ASSESSMENT OF CARDIAC DYSFUNCTION IN PATIENTS WITH END STAGE RENAL DISEASE IN A TERTIARY CARE HOSPITAL

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ABSTRACT

BACKGROUND

End stage renal disease (ESRD) is the irreversible deterioration of renal function which results from impairment of excretory, metabolic, endocrine functions leading to the development of the clinical syndrome of uraemia. Chronic Kidney disease (CKD) is recognised worldwide as a public health problem. In India, prevalence of CKD is high, and as per data available from various studies, approximate prevalence of CKD is around 800/million population.[2-4] Diminished estimated glomerular filtration rate (eGFR) is a powerful, graded, independent predictor of cardiovascular morbidity and mortality[5] and all-cause mortality.

METHODS

Patients with chronic kidney disease with End Stage Renal Disease admitted in King George Hospital, Visakhapatnam during the period from November 2018 to March 2019 were included in the study. This is a retrospective observational study.

RESULTS

A total of fifty CKD patients with ESRD were studied to determine the range of abnormalities of cardiac function. The predominant gender in the study group was male, constituting 68%. Hypertension was the most common aetiology of CKD with 21 (42%) patients, followed by hypertension & diabetes together (22%) and diabetes mellitus alone (20%). Other causes were NSAID abuse (6%), IgA Nephropathy (2%), Polycystic Kidney Disease (2%) & unknown aetiology (6%). Cardiovascular abnormalities were observed in large number of patients with ESRD (76%). LVH was the most common echocardiographic abnormality in CKD cases. Diastolic function was deranged more when compared to systolic function in patients with CKD.

CONCLUSIONS

High prevalence of left ventricular hypertrophy, diastolic dysfunction on echocardiography implies that these patients require detailed cardiovascular evaluation despite the absence of symptoms. Early detection of cardiac abnormalities by echocardiography before the development of overt cardiac symptoms might contribute to better prognosis in these patients.

KEYWORDS

Cardiac Dysfunction, ESRD, LVH.

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BACKGROUND

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In India, prevalence of CKD is high, and as per data available by various studies, approximate prevalence of CKD is around 800/million population.[2-4] Diminished estimated glomerular filtration rate (eGFR) is a powerful, graded, independent predictor of cardiovascular morbidity and mortality[5] and all-cause mortality.[6]

Even subtle kidney dysfunction, as suggested by albuminuria increases cardiovascular risk[7] because it may reflect microvasculature health, including endothelial function. ESRD patients face an extraordinary risk for premature death, largely because of cardiovascular complications.

Prospective studies have shown that End stage renal disease predisposes to LVH (left ventricular hypertrophy) in most (70–80%) patients, which is a marker of poor prognosis.[8] Like conventional atheromatous occlusive vascular disease, CKD is characterized by generalized vasculopathy with other characteristics, including LVH, vascular calcification, and vascular noncompliance. Various epidemiological characteristics of derangement in cardiac function among CKD patients with ESRD have not been examined well and needs detail exposition. Assessment of Cardiac dysfunction by Echocardiography, with detailed evaluation of Left Ventricular structure and functions, is an essential step in patients with ESRD.

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Aims and Objectives

To assess the prevalence of cardiac dysfunction in patients with Chronic Kidney Disease with End stage renal disease, at the time of initiation of haemodialysis.

METHODS

Source of Data and Duration

Patients with Chronic kidney disease with End Stage Renal Disease admitted in King George Hospital, Visakhapatnam during the period from November 2018 to March 2019.

Study Design

Retrospective observational Study.

Inclusion Criteria

Patients with Chronic Kidney Disease (CKD) with End Stage Renal Disease (ESRD i.e. Stage V CKD) with age 18 years and above. A patient was diagnosed to have CKD, if his/her illness was of more than 3 months duration, with abnormal renal ultrasonographic findings and reduced creatinine clearance. A patient with CKD was labelled as ESRD if his eGFR (estimated Glomerular Filtration Rate was below 15 ml/min/1.73 m^2 as per Cockcroft gault equation.

Exclusion Criteria

Patients with pre-existing cardiovascular disease like congenital heart disease, Rheumatic heart disease, myocarditis (due to any infective aetiology) and Primary heart muscle disease like cardiomyopathies.

Method of Collection

Fifty patients admitted in King George Hospital, Visakhapatnam, during the period from November 2018 to March 2019, who were diagnosed as Chronic Kidney disease with ESRD were taken up for the study, at the time of initiation of Haemodialysis. Patient were selected by simple random sampling. All the patients were evaluated by meticulous clinical examination and with the following laboratory investigations, viz. complete blood count, renal function tests, serum electrolytes, blood glucose levels, serum lipid profile, electrocardiography (ECG), chest X-ray and 2D echocardiogram. 2D Echocardiography: One-time echocardiography was done in all the patients to study the range of echocardiographic abnormalities. Two-dimensional echocardiography and M Mode echocardiography were performed. The Left Ventricular Ejection Fraction (LVEF) and Fractional shortening (FS) were taken as a measure of systolic function and LVEF <50% or FS <25% was considered as systolic dysfunction. 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. Left Ventricular Hypertrophy (LVH) was diagnosed when interventricular septal thickness or Left ventricular posterior wall thickness was ≥ 12 mm.

Fractional Shortening was Calculated as-

$$FS\ (\%) = \frac{(LVIDd - LVIDs)}{(LVIDd)} \times 100 \text{ (Normal range being 25\% to 45\%)}$$

LVIDd: Left ventricle internal diameter in diastole
LVIDs: Left ventricle internal diameter in systole
Ejection fraction was calculated as

$$LV\ EF\ (\%) = \frac{LVVd - LVVs}{(LVVd)} \times 100 \text{ (Normal} = 60 \pm 6\%)$$

LVVd: Left ventricle volume in diastole
LVVs: Left ventricle volume in systole

Statistical analysis was conducted using Epi Info software (version 7). P value of <0.05 was considered to indicate statistical significance.

RESULTS

A total of fifty CKD patients with ESRD were studied to determine the range of abnormalities of cardiac function. The following observations were made in the study-

1. The predominant gender in the study group was male, constituting 68%.
2. Hypertension was the most common aetiology of CKD with 21 (42%) patients, followed by hypertension & diabetes together (22%) and diabetes mellitus alone (20%). Other causes were NSAID abuse (6%), IgA Nephropathy (2%), Polycystic kidney disease (2%) & unknown aetiology (6%).
3. Minimum recorded weight was 43 Kg & maximum was 75 Kg. Mean value for weight was 58.89 ± 8.03 kg. Mean value for systolic blood pressure was 148.16 ±18.22 and diastolic blood pressure was 93.26 ±10.68 mmHg. Mean Serum Creatinine was 6.86±1.699 mg/dl. Mean Blood urea value was 86.38 ± 34.369 mg/dl. Mean value for Serum sodium and serum potassium were 133.54 ± 18.266 mEq/l and 4.57 ±0.87 mEq/l respectively. Mean Haemoglobin was 7.410± 1.608 gm/dl. Mean serum calcium and mean serum phosphorous were 7.92 ± 1.318 mg/dl and 4.97 ± 0.879 mg/dl respectively. The mean value for serum total cholesterol was 191.46 ± 49.683 mg/dl. Mean serum albumin value was 2.408 ± 0.792 g/dl.
4. Most common electrocardiographic abnormality found was LVH (72%) followed by ST-T changes (54%) and QT prolongation (42%). Other ECG abnormalities include abnormal P wave (28%), sinus tachycardia (18%), low voltage pattern (8%), tall T waves (6%) & sinus bradycardia (2%).
5. The Following echocardiographic parameters were studied & analysed. (Table 1)
6. Among the 50 patients in the present study, 38 patients (76%) had echocardiographic abnormality. LVH was the most common abnormality seen in 92% of the patients, followed by diastolic dysfunction (54%), mitral regurgitation (46%) and pericardial effusion (40%). About 20% of the study population had both systolic and diastolic dysfunction. Echocardiographic abnormalities in the study group are summarized in Table 2.

7. An elevated total serum cholesterol value of >200 mg/dl was significantly associated with major echocardiographic abnormalities viz. systolic dysfunction, diastolic dysfunction, mitral regurgitation and global hypokinesia. (Table 3).
8. In the present study, prevalence of systolic dysfunction was comparable to the systolic dysfunction observed in the study of Mukesh Laddha et al (24.3%).[1] The prevalence of diastolic dysfunction in the present study was similar to that reported by NP Singh et al[9] (2000) (72%) & Mukesh Laddha et al[1] (72.9% in hypertensive patients). (Table 4).

Parameter	Mean ± S.D.
Left ventricular internal diameter in Diastole (LVIdD) (cm)	5.347±0.5072
Left ventricular internal diameter in Systole (LVIdS) (cm)	3.691 ± 0.6489
Left ventricular Posterior wall Diameter (LVPWd) (cm)	1.597 ± 1.7985
Interventricular septal diameter (IVSd) (cm)	1.358 ± 0.2507
Fractional shortening (FS)	30.838 ± 7.8695
Ejection Fraction (EF)	56.588 ±11.203
Left Ventricular Mass (LVM)	316.24 ± 92.225
'E' peak early diastolic velocity (mm/sec)	0.751 ± 0.3494
'A' Peak atrial filling velocity	0.771 ± 0.201
E/A ratio	1.0063 ±0.488

Table 1. Mean Echocardiographic Parameters in The Study Group

Echocardiographic Finding	Frequency	Percentage
LVH	46	92%
Diastolic dysfunction	27	54%
Mitral Regurgitation	23	46%
Pericardial Effusion	20	40%
Systolic & Diastolic dysfunction	10	20%
Global Hypokinesia	8	16%
Systolic Dysfunction alone	2	4%
RWMA	0	0%

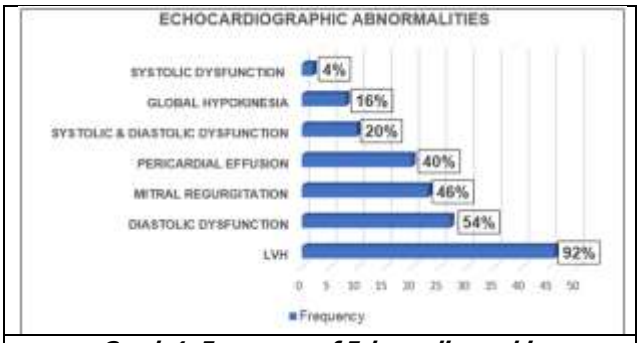
Table 2. Echocardiographic Findings in The Study Group

Parameter	Total Cholesterol >200 mg/dl		p Value
	Yes	No	
LVH	25(54.35%)	21(45.65%)	0.42
Diastolic dysfunction	15(41.67%)	21(58.33%)	0.003*
Mitral Regurgitation	17(73.91%)	6(26.09%)	0.03*
Pericardial Effusion	12(60%)	8(40%)	0.86
Systolic & Diastolic dysfunction	1(10%)	9(90%)	0.003*
Global Hypokinesia	1(12.5%)	7(87.5%)	0.02*
Systolic Dysfunction	2(15.38%)	11(84.62%)	0.001*

Table 3. Correlation of Echocardiographic Findings and Serum Cholesterol

Authors	Prevalence of Systolic Dysfunction	Prevalence of Diastolic Dysfunction
Mukesh Laddha et al[1]	24.3%	72.9% (Hypertensive patients) 42.9% (Normotensive patients)
S.N Agarwal et al[10]	15%	60%
NP Singh et al[9]	0%	72%
Present study	24%	74%

Table 4. Comparison of Various Studies



Graph 1. Frequency of Echocardiographic Findings in Study Population

DISCUSSION

Premature cardiovascular disease is a significant cause of morbidity and mortality among patients with CKD. It is driven by multiple risk factors, including dyslipidaemia and oxidative stress. Predominant structural abnormalities of the heart seen in patients with CKD are Left Ventricular hypertrophy, inter myocardiocytic fibrosis, changes in vascular architecture, and myocardial calcification. All these abnormalities promote systolic as well as diastolic LV dysfunction which predisposes to symptomatic heart failure, which results in premature death. Outcome of CKD patients can be changed by early detection and treatment of major cardiac complications.

Various diagnostic modalities both invasive and non-invasive such as electrocardiography, echocardiography, magnetic resonance imaging and radionuclide scans are utilised for the diagnosis of cardiovascular dysfunction. Echocardiography assessment is non-invasive, easy to perform and provides detailed information of cardiac anatomy, measures systole and diastole function and quantification of LVM and the geometry of LVH objectively.

LVH is the most common abnormality and is associated with left ventricle systolic and diastolic dysfunction. LV systolic dysfunction in patients with CKD is a predictor of worse outcome. Hence, these patients require detailed cardiovascular evaluation despite being asymptomatic.

In our study, the most common cause of CKD was hypertension (42%) followed by hypertension & diabetes together (22%). This was comparable to the studies of Goornavar SM, et al,[11] Levin et al,[12] Lewis et al[13] and Greaves et al.[14] In the studies of Owen et al[15] and Gupta et al,[16] the most common cause of CKD was Chronic Glomerulonephritis. Today, hypertension**,** often together with diabetes, is the first cause of CKD.[17,18] The most common considered mechanisms for hypertension in CKD patients are sodium retention and activation of the renin-angiotensin system.[19] Sympathetic nervous system activation also plays a role. Elevation of plasma catecholamine concentrations, and increased sympathetic nerve traffic has been demonstrated in renal failure.[20-22]

In the present study, 97.4% of patients with a positive urinary albumin had LVH which had statistically significant correlation (p value = 0.041). Also, there was a statistically significant association between the findings of 2D– Echo and lipid profile. Correlation of elevated serum cholesterol value of >200 mg/dl with systolic dysfunction (15.38%), diastolic

dysfunction (41.67%) and combined systolic & diastolic (10%) was statistically significant (P value < 0.05). A higher prevalence of mitral regurgitation & global hypokinesia in patients with elevated total serum cholesterol value of >200 mg/dl, was noted which was statistically significant (with p value - 0.03 & 0.02 respectively). These findings suggest that hyperlipidaemia increases risk of cardiovascular involvement in ESRD patients. Hence, management of dyslipidaemia may play an important role in retarding the progression of cardiac dysfunction in patients with CKD with End Stage Renal Disease.

Out of the 50 patients in our study, only 12 patients (24%) had normal echocardiograms, while 38 patients (76%) have echocardiographic abnormality. These results are comparable to Goornavar SM et al study of 50 cases of CKD, in which only 7 (14%) patients had normal echocardiogram and 43 (86%) patients showed presence of echocardiographic manifestations.[11] LVH was the most common abnormality (92%), followed by diastolic dysfunction(54%), mitral regurgitation (46%),pericardial effusion (40%), Systolic dysfunction alone (4%) both systolic & diastolic dysfunction (20%) & Global Hypokinesia (16%).

The reported prevalence of LVH in literature in patients with CKD is high and varies from 40% to 80% in various studies.[23] Parfrey et al reported that the high prevalence of anaemia and hypertension in patients with CKD might also partly account for increased prevalence of LVH in patients with CKD.[24] In the present study, LVH was the most common echocardiographic finding. LVH was observed in about 92.5% of patients with Hypertension. SA Kale et al identified hypertension as an important risk factor for cardiac dysfunction. There being an independent and significant relationship between systolic, diastolic and mean blood pressure with left ventricular disease.[25] This mandates an aggressive control of hypertension in CKD patients. Reduction of left ventricular hypertrophy with control of hypertension is also being reported.

In the present study, systolic dysfunction was observed in 12 (24%) patients. Robert N. Foley et al (1995) and Mukesh Laddha et al observed about 14.8% and 24.3% of systolic dysfunction respectively in their studies.[1,8,] S.N Agarwal et al (2003) had reported systolic dysfunction in 15% of cases with CKD.[10] NP Singh et al (2000) had found LVH in 76.92%, but did not find systolic dysfunction in CKD patients.[9]

There is a high frequency of LV diastolic dysfunction in patients with CKD and it can further result in development of heart failure and increased mortality. The reported prevalence of left ventricle diastolic dysfunction in CKD patients varies from 50 to 65%, including pre-dialysis, dialysis, and post-transplant populations in various studies.[26] It is observed that diastolic dysfunction can develop even before left ventricular hypertrophy. Diastolic heart function is influenced by numerous factors such as myocardial relaxation and compliance, transvalvular pressure gradient, atrial contraction, pre-load, heart rate, passive elastic properties, respiratory variant, the restraint of pericardium and thoracic wall. As well as arrhythmias and valve incompetence.[27] In the present study, diastolic dysfunction was present in 37 (74%) cases. This is similar to the frequency of diastolic dysfunction reported by NP Singh et al (72%)[9] & S.Agarwal et al (60%).[10] Mukesh Laddha et al, observed 72.9% incidence of diastolic dysfunction in hypertensive patients with CKD and 42.9% in normotensive patients with CKD.[1] The prevalence of pericardial effusion in the present study (40%) is comparable to that of the study of Achari et al (50%).[28]

CONCLUSIONS

Cardiovascular abnormalities were observed in a large number of patients with ESRD (76%) LVH was the most common echocardiographic abnormality in CKD cases. Diastolic function was deranged more when compared to systolic function in patients with CKD. High prevalence of left ventricular hypertrophy, diastolic dysfunction on echocardiography implies that these patients require detailed cardiovascular evaluation despite the absence of symptoms. Timely efforts targeted at the prevention and control of left ventricular hypertrophy such as effective control of hypertension, anaemia and dyslipidaemia, may reduce mortality & morbidity in these patients. Early detection of cardiac abnormalities by echocardiography before the development of overt cardiac symptoms might contribute to better prognosis in these patients.

Limitations of the Study

The sample size in the present study is small (n=50).

This is a retrospective observational study for the prevalence of cardiac dysfunction in patients with CKD with End Stage Renal Disease, before initiating haemodialysis. However, the cardiac dysfunction in CKD patient may alter or evolve over a period with interventions like haemodialysis which is not considered in this study.

In the present study, diabetes & hypertension are the predominant aetiologies of CKD. Cardiac dysfunction in patients with CKD caused by other varied aetiologies couldn't be assessed due to lack of appropriate sample.

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