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Left Ventricular Dysfunction in Different Stages of Chronic Kidney Disease

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ABSTRACT

BACKGROUND: *Chronic kidney disease (CKD) is becoming a significant global public health concern. According to the Global Burden of Disease study, it was responsible for approximately 1.4 million deaths worldwide in 2021, marking a 20% increase since 2010—one of the most substantial rises among leading causes of death. Premature cardiovascular disease remains the primary cause of illness and death in chronic kidney disease patients, often leading to fatal outcomes before they reach end-stage kidney disease. Therefore, early intervention is crucial to prevent cardiovascular complications in chronic kidney disease patients. A two-dimensional echocardiogram serves as a simple, non-invasive tool to evaluate left ventricular structure and function, aiding in the early identification of individuals at risk for cardiovascular complications.*

METHODS: *A Cross-sectional study was conducted among 88 patients diagnosed with chronic kidney disease in Adichunchanagiri Hospital and Research Centre. Relevant information was collected from each subject. In all the selected subjects detailed history was taken and physical examination was done through a pretested and structured pro forma. Every patient was subjected to relevant investigations. All of the above was done after taking an informed consent. The percentage of patients with ventricular dysfunction was estimated in each stage and grade of CKD and association between left ventricular dysfunction and stages of CKD was done.*

RESULT: *In this study, the largest proportion of participants (50%) were classified as G5A1, followed by 19.32% as G4A1, 15.91% as G5A2, and 1.14% as G5A3. Overall, 67.05% of the study population had Grade 5 CKD, while 23.86% had Grade 4 CKD. Left ventricular systolic dysfunction was observed in 30.68% of participants, while left ventricular diastolic dysfunction was noted in 64.78%. Among those with CKD stage 5, 28.81% had systolic dysfunction, compared to 38.09% in stage 4 and 28.57% in stage 3b. Diastolic dysfunction was present in 59.32% of stage 5 patients, 76.19% of stage 4 patients, and 71.42% of those in stage 3b.There was a significant association noted between renal parameters and left ventricular dysfunction . No association was noted between staging and left ventricular dysfunction.*

CONCLUSION: *Left ventricular dysfunction is common in patients with CKD. Since there is no association proved between the stages of CKD and left ventricular dysfunction statistically, a strong advocation for early screening is needed. Two-dimensional echocardiogram is a good non-invasive investigation for the same. Patients also need to be screened for risk factors augmenting the ventricular dysfunction.*

Keywords: *Chronic Kidney disease (CKD), Left ventricular systolic dysfunction, Left ventricular diastolic dysfunction, Two-dimensional echocardiogram*

1. INTRODUCTION

kidney disease (CKD), whose incidence continues to rise globally, independently increases the risk of coronary artery disease (CAD), heart failure (HF), and mortality, regardless of traditional cardiovascular risk factors [1–4]. Left ventricular (LV) diastolic dysfunction usually occurs in chronic kidney disease patients and is related to heart failure (HF) and increased mortality [5]. Left ventricular diastolic dysfunction (LVDD) is evident in patients with early-stage chronic renal disease [6]. 15% of patients initiating dialysis therapy exhibit left ventricular systolic dysfunction (LVSD), although the incidence of diastolic dysfunction at the commencement of dialysis is significantly greater.[7] Systolic or diastolic dysfunction may result in clinically manifest congestive heart failure [8]. Left ventricular systolic dysfunction (LVSD) is frequently linked to severe coronary artery disease and is a significant prognostic factor. Diastolic dysfunction of the left ventricle in chronic kidney disease patients is multifaceted [9]. Studies suggest that the advancement of chronic kidney disease stages may impact the rise in left ventricular (LV) preload [10].

Additionally, left ventricular hypertrophy (LVH), coronary artery disease, microvascular abnormalities, interstitial fibrosis, altered fluid and electrolyte metabolism, and neurohumoral changes may contribute to the onset of diastolic dysfunction of the left ventricle in patients of chronic kidney disease [11]. The excessive activation of the rennin–angiotensin–aldosterone system (RAAS) may significantly aid to the pathomechanism, since even moderate chronic kidney disease (CKD) leads to early cardiac fibrosis, accompanied by little left ventricular diastolic dysfunction and retained systolic function [12].
The intent of this study was to evaluate left ventricular dysfunction in chronic kidney disease patients, including those undergoing dialysis, as the correlations between left ventricular dysfunction, two dimensional echocardiographic parameters and renal function remain little explored.

2. MATERIALS AND METHODS

A Hospital based Cross sectional study was conducted at Adichunchanagiri hospital and Research centre, BG Nagara, Mandya for a period of 18 months. Institution ethical committee clearance was taken. Inpatient and outpatient proved to have chronic kidney disease after relevant investigation were included after taking informed consent. KDIGO staging was done to categorize the patient into different stages of chronic kidney disease. These patients underwent two-dimensional echocardiogram investigation to see for left ventricular dysfunction.

SOURCE OF DATA

Study place: Department of General Medicine, Adichunchanagiri Hospital and Research Center, B G Nagara-571448
Study Design: Hospital Based Cross Sectional Study
Study Period: May 2023 to November 2024 (18 months)
Sample Size:
In tertiary care centre, Adichunchanagiri hospital and research centre the prevalence of the disease is 5% in year 2022.
$S=Z^2*P*Q/D^2$
S=sample size
Z=level of confidence according to standard normal distribution (it is 1.96 for 95% confidence level)
P=proportion of prevalence =5% becomes .05
Q=1-P =1-.05 =.95
D= Margin of absolute error =.05
$S=Z^2PQ/D^2$
S= (1.96 x 1.96 x .05 x .95) / .05 x .05 =73
Hence an approximated sample size of 75 was taken
Study population:
The study was conducted among chronic kidney disease patients visiting Department of General Medicine, Adichunchanagiri hospital and research centre, BG Nagara, Mandya

METHOD OF COLLECTION OF DATA

In all subjects meeting the inclusion criteria after taking informed consent, a detailed history was taken. General physical examination was done. They underwent relevant investigations.
Investigations included
a) Two-dimensional echocardiogram was done according to the standard guidelines. All measurements were made following American Society of Echocardiography (ASE)
recommendations. Patients with EF < 50%. Diastolic dysfunction was graded according to the ratio of transmitral early (E) and late (A) flow velocities (E/A ratio). E/A ratio <0.8 is termed Grade 1, 0.8-1.5 termed Grade 2 and >2 termed as Grade 3 diastolic dysfunction. To differentiate Grade 1 and grade 2 further E/e'>14 and Tricuspid regurgitation velocity(>2.8m/s) was used.
b) Blood samples were collected from all participants to estimate

- Hemoglobin
- Blood urea
- Serum creatinine.
- Urine sample will be analysed for albuminuria.

c) Ultrasonography of abdomen and pelvis was done to collect evidence for chronic kidney disease
d) 12 -lead Echocardiography was done

Cases were classified into different stages of chronic kidney disease based on estimated Glomerular filtration rate (eGFR). eGFR was calculated using Modification of Diet Renal Disease study (MDRD) formula.

Modification of Diet in Renal Disease (MDRD) study equation:

eGFR (ml / min / 1.73 m2) = 186.3 × (Plasma creatinine) $^{-1.154}$× (age) $^{-0.203}$

x 0.742 if female

x 1.21 if African American

INCLUSION CRITERIA

Age > 18 years, both sexes, with chronic kidney disease. i.e

Structural or functional abnormalities of the kidneys for 3 months, as manifested by

1. Kidney damage, with or without decreased GFR, as defined by
a. Pathologic abnormalities
b. Markers of kidney damage
c. Urinary abnormalities (proteinuria)
d. Blood abnormalities (renal tubular syndromes)
e. Imaging abnormalities
f. Kidney transplantation
2. GFR <60 ml/min/1.73 m^2, with or without kidney damage

CKD, chronic kidney disease; GFR, glomerular filtration rate; KDIGO, Kidney Disease in Improving Global Outcomes.

3.Patients who agree to give informed consent.

EXCLUSION CRITERIA

1) Age < 18 years and > 80 years
2) Patients with Acute Kidney Injury
3) Patients with history and clinical features suggestive of preexisting cardiac diseases like rheumatic valvular heart disease, congenital heart disease, coronary heart disease, cardiomyopathy, and pericardial diseases.

STATISTICAL ANALYSIS

Data was entered into Microsoft excel sheet. Data was analyzed using descriptive statistics and chi-square test. Qualitative variables were summarized using percentage/proportions and were statistically analyzed using Chi square test and Fischers exact test. Quantitative variables were summarized using mean and standard deviation and statistically analyzed using T test for two groups and ANOVA was applied to assess difference across multiple groups. A p value <0.05 was considered statistically significant. Suitable statistical software – SPSS was utilized for analysis.

3. RESULTS

TABLE 4- AGE

	Age
Minimum	21
Maximum	80
95% Confidence interval for mean	54.36 - 61.09
Mean ± Std.	57.73 ± 15.88

The mean age of the study population was 57.73 ± 15.88 years.

PARAMETERS OF PARTICIPANT GROUP

	Creatinine (mg/dl)	**Urea (Mg/dl)**	**Urine albumin creatinine ratio(uACR)[mg/g]**

Mean	5.17	59.91	66.02
Std. Deviation	2.32	10.26	58.06
Minimum	1.2	38	10
Maximum	9.8	88	310

The mean values of creatinine were 5.17, with mean of urea being 59.91, along with an elevated mean RBS of 139.92, mean Hb 9.61 [low] and elevated mean urine-albumin-creatinine ratio.

TABLE 12 – ESTIMATED GLOMERULAR FILTRATION RATE (eGFR)

	eGFR (mL/min/1.73 $m^{2)}$
Mean	14.47
Std. Deviation	8.32
Minimum	4
Maximum	43

The mean estimated glomerular filtration rate was observed to be 14.47 +/- 8.32, which corresponds to end stage renal disease

STAGING OF CHRONIC KIDNEY DISEASE

Staging	**Frequency**	**Percentage %**
Stage 5	59	67.05%
Stage 4	21	23.86%
Stage 3b	7	7.95%
Stage 3a	1	1.14%

When we stage the patients, it was noted that stage 5 disease was seen 67.05%, followed by stage 4 in 23.86%.

KDIGO GRADING OF CHRONIC KIDNEY DISEASE

Grade	**Frequency**	**Percentage %**
G5A1	44	50%
G4A1	17	19.32%
G5A2	14	15.91%
G3A1	8	9.09%
G4A3	2	2.27%

G4A2	2	2.27%
G5A3	1	1.14%

Most of the study participants were categorised by G5A1 in 50% of the cases, while 19.32% belonged to G4A1, 15.91 % belonged to G5A2 and 1.14 % belonged to G5A3. Most of the study population belonged to Grade 5 which constituted 67.05 %

LEFT VENTRICULAR HYPERTROPHY IN TWO-DIMENSIONAL ECHOCARDIOGRAM

LeftVentricular Hypertrophy	**Frequency**	**Percentage**
Present	51	57.95%
Absent	37	42.05%

LEFT VENTRICULAR (LV)SYSTOLIC DYSFUNCTION

LV Systolic Dysfunction	Frequency	Percentage %
Normal	61	69.32%
Mild	14	15.90%
Severe	9	10.23%
Moderate	4	4.55%

LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN DIFFERENT GRADES OF CKD (KDIGO)

		Left ventricular Systolic Dysfunction	
		Present	Percentage%
Grade	G5A1	16	36.36%
	G5A2	1	7.14%
	G4A1	7	41.17%
	G4A3	1	50%
	G3A1	2	25%

LEFT VENTRICULAR SYSTOLIC DYSFUNCTION IN DIFFERENT STAGES OF CKD.

	Left ventricular Systolic Dysfunction		
		Present	Percentage %
Staging	STAGE 5	17	28.81
	STAGE 4	8	38.09
	STAGE 3b	2	28.57

LEFT VENTRICULAR(LV) DIASTOLIC DYSFUNCTION

LV Diastolic Dysfunction	Frequency	Percentage %
Normal	31	35.23%
Grade 1	39	44.32%
Grade 2	12	13.64%
Grade 3	6	6.82%

LEFT VENTRICULAR(LV) DIASTOLIC DYSFUNCTION IN DIFFERENT GRADES OF CKD (KDIGO)

		LV Diastolic Dysfunction	
		Present	Percentage (%)
Grade	G5A1	28	63.63%
	G5A2	6	42.87%
	G5A3	1	100%
	G4A1	13	76.47%
	G4A2	2	100%
	G4A3	1	50%
	G3A1	6	75%

LEFT VENTRICULAR (LV)DIASTOLIC DYSFUNCTION IN DIFFERENT STAGES OF CHRONIC KIDNEY DISEASE.

		LV Diastolic Dysfunction	
		Present	Percentage %
Staging	STAGE 5	35	59.32%
	STAGE 4	16	76.19%
	STAGE 3a	1	100%
	STAGE 3b	5	71.42%

ASSOCIATION BETWEEN RENAL PARAMETERS AND LEFT VENTRICULAR SYSTOLIC DYSFUNCTION (LVSD)

LVSD	Mean creatinine (mg/dl)	Mean urea(mg/dl)	Mean uACRmg/g)	P value
Normal	3.6	58.8	42	<.001
Mild	4.86	60.2	44.5	
Moderate	4.90	69.75	49	
Severe	5.20	69.90	82.56	

ASSOCIATION BETWEEN RENAL PARAMETERS AND LEFT VENTRICULAR DIASTOLIC DYSFUNCTION (LVDD)

LVDD	MeanCreatinine(mg/dl)	MeanUrea(mg/dl)	Mean uACR(mg/g)	P value
Normal	5.77	56.90	59.4	**<0.001**
Grade1	5.86	60.28	60.56	
Grade 2	6.23	64.58	68.7	
Grade 3	6.90	64.79	83.75	

ASSOCIATION BETWEEN LEFT VENTRICULAR SYSTOLIC DYSFUNCTION(LVSD) AND STAGING OF CHRONIC KIDNEY DISEASE (CKD)

Left ventricular Systolic Dysfunction								
		Normal	**Mild**	**Moderate**	**Severe**	**Total**	**Chi²**	**P**
Staging	STAGE 5	42	11	1	5	59	11.51	**0.242**
	STAGE 4	13	1	3	4	21		
	STAGE 3a	1	0	0	0	1		
	STAGE 3b	5	2	0	0	7		
	Total	61	14	4	9	88		

ASSOCIATION BETWEEN LEFT VENTRICULAR DIASTOLIC DYSFUNCTION (LVDD) AND STAGING OF CHRONIC KIDNEY DISEASE (CKD)

LV Diastolic Dysfunction								
Staging		**Normal**	**Grade1**	**Grade 2**	**Grade 3**	**Total**	**Chi2**	**P value**

	STAGE 5	24	24	6	5	59	13	**0.163**
	STAGE 4	5	10	5	1	21		
	STAGE 3a	0	0	1	0	1		
	STAGE 3b	2	5	0	0	7		
	Total	31	39	12	6	88		

4. DISCUSSION

Cardiovascular illnesses are the predominant cause of mortality in the chronic kidney disease population. [3-4] The extensive use of two-dimensional echocardiography facilitates the early detection of structural and functional cardiac problems. Several factors in the chronic kidney disease population, such as hypervolemia, a persistent inflammatory state, and uremia, lead to cardiac and vascular remodeling, resulting in structural cardiac abnormalities. Early detection of the predictors of ventricular dysfunction becomes important.

AGE

Mean age of the study population was 57.73 ± 15.88 years. The age was observed to be higher in the males. Singh et al. [13] noted that mean age of the study population was 51.56±13.39 years. This was comparable to the findings of our study. Romejko et al. [17] noted that mean age of the CKD patients was 63 ± 11 years. This was in par to the findings of our study.

Chillo P et al. [15] noted that the mean ± SD age of the total study population was 48 ± 13 years.

Franczyk-Skora et al. [18] noted that 63.97 ±12.5 was the mean age of the study population. It was observed that mean age of population in most of the studies ranges from 50 -65 years which was like our study.

STAGING OF THE CKD

The major section of the study participants was categorized as G5A1 that is 50% of the cases. 19.32% belonged to G4A1. When we stage the patients, it was noted that stage 5 disease was seen 67.05%, followed by stage 4 in 23.86%. 7.95% belonged to stage 3b and 1.14% to stage 3a.

In Chillo P et al. [15], the proportions of patients with CKD of stages 3, 4, and 5 were 0%, 2.1%, and 97.9%, respectively, in the total population. In Rao et al, majority of the patients had stage IV and V disease, correlating to the findings of the present study. In a study by Singh et al [13] 27.2% belonged to stage 3b, 46.3% belonged to stage 4 and 26.5% belonged to stage 5 not on hemodialysis.

LEFT VENTRICULAR[LV] SYSTOLIC AND DIASTOLIC DYSFUNCTION

In our study LV systolic dysfunction was observed in 30.68% participants and LV diastolic dysfunction was observed in 64.78% participants. When we observed LV systolic dysfunction, it was noted to be mild in 15.90% of patients, moderate in 4.55%, and severe in 10.23%. When we evaluated LV diastolic dysfunction it was noted to be of grade 1 in 44.32% patient, grade 2 in 13.64% and grade 3 in 6.82%.

Systolic dysfunction was present in 28.81% of stage 5 patients, 38.09% of stage 4 patients, and 28.57% of stage 3b patients. Meanwhile, diastolic dysfunction was observed in 59.32% of stage 5 patients, 76.19% of stage 4 patients, and 71.42% of stage 3b patients.

In Romejko et al. [17], 77 patients with CKD were evaluated. Grade 1 of LVDD was reported in 72 participants (77.4%), Grade 2 of LVDD in 4 patients (4.3%) and Grade 3 of LVDD was found in 1 person (1.1%). In the study by Rao et al. [16], CKD patients were found to have a high prevalence of systolic (47.8%) and diastolic dysfunction (55.2%). The prevalence of systolic dysfunction increased with increasing severity of renal impairment ,39.1% in CKD stage 4 and 67.8% in CKD stage 5.A similar study conducted by Nitin et al. [19], they found that 30.4% of CKD patients had systolic dysfunction and 56.5% had diastolic dysfunction. They also observed that 51.85% of patients with mild/moderate CKD had diastolic dysfunction, whereas 82.6% of patients with severe CKD had diastolic dysfunction. Singal et al. [20] have reported in their study that 23% Of study subjects had systolic dysfunction. Similarly, in a study

conducted by Avijit Debnath et al. [21], 15% of the patients with mild/moderate CKD had systolic dysfunction while 48% of patients with severe CKD had systolic dysfunction.
Losi et al [22] in a cross-sectional study among patient on maintenance hemodialysis observed that nearly 40% of the patients had diastolic dysfunction. Agrawal et al [23] had reported a prevalence of diastolic dysfunction of 30% in early stages of CKD and 53.2% in late stages of CKD.
The prevalence of diastolic dysfunction is more compared to systolic dysfunction in our study which is similar to other studies. The differences between these observations of varied percentage of systolic and diastolic dysfunction in different stages of CKD can be explained on the ground of the different baseline characteristics of the population studied, different methods used to evaluate the dysfunction. From the above observations it can be concluded that there is a significant burden of LV systolic and diastolic dysfunction in CKD patients.

PARAMETERS ASSOCIATED WITH LEFT VENTRICULAR SYSTOLIC AND DIASTOLIC DYSFUNCTION.

There was a significant association noted between Left ventricular dysfunction with renal parameters. In our study, we observed a positive association between creatinine, urinary creatinine-albumin ratio, urea with left ventricular systolic and diastolic dysfunction. Therefore, an elevated creatinine, urine albumin creatinine ratio are good clinical indicators of Left ventricular systolic and diastolic dysfunction. However, we found no significant correlation with grade or stage of the CKD and left ventricular dysfunction.
In Romejko et al. [17], increased inflammatory parameters, elevated serum glucose concentrations and worse nutritional status were the predictors of impairment in the diastolic function of the left ventricle in CKD and non-CKD patients. They noticed a positive association between serum creatinine and left ventricular dysfunction.
Chillo P et al. [15] in multivariate logistic regression analysis, noted that proteinuria is a predictor of left ventricular systolic and diastolic dysfunction. They found no association between staging of CKD and systolic dysfunction. These findings were similar to our study. Franczyk-skora et al [18] noted that stage of renal failure was associated with the significant increase in LV mass, systolic LV, and diastolic LV dimensions and in the size of the left atrium. Decreased estimated glomerular filtration rate (eGFR) was also observed in this study, which varied to the findings of the present study. Singh et al [13] noted that on age and sex adjusted multivariate logistic regression analysis one of the significant indicators of systolic dysfunction was 24 h urine protein (OR–1.725{1.195–2.490} P = 0.0040). They found positive correlation between severity of LVDD and serum creatinine. No association between stages of CKD and dysfunction was found. These findings were similar to our study. Matsushita et al [26] reported higher albuminuria and albumin creatinine ratio to be association with left ventricular systolic dysfunction as in our study. Park et al. [25] reported no significant associations between different stages of eGFR and LVEF in 3487 patients, which was observed in our study too. In J.A.Tharayil et al. [27] there was no association between reduced estimated glomerular filtration rate indicating no association between staging of CKD and diastolic dysfunction. This was similar to our study.

5. CONCLUSION

Left ventricular dysfunction is frequent among CKD patients undergoing care and treatment at our tertiary care center. The prevalence of diastolic dysfunction was more than systolic dysfunction.
In our study we found serum creatinine, urea and urine albumin creatinine ratio to be predictors of both systolic and diastolic dysfunction. We have found no association between staging of CKD with Left ventricular dysfunction. Hence emphasis on screening of all CKD patients at the earliest for ventricular dysfunction becomes important. Screening for risk factors leading to ventricular dysfunction is essential.
In Chronic kidney disease patient maladaptive events lead to left ventricular hypertrophy, structural changes in myocardium as well as diastolic dysfunction. Systolic failure also occurs frequently. Therefore, early identification and intervention of contributing factors are essential to avert this catastrophic progression. Two-dimensional Echocardiography is essential for identifying both overt and subclinical left ventricular failure in individuals with chronic kidney disease.

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