

A Hospital Based Observational Assessment of Cardiac Functions in Patients with Chronic Kidney Disease (CKD)

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Conflict of interest: Nil

Abstract

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

Methods: An observational study was carried out in 100 patients from department of medicine from AIIMS Patna, Bihar, India for the period of one year after obtaining an approval from institutional ethics committee. Data were collected in the predesigned Patient Profile Form along with complete laboratory reports and all relevant history. All the patients were gone through two-dimensional and M mode echocardiography for determination of their cardiac functions.

Results: This study included 100 patients with 60 (60%) male and 40 (40%) 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 65 (65%) patients were hypertensive (BP $>140/90$ mmhg) and 35 (35%) were normotensive. Echocardiography showed that left ventricular hypertrophy (LVH) was present in 75 (75%). Systolic dysfunction as measured by reduced fractional shortening ($<25\%$) and decreased LVEF ($<52\%$) was present in (8) 8% and 18 (12%) respectively. In hypertensive patients with CKD, LVH was present in 40 patients, diastolic dysfunction was present in 45 patients as deliberate by abnormal E/A ratio, systolic dysfunction as considered by reduced LVEF was present in 7 patients and pericardial effusion observed in 17 patients.

Conclusion: LV diastolic dysfunction also happens in patients who having the early stage of CKD. Hypertensive patients along with CKD had found higher widespread presence of diastolic and systolic dysfunction as compared to normotensive.

Keywords: CKD, Dysfunction, Echocardiography, Hypertension.

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Introduction

Heart failure (HF) is a heterogeneous clinical syndrome resulting from injury and cardiac overload that in consequence leads to the elevation of intracardiac pressure and inadequate cardiac output. Due to left ventricular ejection fraction (LVEF), HF is divided into three main categories: HF with preserved (HFpEF; LVEF $\geq 50\%$), mildly reduced (HFmrEF; LVEF 41–49%), and reduced ejection

fraction (HFrEF; LVEF $\geq 40\%$). [1] Nevertheless, right ventricle dysfunction can also result in HF. Patients suffering from HF are at high risk of comorbidities which are strictly connected with higher mortality risk, increased burden of healthcare costs, and adverse outcomes. [2,3] Additional chronic conditions are a major concern in heart failure. According to Chamberlain's research [3], most heart

failure patients have at least two chronic conditions. Furthermore, patients with HFpEF present an increased number of comorbidities compared to patients with HFrEF. The heart and kidney are closely related. Their role is to maintain salt–water homeostasis and normal blood pressure. The Renal impairment and disturbance of salt and water excretion resulted in an increase in cardiac preload and afterload. Furthermore, low cardiac output can decrease kidney perfusion and lead to kidney failure. Therefore, renal impairment is one of the most serious consequences of HF. [4]

The extremity of CKD can be proficient by a reasonable serum creatinine-based estimated glomerular filtration rate (eGFR), which also indicates excretory kidney function, and elevated urinary albumin measured by the urinary albumin-to-creatinine ratio (ACR), which is a best predictor of kidney damage. [5] In 2017, the worldwide prevalence of CKD was 9.1% (95% uncertainty interval [UI] 8.5 to 9.8), which is roughly estimated 700 million cases. Since 1990, the prevalence of CKD has intensified by 29.3% (26.4 to 32.6), but age-standardized prevalence has remained untouched during this period (1.2%, -1.1 to 3.5). A worthwhile rise was noted in age-standardized incidence of end-stage kidney disease (ESKD) which is treated by renal replacement therapy, with dialysis and kidney transplantation. The global strengthen in mortality from CKD since 1990 was 41.5% (95% UI 35.2 to 46.5), such that mortality from CKD, and cardiovascular disease deaths in debt to impede kidney function caused 4·6% (4.3 to 5) of worldwide deaths in 2017, which manifested that CKD is the 12th leading cause of death globally in 2017, as an increase from 17th in 1990. [6]

High blood pressure (BP) is the most considerable risk factor for the development and progression of CKD as well as more deaths and disease worldwide than any other single health risk factor. [7-

9] Early detection of high BP and its appropriate management is required as possible as to makes a difference in the prevention of CKD progression and control of the CKD health burden. [10]

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

Materials and Methods

An observational study was carried out in 100 patients from department of medicine from AIIMS Patna, Bihar, India for the period of one year after obtaining an approval from institutional ethics committee. Data were collected in the predesigned Patient Profile Form along with complete laboratory reports and all relevant history. 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 echocardiography 2-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 ≥ 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 course 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.

Results

Table 1: Subject's demography including clinical characteristic

| Variables | | Total, n (%) |
|---------------------------------|---|-------------------------------|
| Age (Years) | | 18- 75 (Mean 56 ± 12) |
| Gender | Male | 60 (60) |
| | Female | 40 (40) |
| BMI (mean) (kg/m ²) | | 25.5 |
| | Hypertensive | 65 (65) |
| | Normotensive | 35 (35) |
| | Haemodialysis | 40 (40) |
| | End-stage renal disease (Stage 4 and 5) | 45 (45) |
| | Diabetes | 36 (36) |
| Clinical characteristics | Reduced urine output | 70 (70) |
| | Nocturia | 28 (28) |
| | Haematuria | 12 (12) |
| | Pruritus | 13 (13) |
| | Pallor | 64 (64) |
| | Pedal oedema | 60 (60) |
| | Proteinuria | 48 (48) |
| | Primary | 54 (54) |
| Educational status | Secondary | 20 (20) |
| | Tertiary | 12 (12) |
| | None | 14 (14) |
| | Employed | 40 (40) |
| Occupation | Unemployed | 38 (38) |

| | | |
|-----------------------|---------|---------|
| | Others | 22 (22) |
| | Married | 60 (60) |
| Marital status | Single | 15 (15) |
| | Others | 25 (25) |

This study included 100 patients with 60 (60%) male and 40 (40%) 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 65 (65%) patients were hypertensive (BP >140/90 mmhg) and 35 (35%) were normotensive.

Table 2: Analyzed patients based on CKD stages

| Stage of CKD | Hypertensive | Normotensive |
|----------------------------|--------------|--------------|
| Stage 1 (GFR 90 or higher) | 5 | 5 |
| Stage 2 (GFR 89 to 60) | 7 | 5 |
| Stage 3a (GFR 59 to 45) | 7 | 7 |
| Stage 3b (GFR 44 to 30) | 10 | 15 |
| Stage 4 (GFR 29 to 15) | 12 | 8 |
| Stage 5 (GFR less than 15) | 9 | 10 |

The subjects were classified into 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. of cases | Percentage (%) |
|--|--------------|----------------|
| Left ventricular hypertrophy | 75 | 75 |
| Fractional shortening (<25%) | 8 | 8 |
| Ejection fraction (<50%) | 12 | 12 |
| E/A ratio (<0.75 or >1.8) | 60 | 60 |
| RWMA | 12 | 12 |
| Pericardial effusion (<10mm) | 15 | 15 |
| Valvular calcification | 8 | 8 |

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 75 (75%). Systolic dysfunction as measured by reduced fractional shortening (<25%) and decreased LVEF (<52%) was present in (8) 8% and 18 (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 | 40 | 5 | 30 | 25 |
| Fractional shortening (<25%) | 15 | 35 | 5 | 45 |
| Ejection fraction (<50%) | 7 | 40 | 3 | 40 |
| E/A ratio (<0.75 or >1.8) | 45 | 5 | 20 | 30 |

| | | | | |
|---|----|----|---|----|
| RWMA | 16 | 35 | 4 | 45 |
| Pericardial effusion (<10 mm) | 17 | 38 | 3 | 42 |
| Valvular calcification | 14 | 36 | 5 | 44 |

In hypertensive patients with CKD, LVH was present in 40 patients, diastolic dysfunction was present in 45 patients as deliberate by abnormal E/A ratio, systolic dysfunction as considered by reduced LVEF was present in 7 patients and pericardial effusion observed in 17 patients.

Discussion

Cardiovascular disease (CVD) is the supreme cause of morbidity and mortality amid patients with CKD. In spite of alteration for known CAD risk factors, including hypertension and diabetes and mortality risk dynamically intensifying with worsening condition of CKD. Chronic kidney disease is a non-communicable disease typically caused by diabetes and hypertension. [12] The concept that CVD and CKD can initiate and perpetuate one another led to the creation of cardio renal syndrome as a separate clinical entity. [13] The mechanism underlying the increased risk of cardiovascular events in patients with CKD has not been well defined. Several factors are believed to be responsible for such an association. Even after adjusting for the coexisting multiple risk factors, CKD appears to be the major factor in determining cardiovascular morbidity and mortality. [14]

In hypertensive patients with CKD, LVH was present in 40 patients, diastolic dysfunction was present in 45 patients as deliberate by abnormal E/A ratio, systolic dysfunction as considered by reduced LVEF was present in 7 patients and pericardial effusion observed in 17 patients. Rao et al found that 67.2% of subjects had diastolic dysfunction. [15] Losi et al in a cross-sectional study declare that nearly 40% of the patients had diastolic dysfunction. [16] Agrawal et al

had distinguish a prevalence of diastolic dysfunction of 30% in early stages of CKD and 53.2% in later stages of CKD. [17]

Moreover, systolic dysfunction in 8 (8%) basically related with coronary artery disease hence major determinant of prognosis. It is present in greater proportion in later stages of CKD. Similarly, a study by Kulkarni et al and Foley et al concluded that systolic dysfunction was present in 29 (41.4%) and 14.8 % patients. [18,19] A study by Singh et al. [20] LV systolic dysfunction was 15.6%. Furthermore, systolic dysfunction was reported 24.6% with CKD in a European multicenter study reported by Chinali et al but higher than the 8.3% reported by Adiele et al. [21,22] These findings suggest that there is a significant burden of LV systolic and diastolic dysfunction in CKD patients. We found LVEF was present in 12 (12%). Similar result was also stated by Shin et al that LVEF was present in 57.2% of hemodialysis patients. [23] Hensen et al LVEF was observed in 32% of patients although same was higher as compared to our study. [24]

Echocardiography showed that left ventricular hypertrophy (LVH) was present in 75 (75%). Systolic dysfunction as measured by reduced fractional shortening (<25%) and decreased LVEF (<52%) was present in (8) 8% and 18 (12%) respectively. Similar result were also produced by Hayashi et al and Foley et al that LV hypertrophy was observed in 63% and 73.4% patient by Ramegowda et al left ventricular hypertrophy was seen in 24 patients (48%). [19,25,26] Ejection fraction (<50%) was detected in 12% patients similar result were also concluded by Mavrakanas et al. [27] That EF was confirmed in 12.7% patients. Another study by Hensen et al have similar result

that LVEF was observed in 32% of patients. [24]

Most common Echocardiographic abnormality was Left ventricular hypertrophy followed by conduction abnormalities, E/A ratio, pericardial effusion and RWMA. Left ventricular hypertrophy is the commonest morphological abnormality observed in our study, followed by RWMA. Left ventricular dysfunction is commonest cardiovascular abnormality detected. Echocardiography is a more sensitive diagnostic procedure to detect left ventricular dysfunction in patients with CKD. [28] As the stages of CKD progresses spike ECHO abnormalities were observed like left ventricular hypertrophy, systolic dysfunction, LVDD, regional wall motion abnormalities and pericardial effusion.

Conclusion

We concluded that left ventricular diastolic dysfunction also occurs in patients having early stage of CKD but patients with hypertensive CKD had higher prevalence of diastolic and systolic dysfunction as compared to normotensive counterparts and that Doppler indices combined with conventional and TDI can be used to detect subtle changes of diastolic function due to kidney dysfunction. Also, CKD causes a systemic, chronic pro-inflammatory state contributing to vascular and myocardial remodeling. In this respect to our study, CKD mimics a hastened aging of the cardiovascular system.

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