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Echocardiographic Assessment of Systolic Myocardial Dysfunction in Children with Chronic Kidney Disease

Abdullah Al Mamun*
Md. Habibur Rahman
Tahmina Jesmin
Saimul Huque
Afroza Begum
Golam Muin Uddin
Ranjit Ranjan Roy

Department of Pediatric Nephrology, Bangabandhu Sheikh Muijib Medical University, Dhaka, Bangladesh.

*Corresponding Author
Dr. Abdullah Al Mamun
Email:
mamunbdcn@gmail.com

Abstract

Background and Aim: Chronic Kidney Disease (CKD) is associated with significantly increased morbidity and mortality. Cardiovascular causes contribute to the large proportion of morbidity and mortality in this group. The aim of the current study was to assess systolic myocardial dysfunction of the heart in children with chronic kidney disease (stage V).

Methods: This cross-sectional study was carried out in a tertiary center from January 2018 to December 2018. Children aged 1 to 18 years having chronic kidney disease (stage V) were included in the study. All the patients underwent color Doppler echocardiography for the evaluation of cardiac abnormalities. Age and sex-matched healthy children with no clinical evidence of renal and cardiovascular disease were taken as a comparison group.

Results: Out of Thirty children with Chronic kidney disease (stage V), 21(70%) were male and 9 (30%) female. Echocardiographic findings revealed a statistically significant difference in case of CKD patients group and a comparison group in relation with left atrium (LA), left ventricular internal diameter in diastole (LVIDd), left ventricular internal diameter in systole (LVIDs), interventricular septum in diastole (IVSd), interventricular septum in systole (IVSs), left ventricular posterior wall thickness in diastole (LVPWd) and left ventricular posterior wall thickness in systole (LVPWs) ($p<0.001$) but no difference in relation to FS and EF (p-0.934 & p-0.754 respectively).

Conclusion: It can be concluded from the present study that children with chronic kidney disease are prone to develop left ventricular structural abnormality but systolic functional changes are less frequent.

Keywords: Children; Chronic kidney disease; Systolic myocardial dysfunction.

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Introduction

Chronic kidney disease (CKD) is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health. CKD, although uncommon in children, can be a devastating disorder with many long term consequences. One of the important consequences is cardiovascular events. Population-based studies have demonstrated an increased risk of death and cardiovascular mortality as glomerular filtration rate (GFR) falls below 60 mL/min/1.73 m^2 or when albumin is detected on urinalysis (1).

The life expectancy of children with end stage renal disease (ESRD) who remain on dialysis is shortened by as much as 40–60 years with 30% to 50% of all deaths in this population attributed to cardiovascular causes (2, 3). However, the cardiovascular causes of mortality are different in children with CKD than in adults. Adult cardiovascular deaths are frequently from coronary artery disease and congestive heart failure while the leading causes of cardiac death in children with CKD are arrhythmia, valvular disease, and cardiomyopathy (4).

In 156 children with CKD stage II to IV, the prevalence of left ventricular hypertrophy was 35%, and age-corrected left ventricular mass was correlated with the degree of renal dysfunction (5). In a prospective study performed in 31 CKD children (stage II to IV), 32% of patients developed left ventricular hypertrophy within 2 years (6). These findings confirm single-center experience reporting a left ventricular hypertrophy prevalence of 20% to 25% for CKD stage II to IV and 70% in CKD stage V patients. At attainment of end-stage renal disease and during dialysis treatment, 70% to 90% of pediatric patients present with left ventricular hypertrophy, which usually persists even after successful renal transplantation (4). Left ventricular hypertrophy in children and young adults is usually associated with male gender, obesity, and high parathormone level and its treatment (7). Furthermore, 25% of 130 children with CKD stage II to IV presented with subclinical systolic dysfunction which was associated with concentric left ventricular hypertrophy (7). In pediatric dialysis patients, systolic dysfunction can be often detected by use of tissue Doppler imaging (8). Cardiac complications are not infrequent in children with CKD, especially in End Stage Renal Disease (ESRD). The European Dialysis and Transplant Association (EDTA) reported that 41% deaths in children less than 15 years of age with ESRD were attributable to cardiovascular cause. Alterations of cardiac morphology and function are a common characteristic of ESRD in adult patients and contribute to the higher cardiovascular risk that is associated with this condition (9).

Even in the pediatric age a good number of deaths in patients with ESRD are attributable to cardiovascular disease (10). Previous Echocardiographic studies indicate that young patients with chronic kidney disease (CKD) and ESRD have abnormal left ventricular geometry and high prevalence of left ventricular hypertrophy (5). Though few, previous studies in children have shown CKD related risk factors are strongly associated with the prevalence and severity of cardiovascular change.

Knowledge about cardiac dysfunction will help to manage cardiac complications in children with CKD to decrease mortality and morbidity. Moreover, cardiovascular disease is likely to become more important in children with CKD because treatment with renal replacement therapy (Renal transplantation) has increased the lifespan of these patients markedly. With this view, present study was designed to assess the cardiac dysfunction by Echocardiography in children with CKD.

Methods

This cross sectional study was carried out in the department of Pediatric Nephrology, in a tertiary care hospital in Dhaka, Bangladesh from January 2018 to December 2018 with a view of assessing systolic myocardial dysfunction of the heart in children with chronic kidney disease (stage V). Patients were divided into two groups. Children aged 1 to 18 year having Chronic Kidney Disease (Stage V) admitted in the department of pediatric nephrology were considered as case group and children having no clinical evidence of renal or cardiovascular disease visiting hospital for other purpose having normal echocardiographic findings were taken as comparison group. Children with valvular heart disease and other congenital heart disease, renovascular hypertension due to other cause, having arterio-venous fistula and patients who refused to participate were excluded from study. Prior to the commencement of this study, the study was approved by the Institutional Review Board of the institution.

Echocardiography procedure

All patients underwent color doppler echocardiography performed on (Vivid 7, GE-brand, Echo machine) in left lateral decubitus position using 4 or 7 MHz transducer by a consultant physician experienced in echocardiography in the department of pediatric cardiology, of the respective institution. The left ventricular ejection fraction (EF) and fractional shortening (FS) were taken as measures of Left ventricular systolic function. EF was determined by measuring left ventricular volume in apical 2 - chamber view.

Left ventricular volume was measured by Area-length method, both in end diastole (LVVd) and in end-systole (LVVs). Ejection fraction was measured by, **EF = LVVd - LVVs/ LVVd** (which was automatically generated by machine). Fractional shortening (FS) was determined by measuring left ventricular internal diameter in diastole (LVIDd) and left ventricular internal diameter in systole (LVIDs) by 2D directed M mode

echo at the level of papillary muscle. Fractional shortening was measured by, **FS = (LVIDd-LVIDs)/ LVIDd × 100** (which was automatically generated by machine) Left atrial diameter**,** left ventricular structure**,** fractional shortening (FS) and **e**jection fraction (EF) was considered as outcome variable. Blood pressure was measured in a standard fashion by using an aneroid Sphygmomanometer by palpatory and auscultatory method. Appropriately sized cuffs were used which covered two third of the arm. Three measurements were taken at 15 minutes intervals in the patient's right arm in comfortable position and the average of the three readings was recorded as the patient's blood pressure. Anthropometry was assessed by measurement of height and weight and body mass index (kg/m²). Height/length was measured in bare feet. Height was measured using a stadiometer in all children > 2 years who can stand. Length was measured in children less than 2 year of age or who were unable to stand by using a firm box in the supine position. Weight was measured by digital weight machine and was plotted on CDC chart according to age and sex. BMI was calculated as weight (kg)/height (m)². Percentiles of BMI were calculated using standard CDC chart. Each case was selected as per inclusion criteria. After case selection, informed written consent was taken from legal guardians of individual patients. Then patient's name and particulars were recorded in the case record file. Initial evaluation of the patients by detailed history and physical examination were collected by researcher himself and recorded in the pre-formed data collection sheet. Then all the cases were numbered chronologically. Data was collected by structured questionnaire which included all the variables of interest. After collection, all the data were cheeked and edited. Then data were entered into computer with the help of SPSS software for windows programmed version 21. After frequency run, data were cleaned and frequencies were cheeked. An analysis plan was developed keeping in view with the objectives of the study. Chi-square and independent samples t-test and other appropriate statistical tests were done based on the objective of the study.

Results

Sixty patients were included in the study. Thirty in case group and thirty in control group. Thirty children with Chronic kidney disease (stage V), 21 (70%) were male and 9 (30%) female. Most of the patients belonged to 11-15-year group (53.33%) and their mean age at presentation was 12.23 ± 3.20 year and in control group, most of the children belonged to 11-15-year group and their mean age at presentation was 10.76 ± 5.25 year (Table 1).

Table 1. Age and sex distribution of study subjects (n=60)

	CKD patients group (n=30)			Comparison group (n=30)		
Age ranges (year)	**Male n (%)**	**Female n (%)**	**Total n (%)**	**Male n(%)**	**Female n(%)**	**Total n(%)**
1-5	1 (3.33)	1 (3.33)	2 (6.67)	2 (10.0)	1 (5.0)	3 (15.0)
6-10	5 (16.67)	2 (6.67)	7 (23.33)	3 (15.0)	1 (5.0)	4 (20.0)
11-15	12 (40.0)	4 (13.33)	16 (53.33)	6 (30.0)	3 (15.0)	9 (45.0)
>15	3 (10.00)	2 (6.67)	5 (16.67)	2(10.0)	2 (10.0)	4 (20.0)
Total	21 (70.00)	9 (30.00)	30 (100.00)	13 (65.0)	7 (35.0)	20 (100.0)
	Mean age 12.23±3.20 year			Mean age 10.76±5.25 year		

Mean pulse was 93.52 ± 10.13, mean systolic blood pressure 120 ± 16 and mean diastolic blood pressure 77 ± 14 and mean body mass index was 16.68 ± 3.50 kg/m^2 in case group (Table 2).

Mean hemoglobin level (8.00 ± 1.48) shows moderate anemia, mean estimated GFR (eGFR) was 7.98 ± 3.17 mL/min/1.73m^2, mean PTH level (548.46 ± 309.01) indicates hyperparathyroidism and inorganic phosphate level (6.86 ± 2.98) is in higher range (Table 3). Echocardiographic findings revealed statistically significant difference in case of CKD patients group and comparison group in

relation with left atrium (LA), left ventricular internal diameter in diastole (LVIDd), left ventricular internal diameter in systole (LVIDs), interventricular septum in diastole (IVSd), interventricular septum in systole (IVSs), left ventricular posterior wall thickness in diastole (LVPWd) and left ventricular posterior wall thickness in systole (LVPEs) ($p<0.001$) but no difference in relation to FS and EF (p-0.934 and p-0.754, respectively)(Table 4).

Table 2. Clinical variables of CKD patients (n=30)

Variable	Mean ± SD	Min - Max
Pulse (beats/minute)	93.52 ± 10.13	80 - 120
Blood pressure		
• **Systolic (mmHg)**	120 ± 16	90 – 150
• **Diastolic (mmHg)**	77 ± 14	50 - 100
Body mass index (kg/m^2)	16.68 ± 3.50	11.2 - 25.29

Table 3. Laboratory parameters of CKD Patients (n=30)

Biochemical parameters	Mean ± SD	Min - Max
Serum creatinine (mg/dL)	9.25 ± 4.24	3.2 - 16.9
eGFR (mL/min/1.73m^2	7.98 ± 3.17	3.58 - 14.05
Hb (mg/dL)	8.00 ± 1.48	5.80 - 10.20
PTH (pg/mL)	548.46 ± 309.01	109 - 1113
Inorganic phosphate (mg/dL)	6.86 ± 2.98	2.8 - 11.2

Table 4. Echocardiographic findings in CKD patients and comparison group

Parameters	Group		p-value*
	CKD patients (n=30) (Mean ± SD)	Comparison group (n=30) (Mean ± SD)	
Aortic diameter (mm)	18.73 ± 4.13	15.17 ± 4.79	0.017
LA (mm)	26.67 ± 6.86	17.40 ± 5.98	<0.001
LVIDd (mm)	46.23 ± 7.28	33.59 ± 7.40	<0.001
LVIDs (mm)	30.19 ± 7.06	21.21 ± 5.45	<0.001
IVSd (mm)	8.34 ± 2.44	5.47 ± 2.44	<0.001
IVSs (mm)	10.67 ± 2.45	7.88 ± 2.55	<0.001
LVPWd (mm)	8.10 ± 2.03	5.52 ± 2.00	<0.001
LVPWs (mm)	12.31 ± 2.44	8.38 ±1.64	<0.001
LVEF (%)	63.50 ± 11.16	64.47 ± 9.06	0.754
FS (%)	36.33 ± 6.09	36.47 ± 4.92	0.934

*Unpaired t test was done to measure the level of significance.

Discussion

This study analyzed 30 children with chronic kidney disease (stage V) to detect the cardiovascular abnormalities by echocardiography.

The current study showed a male predominance with a male to female ratio of 2.33:1. This finding is similar to Adiele et al. (11). The cause of male predominance might be the etiology as obstructive uropathy and glomerulo-nephropathy are more common in male gender.

It had been also observed that, most of the patients were of 11-15 year (53.33%) age group and mean age of presentation was 12.23 ± 3.20. Adiele et al (11) also found similar type of findings in their study over 24 children, where mean age at presentation was 12.33 ± 4.24 years and Demirpence et al (12) observed mean age at presentation of 12.3 ± 5.3 years. This similarity may be due to both countries have similar economic and social background and both studies were performed in tertiary level hospital where patients usually attained hospital lately.

In present study, the mean systolic blood pressure and diastolic blood pressure was 120 ± 16 mm of Hg and 77 ± 14 mm of Hg respectively. It was observed that most of the patient was hypertensive. Hypertension is an independent risk factor for development of cardiovascular complications. Metnefes MM (10) also observed 48% to 81% children had hypertension associated with cardiac abnormalities in his study conducted over children on CKD. Demirpence et al (12) observed significantly higher blood pressure in children with CKD compared to control. Chronic kidney disease itself is a factor for developing hypertension and 60% to 80% of patient with glomerulonephritis present with hypertension in the initial episode of the disease (13). Most of the children found to have moderate pallor (73.33%) and mean hemoglobin level was 8.00 ± 1.48 gm/dl. United states renal data system (2003) (14) observed 40% to 67% patient was anemic in stage IV and stage V CKD. Demirpence et al (12) also found to have Hb level of 10.7 ± 1.1 g/dL. In the present study, the cause of decreased hemoglobin level than other study is due to, wide prevalence of malnutrition exists in common population in this country.

Hyperparathyroidism is a major factor of cardiac morbidity in children with CKD. In present study, hyperparathyroidism (PTH= 548.46 ± 309.01 pg/mL) was observed in patients. The North American Pediatric Renal Trials Collaborative Studies (15) reported a 30-58% prevalence of risk factors to develop cardiovascular disease in patients having hyperparathyroidism.

Lilien et al. (16) observed 40% of deaths in children with CKD and end-stage renal disease occurred due to cardiovascular complications as compared to healthy children of the same age group and the risk of heart-related deaths increased 700 times in the patient group. In a case series of 656 patients, Chavers et al. (4) reported, the prevalence of cardiac complications of 24% (16% LV hypertrophy, 6% congestive heart failure, 2% cardiomyopathy) in children with end-stage renal disease. The echocardiographic abnormalities detected in children with CKD in the present study, was similar with those reported by other workers who studied similar aged- group of patients (17).

In the present study, the most common cardiac abnormality detected, was left ventricular hypertrophy (LVH). The findings are similar with previous reports that documented LVH as the most common cardiovascular abnormality in children with CKD (17). The specific LVH changes observed in the current study is similar to the reports by El-Hussain et al (18) in similar group of patients. El-Hussein et al. (18) also observed same type of findings in their study on children with end stage chronic kidney disease. However, these findings are dissimilar with some reported cases of similar groups of patients by some authors from United States of America and Canada (11). The relatively high number of LVH in this study could be attributed to factors such as poor standard of health services, low level of health awareness, drug abuse, poor health seeking behavior and extreme poverty, all of which could be a contributor to the late presentation and late initiation of appropriate therapy seen amongst most of the patients with CKD in the region. Most of the cases that present late are often complicated with fluid over-load, which further increase the risk of LVH (19).

Limitation:

This is a single center study and sample size is small.

Conclusion

It can be concluded from present study that children with chronic kidney disease are prone to develop left ventricular structural abnormality but systolic functional changes are less frequent.

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Conflict of Interest
The authors declare no conflicts of interest.

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Not declared.

Ethics
Not declared.

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