Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE7, 2021

Study to evaluate the cardiovascular functioning in individuals diagnosed with chronic kidney disease (CKD): retrospective observational study

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ABSTRACT

Aim: The aim of the present study was to assess the cardiac functions in patients with chronic kidney disease (CKD).

Methods: This 1-year observational study was conducted on a sample of 200 patients from the departments of General Medicine. The researchers gathered data by utilizing a pre-established patient profile form, which included comprehensive laboratory findings and pertinent medical information. All patients underwent two-dimensional and M mode echocardiography to assess their heart functioning from the previous hospital records.

Results: The present study comprised a cohort of 200 individuals, consisting of 140 (70%) males and 60 (30%) females, who had received a diagnosis of chronic kidney disease (stages 1 to 5) or end stage renal disease. The diagnoses were established through laboratory analysis of glomerular filtration rate (GFR) (<90 ml/min/1.73 m2) and serum creatinine levels (>3 mg/dl). Out of the total sample size of 120 individuals, 60% were diagnosed with hypertension, characterized by blood pressure levels exceeding 140/90 mmHg, while the remaining 40% were classified as normotensive. The individuals were categorized into five groups according to their glomerular filtration rate (GFR). Furthermore, it was shown that the E/A ratio had a positive correlation with the degree of renal impairment, with the exception of individuals diagnosed with severe chronic kidney disease (CKD). The echocardiography examination revealed that hypertension played a significant role in the development of left ventricular hypertrophy and diastolic dysfunction. One of the primary factors that significantly contributed to the occurrence of systolic dysfunction was the presence of regional wall motion abnormalities (RWMA), which were primarily caused by ischemia heart illness. The echocardiography results indicated the presence of left ventricular hypertrophy (LVH) in 144 individuals, accounting for 72% of the total sample. Systolic dysfunction, as indicated by fractional shortening below 25% and a reduced left ventricular ejection fraction (LVEF) below 52%, was observed in 20 individuals, accounting for 10% of the sample, and in 24 individuals, accounting for 12% of the sample, respectively.

Conclusion: Patients in the early stages of chronic kidney disease (CKD) may also experience left ventricular diastolic dysfunction. Patients with hypertension and chronic kidney disease (CKD) had a greater prevalence of both diastolic and systolic dysfunction in comparison to individuals with normal blood pressure.

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE7, 2021

Keywords: CKD, Dysfunction, Echocardiography, Hypertension

1. INTRODUCTION

The presence of cardiac anomalies is commonly detected in the pediatric population, namely among children and adolescents who suffer from chronic renal failure (CRF) or end stage renal disease (ESRD), as well as those who have undergone renal transplantation (TX).[1,2] There is a relative scarcity of research on the frequency of cardiac abnormalities in pediatric patients with chronic renal failure (CRF) compared to adults. However, there is currently no recent comprehensive study available that specifically examines the prevalence of cardiac modifications in the pediatric age group. In adult individuals, chronic renal failure (CRF) frequently leads to cardiac lesions, which are often accompanied by other cardiovascular risk factors such as atherosclerosis, essential hypertension, diabetes, myocardial ischemia, or endocarditis. These risk factors are less commonly detected in younger individuals.[3]The user's text is too short to be rewritten academically. Given the increasing significance of these factors as individuals age, it is crucial to promptly identify cardiac abnormalities and implement preventive interventions in children with chronic renal failure (CRF) and following transplantation (TX).

The proposition that cardiovascular disease (CVD) originates from the kidneys was initially put up by Richard Bright in 1836. Multiple epidemiological studies have demonstrated that people with chronic kidney disease (CKD) experience a higher prevalence and severity of cardiovascular disease (CVD) as compared to the general population. Chronic kidney disease (CKD) is commonly regarded as a coronary artery disease (CAD) analogue. Interestingly, individuals in the early stages of CKD face a higher risk of mortality from cardiovascular diseases (CVDs) compared to progressing to end-stage renal disease (ESRD).[4] Despite the frequent discussions over the extent of this risk, the clinical trials have deliberately excluded individuals with renal impairment. Therefore, there is a dearth of evidence-based management strategies for cardiovascular disease in chronic kidney disease. The treatment implications of this finding are noteworthy, as interventions aimed at halting the advancement of chronic kidney disease (CKD) would also serve to decrease cardiovascular morbidity and mortality. The recognition that cardiovascular disease (CVD) and chronic kidney disease (CKD) can mutually originate and sustain each other has resulted in the establishment of cardiorenal syndrome as an independent clinical entity.[5] Heart failure (HF) is a diverse clinical disease that arises from cardiac damage and overload, resulting in increased intracardiac pressure and insufficient cardiac output. Heart failure (HF) is classified into three primary categories based on the left ventricular ejection fraction (LVEF): HF with preserved ejection fraction (HFpEF; LVEF $\geq$ 50%), mildly reduced ejection fraction (HFmrEF; LVEF 41–49%), and decreased ejection fraction (HFrEF; LVEF $\geq$ 40%).[6] However, it should be noted that malfunction of the right ventricle can also lead to heart failure. Individuals afflicted with heart failure (HF) are very susceptible to comorbidities that are closely associated with elevated mortality risk, heightened financial burden on healthcare systems, and unfavorable outcomes.[7,8] Elevated blood pressure (BP) is a prominent risk factor that significantly contributes to the onset and advancement of chronic kidney disease (CKD), surpassing all other individual health risk factors in terms of global mortality and morbidity.[9-11] The timely identification and effective management of hypertension are crucial in order to have a significant impact on preventing the advancement of chronic kidney disease (CKD) and mitigating the associated health burden.[12]

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE7, 2021

The objective of the current investigation was to evaluate the cardiovascular functioning in individuals diagnosed with chronic kidney disease (CKD).

2. MATERIALS AND METHODS

This retrospective observational study was carried out in 200 patients from department of General Medicine for the period of 1 year. Data were collected in the predesigned patient profile form along with complete laboratory reports and all relevant history from the previous hospital records. All the patients were gone through two-dimensional and M mode echocardiography for determination of their cardiac functions. The analysis made from the data was reported in predesigned forms which includes information such as patient demographic details (BP, all vitals, weight, medical & medication history) and required laboratory information (Serum creatinine, GFR).

All patients were evaluated physically, clinically, biochemically and radiological test were done as per discretion of physician. Additionally, all required examinations were performed as and when required.

Echocardiography was executed using a cardiac ultrasound unit with a 2-3.5 MHz transducer. TDI was performed in all patients with images taken. Left ventricular end-diastolic, systolic dimensions, end-diastolic, and systolic wall thickness of the inter-ventricular septum and left ventricular wall were determined using standard echocardiography2-D and M-mode measurements. M mode recording perpendicular to the long axis of and through the center of the left ventricle at the papillary muscle level were taken as standard measurements of the systolic and diastolic wall thickness and chamber dimensions. The LVEF and fractional shortening (FS) were taken as measure of left ventricular systolic function. Diastolic function was determined by measuring E/A ratio by special Doppler inflow velocity (E is peak early diastole velocity and A is peak atrial 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 was $\geq$ 12 mm.

Inclusion criteria

Patients with age about > 18 years, GFR should be <90 ml/min/ 1.73 m2, serum creatinine >3 mg/dl and subjects having confirm diagnosis of CKD >6 month were included in the study.

Exclusion criteria

Pregnant, lactating women, mentally ill or other psychological subjects, subject who are on antineoplastic medication, post traumatic patient, patient who had severe coarse of COVID-19 and other comorbid disease or condition which can interfere with study as per investigators discretion were excluded from the study.

Biochemical estimations

Physical examination, all vitals, GFR, serum creatinine, CBC, cardiac biomarker, kidney function test and echocardiography were performed. Additional tests were performed based on investigator discretion as applicable.

Statistical analysis

The data was represented graphically in MS-excel with median values.

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3. RESULTS

Table 1: Subject's demography including clinical characteristic

Variables		**Total, n (%)**
Age (Years)	18- 75 (Mean 56±12)	
Gender	Male	140 (70)
	Female	60 (30)
Hypertensive	120 (60)	
Normotensive	80 (40)	
Haemodialysis	80 (40)	
End-stage renal disease (Stage 4 and 5)	100 (50)	
Diabetes	70 (35)	
Clinical characteristics	Reduced urine output	140 (70)
	Nocturia	60 (30)
	Haematuria	20 (10)
	Pruritus	24 (12)
	Pallor	130 (65)
	Pedal oedema	120 (60)
	Proteinuria	96 (48)
Educational status	Primary	110 (55)
	Secondary	40 (20)
	Tertiary	20 (10)
	None	30 (15)
Occupation	Employed	80 (40)
	Unemployed	80 (40)
	Others	40 (20)
Marital status	Married	130 (65)
	Single	20 (10)
	Others	50 (25)

This study included 200 patients with 140 (70%) male and 60 (30%) female who were diagnosed with chronic kidney disease (stage 1 to 5) or End stage renal disease based on laboratory interpretation of GFR (<90 ml/min/1.73 m2) and serum creatinine (>3 mg/dl). Among that 120 (60%) patients were hypertensive (BP >140/90 mmhg) and 80 (40%) were normotensive.

Table 2: Analyzed patients based on CKD stages

Stage of CKD	**Hypertensive**	**Normotensive**
Stage 1 (GFR 90or higher)	20	10
Stage 2 (GFR 89 to 60)	15	10
Stage 3a (GFR59 to 45)	15	15

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Stage 3b (GFR44 to 30)	20	30
Stage 4 (GFR 29 to 15)	30	5
Stage 5 (GFR less than 15)	20	10

The subjects were classified in to 5 groups based on GFR. We also found that E/A increased in parallel with the severity of kidney dysfunction, apart from patients with very advanced CKD.

Table 3: Echocardiographic findings in ESRD study cases

Echocardiographic finding in cases of ESRD	**No. ofcases**	**Percentage(%)**
Left ventricularhypertrophy	144	72
Fractional shortening(<25%)	20	10
Ejection fraction (<50%)	24	12
E/A ratio (<0.75 or >1.8)	120	60
RWMA	26	13
Pericardial effusion (<10mm)	30	15
Valvular calcification	20	10

Echocardiography showed that major contributing factors for left ventricular hypertrophy and diastolic dysfunction were hypertension. Major contributing factor for systolic dysfunction was RWMA due to ischemic heart disease. Echocardiography showed that left ventricular hypertrophy (LVH) was present in 144 (72%). Systolic dysfunction as measured by reduced fractional shortening (<25%) and decreased LVEF (<52%) was present in (20) 10% and (24) 12% respectively.

Table 4: Correlation analyses according to echocardiography finding in hypertensive and normotensive ESRD study

Echocardiographic finding in cases of ESRD	**Hypertensive, n**		**Normotensive, n**	
	Present	**Absent**	**Present**	**Absent**
Left ventricular hypertrophy	80	40	64	16
Fractional shortening (<25%)	15	105	5	75
Ejection fraction (<50%)	16	104	8	72
E/A ratio (<0.75 or >1.8)	90	30	30	50
RWMA	20	100	6	74
Pericardial effusion (<10 mm)	25	95	5	75
Valvular calcification	16	104	4	76

In hypertensive patients with CKD, LVH was present in 80 patients, diastolic dysfunction was present in 90 patients as deliberate by abnormal E/A ratio, systolic dysfunction as considered by reduced fractional shortening was present in 15 patients and pericardial effusion observed in 25 patients.

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4. DISCUSSION

Cardiovascular disease (CVD) is the primary contributor to illness and death in individuals with chronic kidney disease (CKD). Despite efforts to modify established risk factors for coronary artery disease (CAD), such as hypertension and diabetes, the risk of mortality increases progressively as chronic kidney disease (CKD) worsens.[13] Chronic kidney disease (CKD) is a non-communicable ailment that commonly arises due to the presence of diabetes and hypertension.[14] The recognition that cardiovascular disease (CVD) and chronic kidney disease (CKD) can mutually originate and sustain each other has resulted in the establishment of cardiorenal syndrome as an independent clinical condition.[15] The precise etiology behind the heightened susceptibility to cardiovascular events in individuals with chronic kidney disease (CKD) remains little elucidated. There are other elements that are thought to be accountable for such a correlation. Despite accounting for many concurrent risk variables, it is evident that chronic kidney disease (CKD) remains the primary determinant of cardiovascular morbidity and mortality.[16]

The present study comprised a sample of 200 individuals diagnosed with chronic kidney disease, including stages 1 to 5, or end-stage renal disease. Among these participants, 140 (70%) were male, while 60 (30%) were female. The diagnoses were established by laboratory analysis of glomerular filtration rate (GFR), which was found to be below 90 ml/min/1.73 m2, and serum creatinine levels, which exceeded 3 mg/dl. Out of the total sample size of 200 patients, 120 individuals (60%) exhibited hypertension, characterized by blood pressure levels exceeding 140/90 mmHg, whereas the remaining 80 patients (40%) were classified as normotensive. The individuals were categorized into five groups according to their glomerular filtration rate (GFR). Additionally, it was observed that the E/A ratio had a positive correlation with the degree of renal impairment, with the exception of individuals diagnosed with highly progressed chronic kidney disease (CKD). The echocardiography examination revealed that hypertension played a significant role in the development of left ventricular hypertrophy and diastolic dysfunction. The study conducted by Rao et al. revealed that a significant proportion of individuals, specifically 67.2%, exhibited diastolic dysfunction.[17] In a cross-sectional study conducted by Losi et al., it was shown that approximately 40% of the patients exhibited diastolic dysfunction.[18] Agrawal et al. (year) identified a prevalence of diastolic dysfunction of 30% in the initial phases of chronic kidney disease (CKD), which increased to 53.2% in the latter stages of CKD.[19]

One of the primary factors that significantly contributed to systolic dysfunction in this case was regional wall motion abnormality (RWMA), which was mostly caused by ischemic heart disease. The results of the echocardiography examination indicated the presence of left ventricular hypertrophy (LVH) in 144 individuals, accounting for 72% of the total sample. Systolic dysfunction, as indicated by a fractional shortening of less than 25% and a lowered left ventricular ejection fraction (LVEF) of less than 52%, was observed in 20 individuals, accounting for 10% of the total sample. Additionally, a decreased LVEF was found in 24 individuals, representing 12% of the sample. In a similar vein, a study conducted by Kulkarni et al and Foley et al yielded findings indicating that 29 (41.4%) and 14.8% of patients, respectively, exhibited systolic dysfunction.[20,21] Moreover, a European multicenter study conducted by Chinali et al. revealed that the prevalence of systolic dysfunction in individuals with chronic kidney disease (CKD) was 24.6%, which is notably greater than the 8.3% reported by Adiele et al.[22,23] The results of this study indicate that individuals with chronic kidney disease (CKD) experience a notable prevalence of left ventricular (LV) systolic and diastolic dysfunction. The presence of left ventricular ejection fraction (LVEF) was seen in

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE7, 2021

12 individuals, accounting for 12% of the total sample. Shin et al. (year) reported a comparable finding, indicating that left ventricular ejection fraction (LVEF) was observed in 57.2% of individuals undergoing hemodialysis.[24] Hensen et al. reported that left ventricular ejection fraction (LVEF) was recorded in 32% of patients, which was found to be greater than the LVEF observed in our study.[25]

The echocardiography results indicated the presence of left ventricular hypertrophy (LVH) in 75 individuals, accounting for 75% of the study population. Systolic dysfunction, as indicated by a fractional shortening of less than 25% and a reduced left ventricular ejection fraction (LVEF) of less than 52%, was observed in 8% (8 individuals) and 12% (18 individuals) respectively. Hayashi et al also reported similar findings, indicating that left ventricular hypertrophy was seen in 63% patients.[26] Ramegowda et al study revealed left ventricular hypertrophy in 24 patients, accounting for 48% of the sample. Ejection fraction below 50% was observed in 12% of the patients[27], a finding that aligns with the conclusions obtained by Mavrakanas et al.[28] the existence of EF was verified in 12.7% of the patients. A similar finding was reported in a study conducted by Hensen et al, where it was revealed that 32% of patients exhibited a reduced left ventricular ejection fraction (LVEF).[25] The prevailing echocardiographic abnormality observed in the study was left ventricular hypertrophy, which was followed by conduction abnormalities, E/A ratio, pericardial effusion, and regional wall motion abnormalities (RWMA). The most often seen morphological anomaly in our study is left ventricular hypertrophy, followed by regional wall motion abnormalities (RWMA). Left ventricular dysfunction is the most often observed cardiovascular problem. Echocardiography is a diagnostic method that exhibits higher sensitivity in the detection of left ventricular failure among individuals with chronic kidney disease (CKD). As the stages of chronic kidney disease (CKD) advance, notable echocardiographic abnormalities emerge, including left ventricular hypertrophy, systolic dysfunction, left ventricular diastolic dysfunction (LVDD), regional wall motion abnormalities, and pericardial effusion.

5. CONCLUSION

It was determined that individuals in the early stages of chronic kidney disease (CKD) also experience left ventricular diastolic dysfunction. However, it was observed that patients with hypertensive CKD have a higher occurrence of both diastolic and systolic dysfunction compared to those without hypertension. Furthermore, it was found that the utilization of Doppler indices in conjunction with conventional and tissue Doppler imaging (TDI) can effectively identify subtle alterations in diastolic function resulting from kidney dysfunction. Additionally, chronic kidney disease (CKD) induces a systemic and persistent pro-inflammatory condition that plays a role in the remodeling of blood vessels and myocardium. In the context of our work, chronic kidney disease (CKD) has similarities to an accelerated aging process in the cardiovascular system.

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