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Echocardiographic Findings in Children of Chronic Kidney Disease

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Background: Patients with Chronic Kidney Disease (CKD) are at significantly increased risk for both morbidity and mortality from cardiovascular disease (CVD). Determining the spectrum of echocardiographic abnormalities in these patients can help in reduction of morbidity and mortality from CKD.

Materials and Methods: This cross-sectional study was held on department of Pediatric Nephrology, Dhaka Shishu Hospital, Dhaka, during July 2018 to December 2018 (Six months). A total of thirty-six children with chronic kidney disease with creatinine clearance <60ml/min/1.73 m2 and age ranged from 2 to 16 years on supportive treatment and hemodialysis were included. In control group equal number of age and sex matched healthy children without any preexisting renal or cardiovascular diseases were included. Both study group and control group were assessed for cardiovascular findings by echocardiography.

Results: The mean age was 9.09±3.01 years (mean±SD) in case group and 7.85±3.69 years (mean±SD) in control group. Regarding sex, 22 patients (61.1%) in the case group were male and 14 (38.9%) were female. In this study, in CKD patients significant (p<0.001) difference was

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observed in following cardiac parameters, left ventricular end diastolic diameter (LVEDD) (38.34 vs 34.52), left ventricular end systolic diameter LVESD (26.64 vs 20.75), interventricular septal thickness (IVS) (9.34 vs 7.27), left ventricular posterior wall thickness (LVPWT) (8.36 vs 7.46), ejection fraction (EF) (56.68% vs 70.36%), fractional shortening (FS) (31.88% vs 38.30%) and peak early diastole velocity/peak atrial filling velocity (E/A ratio) (1.15 vs 1.45) when compared to control group. Most common cardiac abnormality in children with chronic kidney disease were left ventricular systolic dysfunction (44.4%), mild pulmonary hypertension (30.6%) and left atrial dilatation (27.8%).

Conclusion: Left ventricular systolic dysfunction was the commonest echocardiographic findings in CKD children. There was also significant difference in diastolic function between study and control group.

Keywords: Chronic kidney disease; echocardiography; risk factors; child.

1. INTRODUCTION

Chronic kidney disease (CKD) encompasses a spectrum of different pathophysiologic processes associated with abnormal kidney function and a progressive decline in glomerular filtration rate (GFR) [1]. It is an important cause of morbidity and mortality in children worldwide [1,2]. Scientific and technologic improvements during the second half of the 20th century provided renal replacement therapy as a life-sustaining option for many individuals who otherwise may have died [2,3]. In the past 2 decades, the incidence of the chronic kidney disease in children has steadily increased. The Kidney Disease Outcomes Quality Initiative (KDOQI) working group of the National Kidney Foundation (NKF) defined chronic kidney disease as evidence of structural or functional kidney abnormalities (abnormal urinalysis. studies, or histology) that persist for at least 3 months, with or without a decreased glomerular filtration rate (GFR), as defined by a GFR of less than 60 ml/min per 1.73 m² [2,3] Patients with CKD are at significantly increased risk for both morbidity and mortality from cardiovascular disease (CVD) [4]. Patients on dialysis have a 10 to 30 fold increased risk for cardiovascular mortality compared with the general population. CVD is the single most important cause of death among patients receiving long-term dialysis, accounting for 44% of overall mortality [5-8]. Coronary artery disease including myocardial infarction, congestive heart failure (CHF) and pericardial disease are the common manifestations of cardiovascular major abnormalities in the End stage renal disease (ESRD) [4,9]. Heart failure accounts for 15%, myocardial infarction for about 10% pericarditis for about 3% of dialysis associated mortality [10-18]. Sudden cardiac death may be related to the high prevalence of left ventricular

dysfunction secondary to the LVH in dialysis patients [19,20]. The known common cardiac abnormalities in ESRD are increase in LV cavity size, thickened LV posterior wall, thickened interventricular septum, region wall motion abnormality, decrease in LV compliance, pericardial effusion and calcific/sclerotic valves [21,22]. Changes in cardiac structure and function detected by echocardiography are common in patients with CKD undergoing hemodialysis, and have been recognized as key outcome predictors [23,24]. This study is intended to find out the echocardiographic abnormalities and cardiovascular assessment in CKD in children of Bangladesh. This effort was to help target key patient population at risk by quantifying the extent of the problem, and by facilitating an assessment of the impact of intervention.

2. MATERIALS AND METHODS

It was a cross sectional study done on department of Pediatric Nephrology, Dhaka Shishu Hospital, Dhaka, six months from the day of approval. All children aged 2 to 16 years with chronic kidney disease (GFR<60ml/min/1.73m²) got treatment from the Department of Pediatric Nephrology of Dhaka Shishu Hospital, Dhaka were enrolled in the study. Equal number of age and sex matched healthy control were also enrolled. The patient or the guardian who refused to participate in the study, children under 2 years and above 16 years of age and GFR ≥60 ml/min/1.73m² and known case preexisting cardiac diseases were excluded from this study. Patients were approached for participation either in the inpatient or outpatient setting after taking informed written consent. Children with chronic kidney disease getting treatment or follow up, who fulfilled the inclusion criteria were enrolled in the study. Demographic data regarding information about relationship of respondent to child, parental education status and socio-economic status were collected from guardian or parents [25-29]. Medical data regarding diagnosis, treatment status, follow up were obtained from the patient's medical record [33-34]. Demographic and medical data regarding risk factors taken. For checking cardiac status, clinical examination done. Patients with already known cardiac disease were excluded. The purpose of study explained all the to patients. Echocardiography was done by consultant cardiologist of cardiology department of Dhaka Shishu Hospital. All findings were noted and record was kept. Left ventricular systolic function was taken as LVEF and fractional shortening (FS). E/A ratio showed diastolic dysfunction. E is peak early diastole velocity and A is peak arterial filling velocity of left ventricle across mitral valve. E/A ratio less than 0.75 and more than 1.8 was considered as diastolic dysfunction. LVH was diagnosed when interventricular septum thickness or left ventricular posterior wall thickness ≥12 mm.

Fractional shortening (s) calculated as

FS (%) = (LVDd-LVDs) x 100 Normal range being 25% to 45%

LVDd: Left ventricle internal diameter in diastole LVDs: Left ventricle internal diameter in systole

Eiection fraction calculated as

LVEF (%) = (LVVd-LVVs) x 100 Normal= 59.2%±6%

LVVd: Left ventricle volume in diastole LVVs: Left ventricle volume in systole

The data from patients was collected on a proforma.

Data was collected by preformed questionnaires. Data was processed and analyzed by using the SPSS Windows (version 20.0) programs. P value < 0.05 was considered statistically significant.

3. RESULTS

This cross sectional study was carried out with an aim to determine the echocardiographic findings and cardiovascular risk factor assessment in different stages of CKD in children in Bangladesh. A total of 36 children age ranged from 2-16 years with chronic kidney disease receiving treatment from Dhaka Shishu Hospital and equal number age and sex matched control were included in this study.

Table 1 shows the average age was 9.09±3.01 years in case group and 7.85±3.69 years in control group. Male Female ratio in case is 1.5:1 vs 0.8:1 in control. Most of the study cases 61.1% vs 86.1% control were from rural . In socio-economic status 25% were from poor socioeconomic, 47.2% were from lower middle socioeconomic class in cases group, on the other hand 19.4% were from poor socioeconomic 72.2% were from lower middle class, socioeconomic class in control group. In case group, 44.4% father were businessman & 91.7% mother were housewife whereas 94.4% mother in control group were housewife. In both case and control groups 25% were non immunized.

Table 2 shows higher percentage of stage 3 in 2-5 years (100%) and higher percentage of stage 5 in 5-10 years (46.7%). The difference was statistically significant between stage and age group (P=0.010).

Table 3 shows in WAZ 52.8% of case were <3rd percentile, 30.6% were 3rd -50th percentile and 16.7% >50th percentile On the other hand in control 2.8%, 36.1% and 61.1% respectively (p=.001). In HAZ 55.6% case were <3rd percentile 30.6% 3rd -50th percentile and 13.9% were >50th percentile but in control group it was 13.9%, 47.2% and 38.9% respectively (p=.001). BMI shows 88.9% of case were underweight and 11.1% were within normal weight and 69.4% were within normal weight which is also statistically significant.

Table 4 shows 33.3% cases were normotensive and 63.9% had stage 2 hypertension but all were normotensive in control group. The difference is statistically significant between two groups (P=0.001).

Table 5 shows statistically significant difference in hemoglobin and serum parathyroid level between stage 3,4,5. Hemoglobin level is significantly low and parathyroid hormone is high in stage 5 CKD.

This Table 6 shows there is statistically significant difference between case and control among all recorded echocardiographic parameters eg LVEDD, LVESD, IVS, LVPWT, EF(%), FS(%), E/A ratio.

Table 1. Demographic characteristics of case and control (n=72)

Characteristics	Ca	se (n=36)	Cor	ntrol (n=36)	P value
	No	%	No	%	
Mean age (years±SD)	9.09±3.0	1	7.85±3.6	69	0.122
Sex					
Male	22	61.1	16	44.4	0.157
Female	14	38.9	20	55.6	
Male: Female	1.5:1		0.8:1		
Residence					
Rural	22	61.1	31	86.1	0.031
Urban	12	33.3	3 2	8.3	
Urban slum	2	5.6	2	5.6	
Socio-economic					
Poor	9	25.0	7	19.4	0.093
Lower middle	17	47.2	26	72.2	
Upper middle	8	22.2	3	8.3	
Father occupation					
Service holder	6	16.7	5	13.9	0.084
Businessman	16	44.4	8	22.2	
Others:	14	38.9	23	63.9	
(Farmers, Shopkeeper)					
Mother's occupation					
House wife	33	91.7	34	94.4	0.643
Service holder	3	8.3	2	5.6	
Immunized status					
Immunized	22	61.1	25	69.4	0.478
Partially immunized	5	13.9	2	5.6	
Non immunized	9	25.0	9	25.0	

P value reached from chi square test

Table 2. Age distribution of study patients according to stage of CKD (n=36)

Age group	Number	Stage 3		5	Stage 4		age 5	P value
		No	%	No	%	No	%	
2-5	6	2	100	0	00	4	13.3	
5-10	16	0	00	2	50.0	14	46.7	0.010
10-16	14	0	00	2	50.0	12	40.0	

P value reached from chi square test

Table 3. Anthropometry of study patients and control (n=72)

Anthropometry	Ca	se (n=36)	Con	trol (n=36)	P value	
- ·	No	%	No	%	_	
WAZ						
<3 rd percentile	19	52.8	1	2.8	0.001	
3 rd -50 th percentile	11	30.6	13	36.1		
>50 th percentile	6	16.7	22	61.1		
HAZ						
<3 rd percentile	20	55.6	5	13.9	0.001	
3 rd -50 th percentile	11	30.6	17	47.2		
>50 th percentile	5	13.9	14	38.9		
BMI						
Under weight (<18.5)	32	88.9	11	30.6	0.001	
Normal (18.5-24.9)	4	11.1	25	69.4		
Overweight (25 -29.9)	0	00	0	00		
>Obese (>30)	0	00	0	00		

P value reached from chi square test

Table 4. Blood pressure values between case and control (n=72)

Blood pressure		Case (n=36)			P value
	No	%	No	%	
Normotensive	12	33.3	36	100	
Stage 1 HTN	1	2.8	0	00	0.001
Stage 2 HTN	23	63.9	0	00	

P value reached from chi square test

Table 5. Hematological & biochemical features of different stages of CKD (n=36)

Parameters	Stage 3	Stage 4	Stage 5	P value
	Mean±SD	Mean±SD	Mean±SD	
Hb% (g/dl)	11.00±2.12	9.20±1.43	7.34±1.22	0.001
Serum K+ (mmol/L)	4.50±0.42	4.40±0.27	5.35±0.922	0.074
Serum calcium (mmol/L)	2.10±0.28	2.12±0.22	2.00±0.23	0.554
Serum phosphate (mmol/L)	2.10±0.0	2.12±0.18	2.44±0.40	0.07
Serum PTH (pg/ml)	275.50±62.93	611.00±369.80	845.26±546.59	0.027

P value reached from anova test

Table 6. Echocardiographic measurement of different cardiovascular parameter between case and control (n=72)

Parameter	Case (n=36)	Control (n=36)	t value	P value	
	Mean±SD	Mean±SD			
LVEDD (mm)	38.34±8.80	34.52±6.56	2.082	0.041	
LVESD (mm)	26.64±3.46	20.75±4.84	3.594	0.001	
IVS (mm)	11.34±2.08	7.27±1.81	4.502	0.001	
LVPWT (mm)	10.36±3.69	7.46±1.61	2.287	0.025	
EF (%)	54.68±14.32	70.36±7.69	5.047	0.001	
FS (%)	29.88±9.93	38.30±7.58	3.079	0.003	
E/A ratio	1.15±0.58	1.45±0.25	2.807	0.007	

P value reached from student 't' test

LVEDD : Left Ventricular End Diastolic Diameter, LVESD: Left Ventricular End Systolic Diameter IVS: Interventricular Septal Thickness

LVPWT: Left Ventricular Posterior Wall Thickness, EF: Ejection Fraction, FS: Fractional Shortening, E: Peak early diastole velocity, A: Peak atrial filling velocity

Table 7. Echocardiographic parameters in different stage of CKD (n=36)

	Stage 3	Stage 4	Stage 5	P value
	Mean±SD	Mean±SD	Mean±SD	
Left ventricular struc	ture			
LVEDD (mm)	29.50±4.94	34.56±7.14	39.43±8.88	0.204
LVESD (mm)	17.50±3.53	23.13±5.35	27.71±8.73	0.182
IVS (mm)	9.00±1.41	9.42±2.32	10.56±2.07	0.390
LVPWT (mm)	9.50±0.70	9.92±2.07	11.41±1.72	0.866
Systolic function				
FS	41.50±0.70	31.75±3.50	31.26±10.54	0.116
EF	74.00±1.41	63.00±5.88	54.68±14.62	0.381
Diastolic function				
E/A ratio	1.05±0.21	1.17±0.09	1.53±0.61	0.316

P value reached from anova test

Table 8. Comparison of Echocardiographic findings between case and control (n=72)

Outcome		Case (n=36)		
	No	%	No	%
Left ventricular systolic dysfunction	16	44.4	0	00
Mild pulmonary hypertension	11	30.6	0	00
Left Atrial Dilatation	10	27.8	0	00
Minimum pericardial effusion	3	8.3	0	00
Mitral Regurgitation	4	11.1	0	00
Concentric LVH	2	5.6	0	00
Hypertrophied cardiomyopathy	2	5.6	0	00
Trivial Mitral Regurgitation	2	5.6	2	5.61
Patent foramen ovale (PFO)	3	8.3	0	00

Table 9. Percentage of Left Ventricular Dysfunction in Study Cases

Echocardiographic finding in cases	No. of cases	Percentage
Left ventricular systolic dysfunction :		
Fractional shortening (< 25%)	10	27.7%
Ejection fraction (< 59%)	16	44.4%
Left ventricular diastolic dysfunction:		
E/A ratio (<0.75 or >1.8)	7	19.4%
Left ventricular hypertrophy:		
IVS (>12mm)	3	8.3%
LVPWd (>12mm)	3	8.3%

Table 7 shows there was no statistically significant difference in left ventricular structure, systolic and diastolic function between stage 3, stage 4 and stage 5.

Table 8 shows that 44.4% case had left ventricular systolic dysfunction, 30.6% had mild pulmonary hypertension, 27.8% had left atrial dilatation, 8.3% minimum pericardial effusion, 5.6% had concentric LVH and 5.6% had hypertrophied cardiomyopathy as their ultimate outcome on echocardiography.

This Table 9 shows FS (<25%) present in 27.7%, EF(<59%) in 44.4% cases both of which indicates Left Ventricular Systolic Dysfunction. Altered E/A ratio present in 19.4% patients which indicates Left Ventricular Diastolic Dysfunction. IVS (>12mm) and LVPWd (>12mm) both present in 8.3% cases respectively which indicate Left Ventricular Hypertrophy.

4. DISCUSSION

This cross-sectional study was carried out with an aim to determine the common echocardiographic findings and cardiovascular risk factors assessment in different stages of CKD in children in a tertiary care hospital in Bangladesh as well as their socio demographic parameters. A total of 36 children age ranged from 2-16 year with chronic kidney disease receiving treatment from the Department of Pediatric Nephrology, Dhaka Shishu Hospital and equal number to age and sex matched control were included in this study. The present study findings were discussed and compared with previously published relevant studies.

The present study shows the average age was 9.09±3.01 years (mean±SD) in case group and average age was 7.85±3.69 years (mean±SD) in control group similar to Hafiz I.N. et al. [35] where average age 9.88±3.92 years in case vs 10.72±2.88 years in control. The findings of the study are in well agreement with the findings of the other research works (Al-Doori et al.) [36].

In this study, 22 patients (61.1%) in the case group were male and 14 case (38.9%) were female and ratio was 1.5:1. However, this consistent results obtained in other studies, like Harambat et al. [37] where the higher prevalence of CKD in males. Another study Al-Doori et al. found 19 patients (47.5%) in the cases group were male and 21 cases (52.5%) were female which was not similar.

In the present study we found that a statistically significant decrease in Z-score for (Weight, Height and Body Mass Index) in the CKD patients group than control. Our study was in agreement with Hafiz I.N. et al. who found that there were growth deficit in anthropometric parameters in dialysis children compared to healthy control.

In terms of blood pressure, 66.7% of patients in the cases group were hypertensive (P = 0.001), though other studies show a similar prevalence. Mukesh L. et al. [38] found 37.1% cases were hypertensive which was contrary with our results. Many factors contribute to the raised incidence of hypertension in CKD patients. They include sodium retention, increased activity of the reninangiotensin-aldosterone system, an exaggerated activity of the sympathetic nervous system, secondary hyperparathyroidism, deficient nitric oxide and endothelium-mediated vasodilation. Kale et al. [39] had found that hypertension was identified as important risk factor for all three Left ventricular disorder (Left ventricular hypertrophy, diastolic & systolic dysfunction). Systolic. diastolic and mean BP was separately and significantly associated with LV disease. There was no significant difference of hypertension among CKD stages in this study.

In the present study, the CKD Patients were anemic with significant decrease in hemoglobin level. Anemia found in 35 patients (97.2%) in the case group than control (P=0.001), in agreement with our results Mukesh L. et al. who found that CKD patients (patients vs controls) presented with anemia with significant low Hb (9.1 gm/dL vs 12.04 gm/dL) with P value <0.001. In this study there was statistically significant difference in hemoglobin level among different stages of CKD (P = .001). CKD stage 5 children had significantly lower hemoglobin level.

In this study, CKD patients had a left ventricular end diastolic diameter (LVEDD) (38.34 vs 34.52, P = 0.041), left ventricular end systolic diameter (26.64 vs 20.75, P = LVESD 0.001), interventricular septal thickness (IVS) (9.34 vs 7.27, P=0.001), left ventricular posterior wall thickness (LVPWT) (8.36 vs 7.46, P=0.025), ejection fraction (EF) (56.68 vs 70.36, P=0.001), fractional shortening (FS) (31.88 vs 38.30, P=0.003) and peak early diastole velocity/peak atrial filling velocity (E/A ratio) (1.45 vs 1.15, P= 0.007) in comparison to controls. These results are consistent with those obtained by Adiele et al., Malikenas et al. [40] and van Huis et al. [41].

Increased LVEDD, LVESD, IVS, LVPWT in comparison to control indicate LVH. In this study 16.6% case had definite Left Ventricular Hypertrophy.

In this study left ventricular systolic dysfunction (44.4%), mild pulmonary hypertension (30.6%), left atrial dilatation (27.8%), minimal pericardial effusion 8.3% was noted in this study to be the most common cardiac abnormality in children and tends to develop early in the disease and cuts across all the stages of CKD. Therefore, the findings of the study are in well agreement with the findings of the other research works (Adiele et al.).

In studies using different methodologies, the prevalence of the LV systolic dysfunction varied from 15% to 18% in patients undergoing dialysis (starting the treatment or undergoing regular chronic therapy, respectively), reaching 28% in individuals assessed at the moment of the renal transplant. In this study we found systolic dysfunction in 44.4% cases among them all had low ejection fraction (<59%) and 27.7% had low fractional shortening (<25%).

The analysis of LV diastolic parameters on the basis of E/A ratio was significantly altered in CKD patients as compared to controls, P value in our study is 0.007 in comparison to controls. Left ventricular diastolic dysfunction is an important cause of cardiac morbidity in end stage renal disease. We found 19.4% case had definitive left ventricular diastolic dysfunction. In concordance with our results Schoenmaker et al. [41] who found that diastolic dysfunction in 20-22% of children on regular hemodialysis but S.Agarwal et al. [42] had observed diastolic dysfunction in 60% and systolic dysfunction in 15% of patients and its findings were not consistent with our study.

specific Left ventricular hypertrophy The prevalence documented in this study is similar to the reports by Nashwa et al. [43] in similar group of patients in Australia and El-Husseini et al. [44] in post- transplant patients in Egypt. However, this Left ventricular hypertrophy prevalence rate similar compared to 16-31% reported in similar groups of patients by some authors from Cincinnati, United States of America and Canada. The relatively high prevalence rate of systolic dysfunction in this study could be attributed to factors such as poor standard of health services, low level of health awareness, drug abuse and use of herbal concoctions, 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 sub region.

5. CONCLUSION

Left ventricular systolic dysfunction was the commonest echocardiographic findings in CKD children.

ETHICAL APPROVAL AND CONSENT

Certificate from the ethical review committee of Dhaka Shishu Hospital, Dhaka was obtained for the study. Written informed consent was taken from the legal guardian of the patient.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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