Left ventricular mass index as a prognostic factor in children with chronic kidney disease

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Objective
The objective of this study was to evaluate the effect of decreasing renal function on left ventricular mass index (LVMI) in children with chronic kidney disease (CKD) on regular hemodialysis attending Assiut University Hospital for Children, and also to evaluate left ventricular mass changes as predictor of morbidity and mortality of uremic children by using echocardiography, aiming to use it in the future.

Patients and methods
Baseline clinical characteristics were collected by careful history and examination. Routine laboratory methods were used to measure biochemical parameters: hemoglobin, C-reactive protein, phosphorus, calcium, parathyroid hormone, and lipid profile after patients fasted for 8 h. Echocardiographic parameters were measured within 2–24 h after a dialysis session.

Results
In this study, we studied 36 children on regular hemodialysis. The age of our patients ranged from 3.5 to 16 years, and the number of male patients was similar to female patients. In our study. we found eccentric left ventricular hypertrophy was predominant (38.9%) compared with concentric left ventricular hypertrophy (13.9%). We found that 52.8% of patients had increased LVMI and 47.2% had normal LVMI. Regarding the fate of our cases, 39% died during the study period, whereas the other 61% survived. Mortality among patients with increased LVMI was higher (28%) than among patients with normal LVMI (11%).

Conclusion
Children with CKD are prone to development of cardiac dysfunctions, so early and regular echocardiographic studies of all children with CKD to detect early cardiac changes and institute interventions and follow-up are required.

Keywords:
Assiut, children, chronic kidney disease (CKD), left ventricular mass

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Introduction

The evaluation and treatment of patients with chronic kidney disease (CKD) requires understanding of separate but related concepts of diagnosis, comorbid conditions, severity of disease, and complications of disease including cardiovascular complication.

Left ventricular hypertrophy (LVH) develops early in the course of CKD and is thought to maintain cardiac function and reduce left ventricular wall stress during conditions of increased afterload and preload. Numerous hemodynamic and nonhemodynamic factors have been associated with the development of LVH [1]. Consistent with this association, left ventricular adaptation occurs through two distinct geometric patterns: concentric and eccentric geometry [1].

Echocardiography is an ideal tool for cardiac assessment, as it is noninvasive, portable, and efficacious in providing detailed anatomic, hemodynamic, and physiologic information about the pediatric heart [2].

Echocardiogram is still established as the main device to evaluate left ventricular mass (LVM) in daily clinical practice [3].

Aim

The aim is to evaluate the effect of decreasing renal function on left ventricular mass index (LVMI) in children with CKD stage 5 on regular hemodialysis attending Assiut University Hospital for Children and also to evaluate LVMI changes.

Patients and methods

Patients

This study included 36 patients with CKD stage 5 on regular hemodialysis after obtaining their informed

consent. The study was carried out at the Pediatric Nephrology department and the Echocardiography room of the University of Assuit Teaching Hospital. The hospital serves as a major referral Centre to the surrounding health facilities in the government and beyond. The Pediatric Nephrology clinic of offers services to patients from the catchment area of the hospital. Ethical Clearance was obtained from the Independent Hospital. Research and Ethical Committee (IHREC) of the university of Assuit hospital and written informed consent and assent obtained from parents and patients where applicable. Patients with diabetes, epilepsy, rhythm or conduction abnormality, and valvular heart disease were excluded.

Methods

Hemodialysis was carried out three times a week for 4 h with standard bicarbonate dialysis. Hemodialysis was carried through an upper limb arteriovenous fistula.

Baseline clinical characteristics were collected by careful history and examination.

Routine laboratory methods were used to measure biochemical parameters: hemoglobin (HB), C-reactive protein, phosphorus, calcium, parathyroid hormone, and lipid profile after patients fasted for 8 h. Echocardiographic parameters were measured within 2–24 h after a dialysis session.

Echocardiography was done by an experienced echocardiologist in the cardiology unit of Assiut University Hospital for Children. Two-dimensional guided M-mode echocardiography was performed by standard methods. Left ventricular internal dimension and interventricular septal and posterior wall thickness were measured at end-diastole and end-systole, according to the American Society of Echocardiography guidelines. LVH was determined as LVMI. LVMI was calculated using the anatomically validated formula:

LVM was calculated at end-diastole by using the American Society of Echocardiography convention [4]:

$$\text{LV mass} = 0.8(1.04([\text{LVIDD}+\text{PWTD}+\text{IVSTD}]3-[\text{LVIDD}]))+0.6\text{g},$$

Where LVIDD is the left ventricular internal diameter in diastole, PWTD is the posterior wall thickness in diastole, and IVSTD is the interventricular septal thickness in diastole.

LVMI was measured as follows:

LVMI = LVM/body surface area.

Statistical analysis

Statistical package for social sciences, version 24, May 2016 (IBM Corp., Chicago, Illinois, USA), were used for statistical data analysis.

Data were expressed as mean, SD, number, and percentage. Mean and SD were used as descriptive value for quantitative data, whereas number and percentage were used to describe qualitative data.

Student's *t*-test was used to compare the means between two groups.

Pearson's χ^2-test was used to compare percentages of qualitative data.

Univariate and multivariate regression analyses were done to predict the possible independent risk factors for LVMI and death among CKD.

For all these tests, the level of significance (P) can be explained as follows:
(1) No significance ($P > 0.05$)

Table 1 Demographic data of the study group

Items	Values
Age (years)	
Mean	12.264±3.656
Median (range)	13 (3.5-16)
Sex [*n* (%)]	
Male	18 (50)
Female	18 (50)
Total	36

Table 2 Laboratory investigations of the study group

	Mean	Median	SD
CRP	9.212	5.045	8.534
Serum albumin (mg/dl)	3.392	3.500	0.733
Serum creatinine (mg/dl)	7.156	6.750	2.217
Blood urea (mmol/l)	138.694	135.000	59.201
GFR (ml/min)	11.531	9.650	4.991
WBCs	7.486	6.700	2.842
HB (mg/dl)	9.272	8.550	1.862
PLT	239.083	230.000	77.347
Neutrophils (%)	59.125	58.500	12.350
Band (%)	0.856	1.000	0.456
Lymphocytes (%)	48.250	32.000	65.173
Cholesterol (mg/dl)	146.59	141.00	45.473
Triglyceride (mg/dl)	146.36	127.50	67.387
HDL (mg/dl)	35.68	33.00	13.816
LDL (mg/dl)	81.59	73.50	39.235
Serum calcium (mg/dl)	8.400	8.500	1.424
Serum phosphorus (mg/dl)	5.586	5.650	2.404
Parathyroid hormone (mg/dl)	268.567	273.000	170.693

CRP, C-reactive protein; GFR, glomerular filtration rate; HB, hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PLT, platelet; WBC, white blood cell.

(2) Significance ($P < 0.05$)
(3) High significance ($P < 0.001$).

Results

Table 1 shows that the mean age of the study population was 13 years, with a very wide range from 3.5 to 16 years, which was reflected in the high SD of more than 3.5. Moreover, Table 1 shows that half of our cases were males and the other half were females. Table 2 shows that C-reactive protein was mildly elevated in most of the cases, with a mean of 9.212. Most cases showed mild degree of hypoalbuminemia, with a mean of 3.4 ± 0.7. Serum creatinine was highly elevated, with a mean of 7.2 mg/dl. The glomerular filtration rate was very much lowered with a mean of 11.5 mg/min. The complete blood count showed only anemia, with a mean HB level of 9.3 ± 1.9 g/dl. Lipid profile was more or less normal in nearly all cases. In contrast, serum calcium showed mild reduction, with a mean of 8.4 ± 1.4 mg/dl.

Table 3 shows that LVH was found in more than half of the cases [19 (52.8%) of 36 cases].

Table 4 shows that among our two groups, 52% of patients had increased LVMI and 47% had normal LVMI.

Table 3 Echocardiography of the study population

	Mean	Median	SD
RVAW	5.200	5.000	1.110
RV	14.95	14.00	4.613
IVS	7.781	7.550	2.081
Left ventricular end-diastolic diameter	44.142	43.500	6.777
Left ventricular end systolic diameter	29.950	28.500	6.409
LVPW	8.006	7.950	1.659
Aortic velocity	126.111	125.000	23.054
Mitral E	105.639	104.000	20.178
Mitral A	82.417	81.500	18.554
Mitral E/A	1.3483	1.3250	0.364
Pulmonary artery flow	126.194	121.000	29.696
Tricuspid regurge PG	35.789	33.000	11.090
LVM (g)	117.61	96.00	59.07
Left ventricular mass index	113.31	104.50	49.19
RWT	0.36	0.35	0.07
Left ventricular hypertrophy [*n* (%)]		19 (52.8)	

A, early diastolic; E, late diastolic; IVS, interventricular septum; LVM, left ventricular mass; LVPW, left ventricular posterior wall; RV, right ventricle; RVAW, right ventricular anterior wall; RWT, relative wall thickness.

Table 4 Left ventricular mass index

	Frequency (%)
Normal	17 (47.2)
Mild	4 (11.1)
Moderate	5 (13.9)
Severe	10 (27.8)
Total	36 (100.0)

Table 5 shows eccentric LVH (38.9%) to be predominant, followed by concentric (13.9%) and concentric remodeling (8.3%).

Table 6 shows that nearly 39% of cases died during the study period, whereas the other 22 patients survived.

Discussion

LVH develops early in the course of CKD and is thought to maintain cardiac function and reduce left ventricular wall stress during conditions of increased afterload and preload. However, the development of LVH is also associated with long-term cardiovascular morbidity and mortality.

LVH is one of the most consistent predictors of mortality in adults with CKD. However, little is known about its significance as a predictor of mortality in children with CKD. The reported prevalence of LVH in children with CKD ranges from 17 to 80%, dependent mainly on the stage of disease [5].

In this work, we studied 36 children on regular hemodialysis. The mean age of our patients is from 3.5 to 16 years. This was similar to studies done by Malikenas and colleagues [6,7], as the mean age of their patients was 12.33 ± 4.24 years.

There are many risk factors for LVH in patients with CKD. Anemia, hypertension, extracellular fluid expansion, arteriovenous fistulas, and abnormalities of calcium phosphate homeostasis are some of the common mechanisms described [1].

Anemia is considered to be a risk factor in developing LVH. It was also reported as a major contributor in cardiac morbidity and mortality, and in all-cause mortality in patients on dialysis (Kazmi *et al.*) [6]. HB levels are observed to predict the grade of LVH, where every 1 U decrease of HB (g/dl) level was reported to be associated with 50% increased risk for dilatation

Table 5 Left ventricular hypertrophy type

	Frequency (%)
Concentric	5 (13.9)
Concentric remodeling	3 (8.3)
Eccentric	14 (38.9)
Normal	14 (38.9)
Total	36 (100.0)

Table 6 Fate of the study patients

	n (%)
Living	22 (61.1)
Died	14 (38.9)
Total	36 (100.0)

and left ventricular systolic dysfunction (Culleton and Hemmelgarn) [7].

Strict control of blood pressure (BP) is known to be one of the best practices to prevent LVH [8]. In our study, the percentage frequency of cases with hypertension was higher ($P < 0.048$) in group with increased LVMI group than group with normal LVMI. This is in accordance with Ruggenenti *et al.* [9]. This is attributed to the role of hypertension in the pathogenesis of LVH. This was a significant result, because BP control should not be a difficult target to be reached to modulate ventricular hypertrophy and affect cardiovascular morbidity in uremic patients.

In this study, regarding M-mode echocardiography, we found that left ventricular end-diastolic diameter, left ventricular end-diastolic, left ventricular posterior wall, interventricular septum, and aortic velocity were higher in increased LVMI group than normal group. Transmitral early-diastolic and late-diastolic wave peaks, mitral early-diastolic/late-diastolic, pulmonary artery flow, and tricuspid regurge were obtained by using the pulsed wave Doppler, which were higher in increased LVMI group than normal group. This difference was nonsignificant except in LVM (g), and interventricular septum as it was significant. Moreover, in left ventricular end-diastolic diameter and left ventricular end-systolic diameter, there was a highly significant difference ($P < 0.001$).

In our study, we found eccentric LVH was predominant (38.9%) compared with concentric LVH (13.9%) and concentric remodeling (8.3%), signifying that volume overload with high cardiac output is a major factor in children with CKD. This is similar to the study by Adiele DK *et al*. who found that eccentric LVH was predominant (33.3%) compared with concentric LVH (16.7%), signifying that volume overload with high cardiac output is a major factor in Nigerian children with CKD. In contrast, concentric LVH, which occurs owing to excessive pressure (hypertension) on the ventricular muscles, is associated with increased incidence of cardiac ischemia and sudden death [10]. There are varying reports as to whether eccentric or concentric LVH is more common in children [11]. Generally, reports from the developed part of the world show more of concentric hypertrophy [12] which could be because they can afford chronic dialysis and ultrafiltration with resultant marked reduction in volume overload. This is not an absolute finding as other authors in Europe and USA documented predominance of eccentric LVH [13,14].

Conclusion and recommendation

(1) Early and regular echocardiographic studies of all children with CKD on hemodialysis, as they are prone to the development of cardiac dysfunctions in the early state of the disease
(2) Strict control of BP is known to be one of the best practices to prevent LVH because BP control should not be a difficult target to be reached to modulate ventricular hypertrophy and affect cardiovascular morbidity in uremic patients
(3) Evaluation and treatment of anemia in children with CKD, as it is an important factor related to uremia that also contributes to LVH.

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Conflicts of interest

There are no conflicts of interest.

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