduce the risk of heart problems in these patients and lead to improved treatment outcomes and better disease management. On the other hand, a 25% rate of occult hypertension indicates that the auditory blood pressure measurement alone is not sufficient to diagnose hypertension in patients with chronic kidney disease and should be used in conjunction with the ABPM method.

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