Original Article

Study The Influence of Chronic Kidney Disease in Children on Cardiac Function and Cardiac Biomarkers.

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ABSTRACT

Introduction: Chronic kidney disease (CKD) in children poses a significant health challenge, potentially affecting cardiac function.

Aim of the study: To investigate the impact of chronic kidney disease in children on cardiac functions using 2D echocardiography and tissue Doppler, as well as measuring cardiac biomarkers (Troponin I & CK-MB) to correlate the results with the degree of cardiac affection.

Methods: This cross-sectional study conducted at the pediatric nephrology unit of our university hospital from February 1, 2022, to January 31, 2023. Patients aged 1 year to 18 years diagnosed with CKD were included, with a control group matched for age and sex. Comprehensive medical history, systemic examinations, routine assessments, and cardiac evaluations with echocardiography were performed. Cardiac biomarkers were measured at the beginning of the study and after 6 months.

Results: The study revealed higher systolic blood pressure, altered growth patterns, and a variety of etiologies for CKD. Significant differences were observed in serum creatinine, eGFR, serum CKMB activity, and Troponin I level between patients and controls. Echocardiographic parameters such as IVSD (interventricular septum thickness), LVPWD (left ventricular posterior wall thickness), and LVMI (left ventricular mass index) were significantly higher in the CKD group. Tissue Doppler analysis indicated diastolic dysfunction in patients with CKD, with correlations between biomarker levels and cardiac parameters.

Conclusion: Children with CKD exhibit notable cardiac alterations, as evidenced by elevated biomarker levels and echocardiographic findings. Hypertension, CKMB, and Troponin I emerge as significant predictors of cardiac affection in this population.

Keywords: Chronic Kidney Disease; Echocardiography; Cardiac Function.

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INTRODUCTION

Chronic kidney disease (CKD) is characterized by a glomerular filtration rate < 60 mL/min/1.73 m^2 persisting for over 3 months and impacting overall health. The intricate relationship between the cardiovascular system and the kidneys contributes to a complex interplay between heart and kidney function, acknowledged in literature as independent factors influencing each other's morbidity. [1] CKD patients face an increased cardiovascular risk, presenting with conditions such as coronary artery disease, heart failure, arrhythmias, and sudden cardiac death. Notably, the risk is significantly elevated in advanced CKD stages (stages 4–5), although even early CKD stages (stages 1–3) show a higher incidence of cardiovascular events compared to the general population. Cardiovascular disease plays a major role in CKD-related deaths, underscoring the profound impact of this intricate interconnection on patient outcome [2].

CVD in CKD is influenced by two major mechanisms. Firstly, the kidneys respond to injury or insufficiency by releasing hormones, enzymes, and cytokines, causing distinct vascular changes. Secondly, CKD-associated mediators and hemodynamic alterations contribute to cardiac damage. CKD induces a chronic proinflammatory state, fostering vascular and myocardial remodeling processes that lead to atherosclerotic lesions, vascular calcification, vascular senescence, myocardial fibrosis, and calcification of cardiac valves [2]. This systemic impact mirrors an accelerated aging of the cardiovascular system. Patients with CKD exhibit myocardial changes, including pathological fibrosis with collagen deposition between capillaries and cardiomyocytes, and cardiac hypertrophy, representing the hallmarks of uremic cardiomyopathy. [3]

It is well known that cardiac biomarkers are often increased in patients with impaired renal function, which makes the interpretation of these biomarkers ambiguous, and the diagnosis of CVD is challenging in patients with impaired renal function.[4] The reduced eGFR may cause myocardial injury via chronic low-grade inflammation and endothelial dysfunction and may also reduce the renal elimination of cardiac biomarkers.[5]

The purpose of this study was to investigate the impact of chronic kidney disease in children on cardiac functions using 2D echocardiography and tissue Doppler, as well as measuring cardiac biomarkers (Troponin I & CK-MB) to correlate the results with the degree of cardiac affection.

METHODS

This cross-sectional study, conducted from February 1, 2022, to January 31, 2023, at the Pediatric Nephrology Unit of our University Hospital, aimed to explore the influence of CKD on cardiac functions in children. Inclusion criteria were children aged 1 year to 18 years, diagnosed with CKD for 1 year before the study at our University Hospital with eGFR <15mL/min/1.73m2 according to Schwartz formula [6]: eGFR= k×(Height in cm)÷ serum creatinine. K=0.45 in term infant to 1 year of age, K=0.55 in chidren aged 1 to 12 years and adolescent girls and K=0.7 in adolescent boys. Exclusion criteria were acute kidney injury, infants under 1 year, age exceeding 18 years and known congenital or acquired heart disease.

Participants were categorized into two groups: Group I consisted of 24 patients with chronic kidney disease undergoing

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regular hemodialysis in accordance with Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines, utilizing Fresenius 4008B and 5008s machines with specified parameters. Meanwhile, Group II comprised 22 healthy children matched for age and sex, serving as the control group .

Full Medical History: Participants underwent a comprehensive history, including personal details (name, age, sex, and residency), with a specific emphasis on the present illness and symptoms related to renal and heart diseases. The history review concentrated on symptoms associated with renal and heart conditions

Full Regional and Systemic Examination including a thorough evaluation of vital signs, anthropometric measurements, general examination, full cardiac examination, and systemic examination .

Investigations: under complete aseptic condition 6 ml of venous blood was withdrawn from each subject predialysis then it was transferred into two serum gel separator tubes and centrifuged for separation of serum. We divided the serum into two parts. The 1st part of the serum was used for the measurement of serum BUN, creatinine, and electrolytes, 2nd part was used for the measurement of serum cardiac troponin I level by ELISA method using ELISA Kit (ab200016) and creatine kinase (CK-MB) activity level by immunoinhibition method. We measured serum cardiac troponin I and creatine kinase (CK-MB) activity level initialy and after 6 months from beginning of the study .

Conventional Echocardiography: an experienced echocardiologist assessed various cardiac parameters, including left ventricular dimensions and function, right ventricular dimensions and function, and the calculation of LV mass index .

Tissue Doppler analysis: a range of parameters such as S wave, E wave, A wave, isovolumetric contraction time (IVCT), isovolumetric relaxation time (IVRT), ejection time, and myocardial performance index (MPI) were evaluated to provide a comprehensive understanding of cardiac function.

Statistical analysis

The collected data underwent thorough revision, coding, and tabulation using the Statistical Package for Social Science (IBM Corp. Released 2017, IBM SPSS Statistics for Windows, Version 25.0, Armonk, NY: IBM Corp.). Subsequently, the data were presented, and appropriate analyses were conducted based on the nature of the obtained data for each parameter. Descriptive statistics, including mean, standard deviation (±SD), standard error (±SE), median, range, frequency, and percentage, were employed for numerical and non-numerical data description. Analytical statistics involved the utilization of various tests, such as the Student T Test, Mann Whitney Test, Wilcoxon Test, Chi-Square test, Fisher-Exact test, and correlation analysis, to assess statistical significance, differences, and relationships between variables.

The probability of results was determined with a significance level set at $p < 0.05$ and a confidence interval of 95%. Additionally, receiver operator characteristic (ROC) curve analysis was performed, evaluating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and the area under the curve (AUC) to determine the accuracy of the diagnostic test. The AUC values were interpreted as follows: AUC < 0.5 (bad), AUC: 0.5-0.69 (fair), AUC: 0.7-0.8 (good), AUC: 0.8-0.9 (very good), AUC > 0.9 (excellent).

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RESULTS

Statistically, there were no significant differences in sex and age among the studied groups. However, there were significant differences in weight and height between the groups, with the control group exhibiting higher values than the CKD group. Additionally, a highly significant difference was observed in systolic blood pressure, which was higher in the CKD group compared to the control group **Table 1.** Twenty-three patients complained of growth failure, 23 patients experienced oliguria, 22 patients reported dyspnea, 18 patients exhibited generalized edema, and 9 patients developed skeletal deformities. One patient complained of polyuria **.**

Patients demonstrated significantly higher serum creatinine values and lower eGFR compared to the control group. Moreover, there were significantly higher values of CKMB, Troponin I. **Table 2**, IVSD (interventricular septum thickness), LVPWD (left ventricular posterior wall thickness), LVIDs (left ventricular internal dimension at end systole) and LVMI (left ventricular mass index) in CKD patients compared to the control group. However, there were no significant differences in TAPSE values, LV diastolic function, and RV diastolic function between the two groups. **Table 3, and Table 4.**

Tissue Doppler analysis revealed significant differences in E wave, ICT, IRT, and MPI in the left ventricle (septum, posterior wall), and right ventricle (anterior wall), indicating diastolic dysfunction in CKD patients **Figure 1**. While **Figure 2** depicts a significant correlation between CKMB levels and LVMI among CKD patients. Troponin I level correlated significantly with various clinical and laboratory parameters, as well as tissue Doppler parameters, systolic function parameters, as detailed in **Tables 5** and **Table 6.**

Table 7 illustrates the diagnostic accuracy of CKMB and Troponin I in detecting cardiac affection in CKD patients. CKMB showed 80.7% accuracy (AUC 0.938), while Troponin I showed 88.66% accuracy (AUC 0.964) at the best cutoff levels. Furthermore, logistic regression analysis indicated that hypertension, CKMB levels, and Troponin I were significant predictors of cardiac affection in CKD patients, while age and gender were deemed insignificant **Table 8.**

Table 1. Comparison between CKD patients and control group regarding to demographics, anthropometric measures and Vital signs.

	CKD N = 24		Control N= 22		Test	P
	No.	%	No.	%		
Sex						
Male	15	62.5	14	63.6%	x^2= 0.006	0.936
Female	9	37.5	8	36.4%		
Age (years)						
Mean ± SD.	14.13 ± 3.38		12.27 ± 4.09		t= 1.503	0.140
Median	14.50		13.0			
Min. – Max.	7.0 – 18.0		2.0 – 18.0			
Weight (kg)						
Mean ± SD.	20.12 ±5.17		26.91 ± 15.20		t= 1.411	0.048*
Median	21.3		23.0			
Min. – Max.	11.40-30.00		8.0 – 50.0			
Height (cm)						
Mean ± SD.	93.16 ±10.18		118.36 ± 31.39		t= 2.541	0.028*
Median	91		125.0			
Min. – Max.	77.00-114.10		77.0 – 165.0			

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Table 1. Comparison between CKD patients and control group regarding to demographics, anthropometric measures and Vital signs. **(Continued)**

	CKD N = 24	Control N= 22	Test	P
Heart rate (min)				
Mean ± SD.	85.0 ± 7.32	85.82±6.26	T=0.406	0.687
Median	84.0	87		
Min. – Max.	68.0 – 100.0	74.00-93.00		
Systolic BP (mmHg)				
Mean ± SD.	117.08 ± 22.36	103.64±10.93	T=2.624	0.013*
Median	120.0	100		
Min. – Max.	80.0 – 170.0	90.00-120.00		
Diastolic BP (mmHg)				
Mean ± SD.	72.71 ± 16.08	75.64±6.57	T=0.820	0.418
Median	75.0	74		
Min. – Max.	40.0 – 100.0	65.00-85.00		
Hypertension	No. (%)			
No	16 (66.7%)	22 (100%)	X^2=8.877	0.004*
Yes	8 (33.3%)	0 (0%)		

Min.: Minimum, Max.: Maximum, SD.: Standard deviation, t, student t test; x^2: Chi-Square, FE: Fisher Exact, P: Comparing between CKD patients and control, *: Significant when p value <0.05. BP: blood pressure

Table 2.: Comparison between CKD patients and control group regarding to creatinine level, eGFR, CKMB activity level, troponin I level.

	CKD N = 24	Control N = 22	Test	P
Creatinine (mg/dL) Mean ± SD.	9.16 ± 2.42	0.54 ± 0.18	t= 17.413	<0.001*
eGFR (ml/min/1.73) Mean ± SD.	6.14 ± 1.33	91.55 ± 22.29	t= 17.939	<0.001*
CKMB (U/L)	**CKD N = 24**	**Control N = 22**	**Test**	**P1**
At presentation Mean ± SD.	39.33 ± 2.73	8.73 ± 0.49	U= 0.02	<0.001*
After 6 months Mean ± SD.	44.58 ± 2.91	8.86 ± 0.48	U= 0.01	<0.001*
Z	276.0	1.342		
P2	<0.001*	0.180		
Troponin I (ng/ml)	**CKD N = 24**	**Control N = 22**	**Test**	**P1**
At presentation Mean ± SD.	0.118 ± 0.010	0.021 ± 0.001	U= 0.02	<0.001*
After 6 months Mean ± SD.	0.129 ± 0.010	0.019 ± 0.001	U= 0.01	<0.001*
Z	36.0	2.50		
P2	0.011*	P2		

SD.: Standard deviation, t: Student t test, P: Comparing between CKD patients and control, *: Significant when p value <0.05, U: Mann-Whitney, Z: Wilcoxon test, P1: Comparing between CKD patients and control, P2: Comparing between before and after 6 months

Table 3: Comparison between CKD patients and control group regarding to echocardiography parameters (systolic function)

Systolic function (LT VENT)	CKD N = 24	Control N = 22	Test	P
IVSD (cm) Mean ± SD.	0.98 ± 0.26	0.67 ± 0.17	t= 4.241	<0.001*
LVPWD (cm) Mean ± SD	1.13 ± 0.12	0.56 ± 0.05	U= 27.0	<0.001*
LVIDd (cm) Mean ± SD.	3.98 ± 0.68	3.57 ± 0.50	t=1.790	0.083
LVIDs (cm) Mean ± SD.	2.49 ± 0.59	1.99 ± 0.44	t=2.521	0.017*
FS (%) Mean ± SD.	36.69 ± 8.04	40.43 ± 5.32	t= 1.402	0.170
EF (%) Mean ± SD.	66.37 ± 11.05	71.95 ± 5.88	t= 1.566	0.127
LVMI (g/m^2) Mean ± SD.	121.41 ± 11.39	62.69 ± 3.72	U= 28.0	<0.001*
Systolic function (RT VENT)	**CKD N = 24**	**Control N = 22**	**Test**	**P**
TAPSE (mm) Mean ± SD.	15.05 ± 1.18	17.18 ± 1.15	U= 182.5	0.072

SD.: Standard deviation, t: Student t test, P: Comparing between CKD patients and control, *: Significant when p value <0.05, U: Mann-Whitney, Z: Wilcoxon test, P1: Comparing between CKD patients and control, P2: Comparing between before and after 6 months. IVSD=interventricular septum thickness, LVPWD= left ventricular posterior wall thickness, LVIDd= left ventricular internal dimension at end diastole, LVIDs= left ventricular internal dimension at end systole, FS%= fraction

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Table 4 : Comparison between CKD patients and control group regarding to echocardiography parameters (diastolic function)

Diastolic function (LT VENT)	CKD N = 24	Control N = 22	Test	P
E WAVE (cm/sec) Mean ± SD.	84.68 ± 21.97	96.90 ± 20.41	t= 1.950	0.058
A WAVE (cm/sec) Mean ± SD.	65.24 ± 16.40	59.99 ± 5.62	t= 1.477	0.151
E/A Ratio Mean ± SD.	1.38 ± 0.10	1.59 ± 0.07	U= 181	0.067
DT (deceleration time msec) Mean ± SD.	122.13 ± 26.52	1 ± 22.42	t= 1.414	0.164
Diastolic function (RT VENT)	**CKD N = 24**	**Control N = 22**	**Test**	**P**
E WAVE(cm/esc) Mean ± SD.	71.37 ± 16.03	71.48 ± 10.750	t=0.028	0.978
A WAVE (cm/sec) Mean ± SD.	60.16 ± 14.39	59.90 ± 17.76	t=0.055	0.956
E/A Ratio Mean ± SD.	1.24 ± 0.08	1.25 ± 0.07	U=257	0.877
DT (deceleration time mesc) Mean ± SD.	120.75 ± 23.22	125.27 ± 25.16	t=0.634	0.529

SD.: Standard deviation, t: Student t test, P: Comparing between CKD patients and control, *: Significant when p value <0.05, U: Mann-Whitney, Z: Wilcoxon test, P1: Comparing between CKD patients and control, P2: Comparing between before and after 6 months.

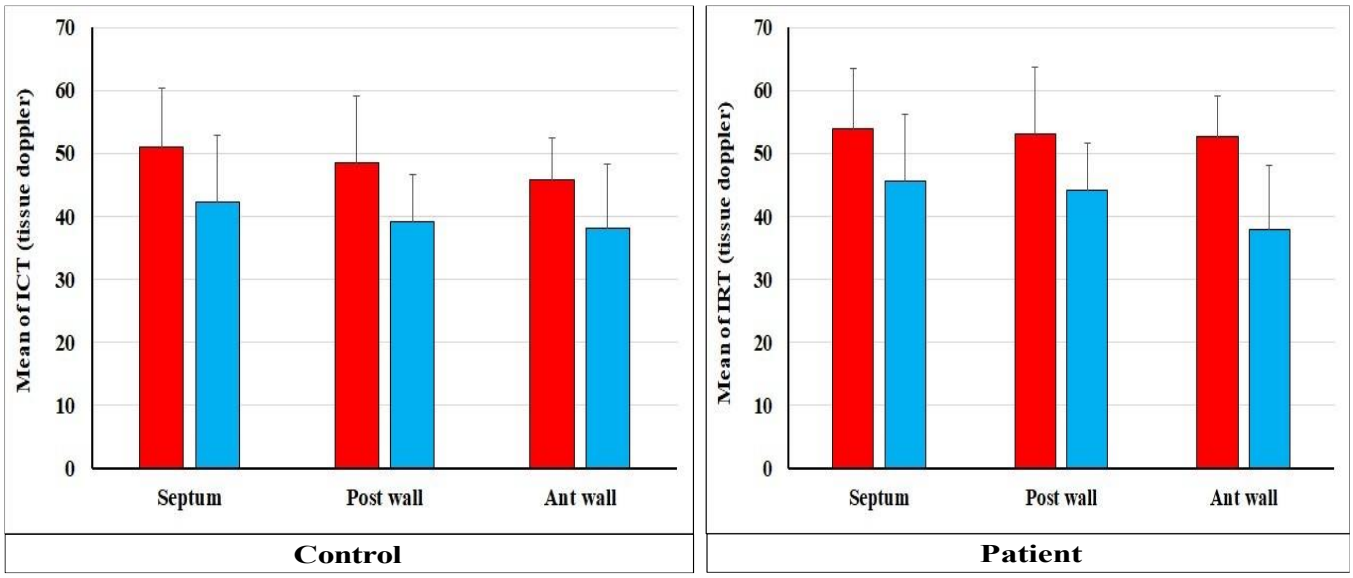

Figure 1: Bar chart for comparing between CKD patients and control group regarding to tissue doppler (ICT) and (IRT).

OR, odds ratio; CI, confidence interval.

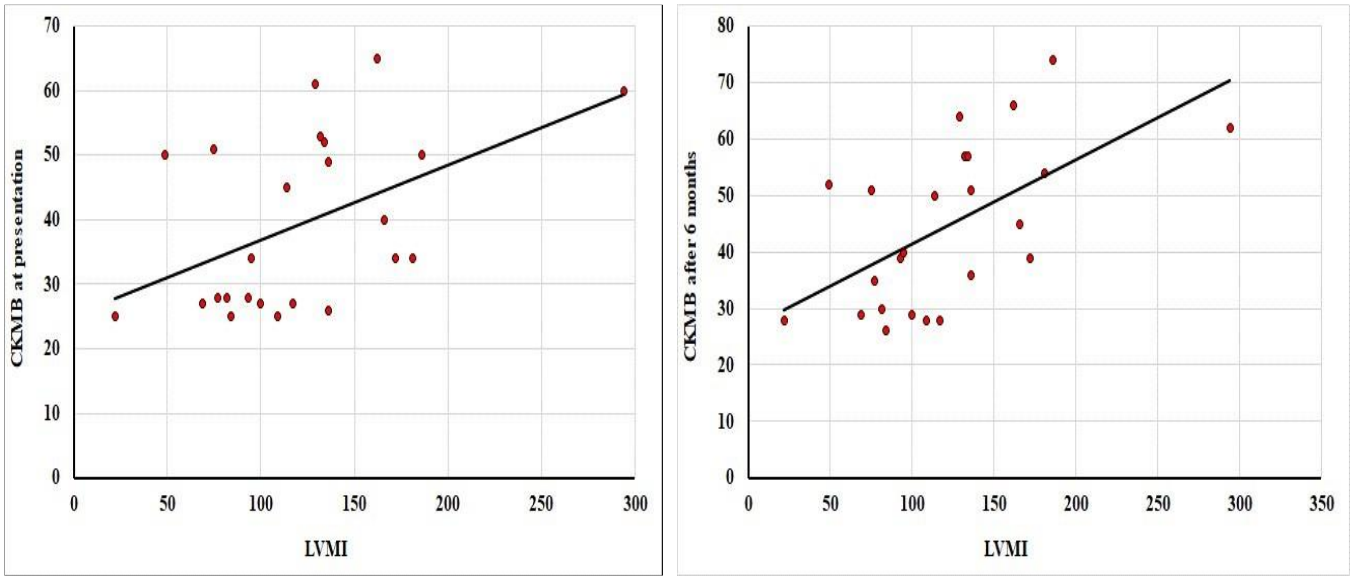

Figure 2: Correlation between CKMB at presentation, after 6 months and LVMI among patients with CKD.

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Table 5: Correlation between troponin I and tissue doppler among patients with CKD.

Tissue doppler	Troponin I			
	At presentation		After 6 months	
	ρ	*p*	*ρ*	*p*
Left ventricle				
S wave (cm/sec)	-0.419	0.041*	-0.329	0.116
E wave (cm/sec)	-0.648	0.001*	-0.514	0.010*
A wave (cm/sec)	-0.325	0.121	-0.199	0.351
ICT (msec)	-0.079	0.714	-0.202	0.343
IRT (msec)	0.423	0.039*	0.446	0.029*
ET (msec)	0.187	0.382	0.203	0.342
MPI (Tie index)	0.043	0.841	0.117	0.586
Right ventricle				
S wave (cm/sec)	0.171	0.424	0.290	0.169
E wave (cm/sec)	-0.156	0.467	0.033	0.877
A wave (cm/sec)	-0.132	0.539	-0.054	0.803
ICT (msec)	0.123	0.566	0.024	0.912
IRT (msec)	0.562	0.004*	0.531	0.008*
ET (msec)	0.252	0.235	0.294	0.164
MPI (Tie index)	-0.135	0.528	-0.031	0.886

ρ, Spearman's correlation coefficient, *: Significant when p value < 0.05.

Table 6: Correlation between troponin I and echocardiography parameters (systolic function), (diastolic function) among patients with CKD.

	Troponin I			
	At presentation		After 6 months	
	ρ	*p*	*ρ*	*p*
IVSD (cm)	0.397	0.055	0.452	0.027*
LVPWD (cm)	0.509	0.011*	0.566	0.004*
LVIDd (cm)	0.276	0.192	0.240	0.258
LVIDs (cm)	0.335	0.110	0.336	0.109
FS%	-0.183	0.393	-0.060	0.780
EF%	-0.194	0.364	-0.088	0.682
LVMI (g/m^2)	0.550	0.005*	0.707	<0.001*
TAPSE (mm)	0.139	0.516	0.243	0.253
	Troponin I			
	At presentation		**After 6 months**	
	ρ	*p*	*ρ*	*p*
LT VENT				
E WAVE (cm/esc)	0.008	0.971	0.073	0.734
A WAVE (cm/esc)	-0.135	0.530	0.026	0.903
E/A Ratio	0.042	0.846	0.019	0.929
DT (deceleration time)	0.244	0.251	0.053	0.805
RT VENT				
E WAVE (cm/esc)	-0.339	0.105	-0.311	0.139
A WAVE (cm/esc)	0.030	0.889	0.009	0.968
E/A Ratio	-0.247	0.245	-0.156	0.465
DT (deceleration time)	0.020	0.925	-0.128	0.552

ρ, Spearman's correlation coefficient. *: Significant when p value < 0.05.

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Table 7: Validity of CKMB and troponin I in diagnosing cardiac affection in patient with CKD.

	CKMB	Troponin I
AUC	0.938	0.964
95% CI	0.865-1	0.913-1
P1	<0.001	<0.001
Cut off	>26.75	>0.080
Sensitivity (%)	80.5	94.44
Specificity (%)	80.9	82.35
PPV (%)	81.7	85.00
NPV (%)	79.7	93.33
Accuracy (%)	80.7	88.66
P2	0.	472

AUC, area under ROC curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value, P1, probability of AUC, P2, comparison of AUC of CKMB and AUC of troponin I

Table 8: Logistic regression analysis for prediction of risk factors for cardiac affection in patient with CKD

	Univariable			Multivariable		
	p	**OR**	**95% CI**	***p***	**OR**	**95% CI**
Age	0.336	1.055	0.946-1.177			
Gender	0.826	1.101	0.466-2.603			
Hypertension	0.025	3.993	1.189-13.409	0.042	1.213	1.105-9.326
CKMB	0.014	1.142	1.027-1.270	0.010	1.929	1.175-2.306
Troponin I	0.027	2.085	1.749-3.483	0.029	1.697	3.713-7.758

OR, odds ratio; CI, confidence interval.

DISCUSSION

Chronic Kidney Disease (CKD) is a global health concern, on the verge of an epidemic, marked by a gradual decline in kidney function over three months, as per KDIGO guidelines. Pediatric patients with severe CKD face a staggering 30-fold increase in mortality risk, predominantly due to cardiovascular disease (CVD), which constitutes 25– 50% of deaths in this demographic. Studies, including the US Renal Data System and ANZDATA Registry, highlight the alarming prevalence of CVD-related deaths in children on dialysis, emphasizing the urgent need for research [7].

The current study investigates the impact of CKD on cardiac function in 24 pediatric patients undergoing hemodialysis, comparing them with a control group of 22 healthy children. Among the pediatric patients in the study, CKD had diverse causes, with vesicoureteric reflux, failed renal transplantation, congenital kidney anomalies, post-COVID-19 infection, obstructive uropathy, nephrotoxic drug exposure, and hemolytic uremic syndrome identified, while a significant portion (29.1%) had an unknown etiology. In agreement with study [8] growth failure was evident in CKD patients, as reflected in lower height and weight compared to the control group. Hypertension was prevalent in 33.3% of CKD patients, with elevated systolic blood pressure observed, mirroring findings in a study [9] on children with CKD. Abnormal vascular regulation, fluid overload, increased cardiac output, peripheral vascular resistance, and the activation of the renin-angiotensin-aldosterone system were implicated in CKD-related hypertension,

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consistent with research [10]. The multifactorial etiology of growth failure in CKD includes factors like age at CKD onset, residual renal function, metabolic derangements, renal osteodystrophy, and disruptions in the growth hormone-insulin-like growth factor-1 axis, as noted in studies [9],[11].

The study reveals a significant elevation in serum CKMB activity and Troponin I levels in pediatric patients with CKD compared to the control group, both at the beginning of the study and after 6 months. This aligns with a study [4] on cardiac biomarkers in individuals with lower eGFR., consistent with a study [12] supports the elevated troponin I levels in children on hemodialysis, conversely another study findings [13] in CKD patients. A study, however, reports normal cardiac troponin I levels in Egyptian children with CKD on regular hemodialysis, emphasizing the variability in results attributed to different patient categories and diagnostic tests. The discrepancy underscores the importance of considering factors such as sampling time and ultrafiltration coefficient in hemodialysis patients when interpreting troponin measurements.

The 2D echocardiography findings in the current study highlight significant differences in left ventricular parameters between pediatric patients with CKD and the control group. These differences include increased IVSD, LVPWD, LVIDs, and LVMI in CKD patients, indicative of LVH (left ventricular hypertrophy). LVH is a common occurrence in CKD, believed to sustain cardiac function and reduce left ventricular wall stress during elevated afterload and preload conditions. The pathophysiological factors contributing to LVH in CKD involve increased systemic arterial resistance, elevated blood pressure, aortic calcification, and activation of the intracardiac renin-angiotensin system. Additionally, intravascular volume expansion, secondary anemia, and arteriovenous fistulas contribute to eccentric or asymmetric LV remodeling. Contrary to our results, a study [14] observed an association between right ventricular dysfunction and CKD, using TAPSE as a measure, suggesting variability in findings across studies.

In current study, there were no significant differences in E waves, A waves, E/A ratio, and deceleration time (DT) for both left and right ventricular diastolic function between pediatric patients with CKD and the control group. However, tissue Doppler findings indicated significant differences in various parameters, including E wave, isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT), and myocardial performance index (MPI), suggesting diastolic dysfunction in CKD patients. These findings align with studies in 2021 and 2020 [15], which also emphasized the impact of CKD on myocardial performance index. In our study, CKMB levels showed a positive correlation with systolic blood pressure and LVMI but no significant correlation with diastolic function in 2D echocardiography, consistent with a study [16] in adult CKD patients, where systolic and diastolic dysfunction were associated with higher CKMB levels over a follow-up period.

In current study, a significant correlation was observed between CKMB levels and S wave of the anterior and posterior walls of the heart, as well as ejection time of the anterior wall in tissue Doppler.

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This contrasts with a study [17], which showed no correlation between CKMB levels and echocardiographic parameters in CKD. On the other hand, our study revealed correlations between Troponin I levels and various systolic and diastolic parameters, both initially and after 6 months among CKD patients, aligning with another study [18] observations of Troponin I's association with LVMI and LVEF (left ventricular ejection fraction). However, unlike their study, we found no correlation between Troponin I levels and LVEF. Current study demonstrated correlations between Troponin I levels and diastolic function parameters in the tissue doppler. These findings parallel with a study [19] on pediatric chronic renal failure patients, where cardiac Troponin levels correlated with cardiovascular abnormalities.

The Current study demonstrated the diagnostic validity of CKMB and Troponin I in detecting cardiac involvement in patients with CKD with sensitivities of 80.5% and 94.44%, specificities of 80.9% and 82.35%, and accuracies of 80.7% and88.66%, respectively. The cutoff values were determined as 26.5 IU/dl for CKMB and 0.08 ng/ml for Troponin I. Hypertension, CKMB levels, and Troponin I were identified as significant predictors of cardiac involvement in CKD patients, while age and gender were deemed insignificant. Our findings align with a study [20] on specificity of cardiac troponin I and creatine kinase-MB isoenzyme in asymptomatic long-term hemodialysis patients. A study [21] supports the associations between cardiac biomarkers and cardiovascular disease in CKD patients. Additionally, a study [22] demonstrated the reliability of cardiac Troponin I across the spectrum of renal disease, including ESRD in dialysis-dependent patients. Elevated cardiac troponins may indicate conditions beyond acute coronary syndrome, such as heart failure, cardiomyopathies, myocarditis, tachyarrhythmia, and pulmonary embolism, even in healthy individuals after strenuous exercise. The prognostic value of routine cTn measurements in CKD patients has been emphasized, with elevated levels associated with a higher risk of coronary artery disease and worse prognosis. However, the precise mechanisms leading to elevated cTn levels in the context of renal dysfunction remain unclear, and caution is needed in interpreting results without consideration of the broader clinical context.

LIMITATIONS OF THE STUDY

This was a single center study with a relatively small sample size which may limit the generalizability of the findings to a broader population. Exclusion criteria, such as patients with known congenital or acquired heart diseases, might have excluded potential contributors to cardiac dysfunction. The study's duration may not capture long-term changes in cardiac function.

RECOMMENDATIONS

Further studies with multi-center corporations and larger sample sizes can improve the generalizability of the results. Additionally, extending the follow-up period beyond the current study duration could provide insights into the long-term trajectories of cardiac function in children with chronic kidney disease (CKD).

While Troponin I and CK-MB are valuable indicators of cardiac injury, a more comprehensive evaluation of cardiac health could involve assessing additional biomarkers such as B-type natriuretic

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peptide (BNP) and NT-proBNP for heart failure severity, myoglobin for early myocardial injury, CRP for inflammation, D-dimer for thrombotic risk, lipid profile for lipid abnormalities, Troponin T for an alternative troponin isoform, and galectin-3 for fibrosis-related cardiac remodelling.

Given the potential impact of medications on cardiac health, future studies should explore the specific medications used by the study participants to better understand their influence on cardiac outcomes.

CONCLUSION

In conclusion, the current study showed a significant correlation between CKD in pediatric patients and cardiac dysfunction, as evidenced through meticulous assessments employing 2D echocardiography, tissue Doppler, and cardiac biomarkers. Clinical manifestations, diverse etiologies, and elevated cardiac biomarkers, notably CKMB and Troponin I, illuminate the intricate relationship between renal and cardiac functions in this population. The identification of significant predictors for cardiac affection, including hypertension, CKMB activity, and Troponin I level, serves as crucial risk stratification markers.

ABBREVIATIONS

CKD	Chronic kidney disease
eGFR	Estimated glomerular filtration rate
IVSD	interventricular septum thickness
LVPWD	left ventricular posterior wall thickness
LVMI	left ventricular mass index
CVD	Cardiovascular disease
KDIGO	Kdney disease improving global outcome
ANZDATA	Australian and New Zealand dialysis and transplant registry
LVH	Left ventricular hypertrophy
LV	Left ventricle
TAPSE	Tricuspid annular plane systolic excursion
ESRD	End stage renal disease

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AUTHORS' CONTRIBUTIONS

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Conception and design of study: W.E. A, E G.A
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STATEMENTS

Ethics approval and consent to participate

This study protocol and the consents were approved and deemed sufficient by the Ethical

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Committee of Benha University and informed written consent was obtained in every case from their legal guardians.

Consent for publication

The contents and material of the manuscript have not been previously reported at any length or being considered for publishing elsewhere.

Availability of data and material

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