International Journal of Medicine Research
ISSN: 2455-7404; Impact Factor: RJIF 5.42
Received: 08-03-2019; Accepted: 10-04-2019
www.medicinesjournal.com
Volume 4; Issue 2; April 2019; Page No. 130-134

Cardiac status in CKD patients on maintenance hemodialysis to detect cardiovascular disease: importance of M mode Echocardiography

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Abstract
Background: CVD mortality rates are much greater in dialysis patients despite stratification for sex, race, or age group. Younger dialysis patients have an approximately 500-foldincreased CVD mortality rate compared with their counterparts in the general population, and rates remain approximately five times higher, even among the oldest patients**.**
Aims and Objectives: To assess cardiac status in CKD patients on maintenance hemodialysis to detect coronary artery disease including myocardial infarction, congestive heart failure (CHF), valvular deformities and pericardial disease by M mode Echocardiography
Materials and Methods: One hundred and fifty patients were studied at Department of Medicine Gandhi Medical College and associated Hamidia Hospital Bhopal from September 2016 to June 2019. After detailed clinical evaluation in patients with feature suggestive of CKD, all the patients had undergone urine (PH, Specific gravity, Protein, Sugar, Microscopy), blood (HB%, FBS/PPBS, Urea, Creatinine, Electrolyte, Calcium, Phosphorous) and ultrasound abdomen. M mode electrocardiography (12 lead ECG) was done on patient with chronic kidney disease.
Results: Majority of the patients belong to age group of 60-70 years. Majority of the patients were male [90 (60.7%)]. ECHO findings revealed that diastolic dysfunction were present in 90.67% patients, LVH in 86.67, RWMA in 57.33 and pericardial effusion in46.67% patients. Most common valve abnormality was MR/TR in 36.2% patients, among most common chamber abnormality DCMP (36.6%) was most common. Hypertensive patients had significantly more LVH (74.66%) as compared to non hypertensive (12%) (P=0.012). Patients with hypertension had higher percentage of diastolic dysfunction (88.67%), RWMA (55.33%) and pericardial Effusion (46%). Patients with anemia had higher percentage of diastolic dysfunction (85.33%), LVH (82%), RWMA (54%) and pericardial Effusion (44.67%). Non diabetes patients had higher percentage of diastolic dysfunction (29.33%) and LVH (60%) as compared to diabetes whereas RWMA (40.67%) and Pericardial Effusion (32.67%) were higher among diabetes.
Conclusion: Cardiovascular abnormalities in chronic kidney disease were observed in maximum no of patients and left ventricular dysfunction was the commonest cardiovascular abnormality.

Keywords: cardiovascular disease, pericardial effusion, echocardiography

Introduction

Patients with chronic kidney disease (CKD) are at significantly increased risk for both morbidity and mortality from cardiovascular disease (CVD). Cardiac disease is the single most important cause of death among patients receiving long-term dialysis, accounting for 44%of overall mortality [1, 2].

It is important to emphasize that the prevalence of CVD is increased among all patients with CKD, not only those with end-stage renal disease (ESRD). That is, the prevalence of LVH increases as glomerular filtration declines, and as many as 30% of patients reaching ESRD already have clinical evidence of ischemic heart disease or heart failure. 3 Furthermore, it is important to note that patients with a reduced glomerular filtration rate (GFR) are more likely to die of CVD than they are to develop ESRD [3].

These data reinforce the need to intervene in the earlier stages of CKD, before ESRD, to both prevent and treat CVD. Unfortunately, there have been few studies of CVD in the earlier stages of CKD. However, the limited data available suggest that although such treatments as β-blockers and aspirin are not used as frequently in patients with CVD and reduced GFR, they are of benefit in this subset of the population [3].

Cross-sectional echocardiography is the first technique providing non invasive visualization of the coronary arteries in man. In fact, the technique has been reported8 to permit accurate prospective identification of obstructive disease of the left main coronary artery. Not only can echocardiography directly visualize the diseased coronary artery, but also it can indirectly detect the effects on the left ventricle of acute and chronic ischemia caused by coronary artery disease [4].

Hence in present study we tried to assess cardiac status in CKD patients on maintenance hemodialysis to detect coronary artery disease including myocardial infarction, congestive heart failure (CHF), valvular deformities and pericardial disease by Echocardiography.

Materials and Methods

Present descriptive-Cross sectional study was performed on 150 patients at Department of Medicine Gandhi Medical College and associated Hamidia Hospital Bhopal from September 2016 to June 2019

Patients with azotemia for more than 3 months, symptoms or signs of uremia, reduced Kidney size bilaterally, broad casts in urinary sediment and symptoms or signs of renal osteodystrophy were enrolled.

After detailed clinical evaluation in patients with feature suggestive of CKD, all the patients had undergone urine (PH, Specific gravity, Protein, Sugar, Microscopy), blood (HB%, FBS/PPBS, Urea, Creatinine, Electrolyte, Calcium, Phosphorous) and ultrasound abdomen. M mode electrocardiography (12 lead ECG) was done on patient with chronic kidney disease

Cases with CKD without considering the etiology, patient with chronic kidney disease on routine dialysis and age more than 18 years and less than 55 years were included whereas patients with documented ischaemic heart disease, congenital heart disease, valvular heart disease and age less than 18 years and age more than 55 years were excluded from the present study. This study is approved by the Institutional ethics committee.

All the data analysis was performed using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was used to prepare the tables. Quantitative data was expressed as mean±SD whereas categorical data was expressed as percentage. Chi square test was used to compare the categorical data. Level of significance was assessed at 5%.

Results

In present study mean Age, serum calcium, phosphate, potassium, sodium, urea, creatinine and hemoglobin was 56.60±16.71, 9.23±0.65, 6.09±1.17, 5.39±0.75, 139.89±2.37, 203.78±93.51,9.93±5.13 and 6.67±2.14 respectively.

A Total of 150 cases of CKD were screened out of them maximum were of age group in between 60-70 years. Majority of the patients were male [90 (60.7%).

A total 101 (68%) patients were having diabetes. ECG findings revealed that majority of the patients had Hyper acute T wave (34.7%) followed by LV strain (26%) and Low Voltage Complexes (16.7%). In present study ECHO findings revealed that diastolic dysfunction were present in 90.67% patients, LVH in 86.67, RWMA in 57.33 and pericardial effusion in46.67% patients. Most common valve abnormality was MR/TR in 36.2% patients, among most common chamber abnormality DCMP (36.6%) was most common.

RVSP (right ventricular systolic pressure) is the estimate of pulmonary artery pressure to assess for pulmonary artery hypertension. Majority (30%) of the patients had RVSP in range of 40-50mmhg and 25.3% patients had RVSP in range of 30-40 mmhg and 3.33% patients had RVSP in range of 20-25mmhg whereas 21.3% patients had RVSP in range of 25-30mmhg (46.6% patients had RVSP in between 20-30mmhg) which suggests that 46.6% patients had mild pulmonary artery hypertension whereas 30%patients having moderate pulmonary artery hypertension and 3.3% patients having severe pulmonary artery hypertension. That means out of 150 CKD patients 80% having pulmonary artery hypertension.

Table 1: Comparing hypertension status with ECHO (Echocardiography)

Variable	Status	HTN (>140/80mmhg); n (%)	Non HTN(<140/80mmhg); n (%)	P value
Diastolic dysfunction	Present	133 (88.67)	3 (2)	0.242
	Absent	13 (8.67)	1 (0.67)	
LVH	Present	112 (74.66)	18 (12)	0.012
	Absent	19 (12.67)	1 (0.67)	
RWMA	Present	83 (55.33)	3 (2)	0.478
	Absent	63 (42)	1 (0.67)	
Valve abnormality	Mild to Moderate MR	35 (23.33)	3 (2)	0.413
	MR/TR	50 (33.33)	3 (2)	
	Mild TR	30 (20)	0 (0)	
	Normal	29 (19.33)	0 (0)	
Chambers	DCMP	82 (54.67)	3 (2)	0.713
	LA/LV enlarged	14 (9.33)	2 (3)	
	RA/RV enlarged	48 (32)	1 (0.67)	
Pericardial Effusion	Present	69 (46)	1 (0.67)	0.372
	Absent	77 (51.33)	3 (2)	

Table 2: Comparing anemia status with ECHO

Variable	Status	Hb<10, n (%)	Hb>10, n (%)	P value
Diastolic dysfunction	Present	128 (85.33)	8 (5.33)	0.369
	Absent	14 (9.33)	0 (0)	
LVH	Present	123 (82)	7 (4.67)	0.002*
	Absent	19 (12.67)	1 (0.67)	
RWMA	Present	81 (54)	5 (3.33)	0.778
	Absent	61 (40.67)	3 (2)	
Valve abnormality	Mild to Moderate MR	35 (23.33)	2 (1.33)	0.964
	MR/TR	51 (34)	3 (2)	
	Mild TR	28 (18.67)	2 (1.33)	
	Normal	28 (18.67)	1 (0.67)	
Chambers	DCMP	81 (54)	6 (4)	0.499
	LA/LV enlarged	14 (9.33)	0 (0)	
	RA/RV enlarged	47 (31.33)	2 (1.33)	
Pericardial Effusion	Present	67 (44.67)	3 (2)	0.581
	Absent	75 (50)	5 (3.33)	

Table 3: Comparing Diabetes Status with ECHO

Variable		DM, n (%)	No DM, n (%)	P value
Diastolic dysfunction	Present	9 (6)	44 (29.33)	0.907
	Absent	93 (62)	4 (2.67)	
LVH	Present	40 (26.67)	90 (60)	0.323
	Absent	9 (6)	11 (7.33)	
RWMA	Present	61 (40.67)	5 (3.33)	0.337
	Absent	41 (27.33)	23 (15.33)	
Valve abnormality	Mild to Moderate MR	26 (17.33)	11 (7.33)	0.140
	MR/TR	31 (20.67)	23 (15.33)	
	Mild TR	21 (14)	9 (6)	
	Normal	24 (16)	5 (3.33)	
Chambers	DCMP	68 (45.3)	9 (6)	0.657
	LA/LV enlarged	16 (10.7)	3 (2)	
	RA/RV enlarged	37 (21.3)	17 (11.3)	
Pericardial Effusion	Present	49 (32.67)	21 (14)	0.586
	Absent	53 (35.33)	27 (18)	

Discussion

Premature cardiovascular disease is a significant cause of morbidity and mortality among patients with CKD. Four main structural abnormalities of the heart have been described in patients with CKD: LV hypertrophy, expansion of the nonvascular cardiac interstitium leading to inter-myocardiocyte 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 in turn is a risk factor for premature death.

In present study mean Age, serum calcium, phosphate, potassium, sodium, urea, creatinine and hemoglobin was 56.60±16.71, 9.23±0.65, 6.09± 1.17, 5.39 ±0.75, 139.89±2.37, 203.78±93.51,9.93±5.13 and 6.67±2.14 respectively. A similar study by Laddha *et al*. found that maximum number of patients belonged to age group of 51-60 years. Mean age of ESRD patients was 53.3 ± 12.8 [5]. Study done by Franczyk-Skóra *et al*. reported that the mean age of patients with CKD II–IV was63.97 ±12.5 years and 67.78 ±12.0 in dialysis group [6]. Reports of Laddha *et al*. reported that mean haemoglobin percentage was 7.78 ± 1.84 gm%. Mean blood urea level was 151.7 ± 51.37 mg%. Mean serum creatinine level was 10.35 ± 5.56 gm% [5].

In present study majority of the patients were male [90 (60.7%)] followed by 59 (39.3%) females. Reports of Laddha *et al*. *et al*. showed that out of 70 patients, there were 53 males (75.7%) and 17 females (24.3) [5]. Franczyk-Skóra *et al*. showed that there were more males in dialysis group than in other CKD group (68.57% vs. 30.12%) [6].

In present study diabetes mellitus was the leading cause of ESRD, 101 (68%) were having diabetes. Laddha*et al*. reported that hypertension (37.1%) was leading cause of ESRD, other causes included diabetes (21.4), diabetes with hypertension (10%), chronic glomerulonephritis (8.6%), polycystic kidney disease (7.1%), obstructive uropathy (5.7%), analgesic nephropathy (2.9%) and aetiology remained unknown in 7.1% cases [5]. Franczyk-Skóra *et al*. reported that In dialysis group hypertension (93.1% vs. 85.54%) Was more frequent [6].

In present study ECG findings revealed that majority of the patients had Hyper acute T wave (34.7%) followed by LV strain (26%) and Low Voltage Complexes (16.7%).In a similar study by Laddha *et al*. showed that ECG changes in decreasing order of frequency were sinus tachycardia in 48.6%, LVH in 45.7%, ST –T changes in 30%, ventricular ectopics and Tall 'T' wave in 7.1%, QT prolongation and low voltage pattern in 5.7%, ventricular tachycardia in 2.9% and complete heart block in 1.4% was noted [5].

Echocardiography provides an excellent non-invasive method to study the details of anatomy of cardiac chambers, wall dimensions, valve movements and is also used to assess the cardiac performance. In present study ECHO findings revealed that diastolic dysfunction were present in 90.67% patients, LVH in 86.67, RWMA in 57.33 and pericardial effusion in 46.67% patients. Most common valve abnormality was MR/TR in 36.2% patients, among most common chamber abnormality DCMP (57.7%) was most common. In the study of Laddha*et al*. [5], LVH was present in 74.3%, systolic dysfunction was present in 24.3% of patients as suggested by reduced LVEF measurement and diastolic dysfunction was observed in 61.4% by abnormal E/A ratio of ESRD patients. Mild pericardial effusion (less than 10 mm thickness) was present in 14.3% patients. Mitral and aortic valve calcification and mitral regurgitation was noted in 7.1% patients [5]. Robert N. Foley *et al*. (1995) had found abnormalities of left ventricular structure and functions were very frequent on baseline echocardiography: 73.9% had left ventricular hypertrophy, 35.5% had left ventricular dilatation and 14.8% had systolic dysfunction in ESRD patients [7]. NP singh *et al*. (2000) had found LVH in 76.92%, diastolic dysfunction in 72% butdid not find systolic dysfunction in CKD patients [8]. Zoccali *et al.* (2000) had found 77% LVH, 22% systolic dysfunction by LVEF measurement in haemodialysispatients [9]. S. Agarwal *et al*. (2003) had observed diastolic dysfunction in 60% and systolic dysfunction in 15%of patients [10]. The above findings were consistent with our study. Franczyk-Skóra *et al*. assessed indices of LV diastolic dysfunction in 118 CKD patients and reported that the analysis of echocardiographic parameters showed that in CKD patients the stage of renal failure was associated with the significant increase in LV mass, IVSd, IVSs, systolic LV and diastolic LV [6]. Parfrey *et al*. [11] study, it has been observed that shortly after the dialysis session, a reduction in diastolic diameter of the LV and an increase in the thickness of the LV wall occur which is associated with volume depletion by ultrafiltration. Also, in this study, the RV diameter was found to be much greater in CKD patients stage V/ dialysis (29.9 ±2.9) than in stages II–IV. Left ventricular muscle mass was over 1.5-times higher in dialysis patients that in CKD stage II subjects in the study done by Franczyk-Skóra *et al.* [6] According to Zoccali *et al*. [9] the increase in mass of 1 g/m 2.7/ month was associated with a 62% increase in the incident risk of

fatal and non-fatal cardiovascular events in dialysis patients. They also suggested that changes in LV mass index represent a stronger predictor of mortality and cardiovascular complications than LV mass itself.

Also Miyzato *et al*. [12] in their study of patients with chronic kidney disease noticed increased LV mass. The data of Robert E. Kleiger *et al*. (1981) suggest that hypertrophy and EF appears to be the first detectable abnormality [13]. Agarwal *et al*. assessed the prevalence of systolic and diastolic dysfunction in patients of chronic renal failure on conservative management and reported that the prevalence of diastolic dysfunction was found to be 66.6% (20 patients) in mild/moderate CRF group and 53.2% (16 patients) in severe CRF group [10]. Also, in a study of ESRD patients by Virtanen *et al*. (1998) [14], mean E/A was 1.5 ± 0.5. London *et al*. (1993) reported a significant reduction in E/A ratio in haemodialysis patients as compared to controls [15]. Study done by Agarwal *et al*. is in agreement to the present study findings as in present study maximum patients had diastolic dysfunction (90.67%) [10]. Left ventricular diastolic dysfunction is an important cause of cardiac morbidity in ESRD patients.

In present study there was statistically significant association between the findings of 2D – Echo in patients having hypertension as compared to normotensive group for LVH. Juan M. *et al*. (1998) had found statistically significant difference in E/A ratio, fractional shortening, and LVEF among hypertensive and normotensive patients [16]. Patrick S *et al*. (1999) had found that rise in mean arterial blood pressure was associated with increase in LVH in ESRD patients [17]. SA Kale *et al*. (2001) had found that hypertension was identified as important risk factor for all three LV disorders LVH, diastolic dysfunction and systolicdysfunction [18]. In agreement to present study Laddha *et al*. assessed the prevalence of systolic and diastolic dysfunction in patients of end stage renal disease (ESRD) on haemodialysis and reported that LVH was more common in hypertensive (87.5%) patients as compared to non hypertensive (45.5%) patients (p=0.01), whereas RWMA (16.7% vs.4.5%) and pericardial effusion (14.6% vs.13.6%) was similar among both the groups in hypertensive and non-hypertensive patients respectively) [5]. Franczyk-Skóra *et al*. showed that subjects with hypertension were more likely to have atrial fibrillation, increased diameter of LA, increased atrial volume before dialysis and decreased after it as well as reduced early diastolic velocity (E') and ejection fraction [6].

In anemia, two peripheral effects greatly increased the total peripheral resistance. Those are reduced viscosity of the blood resulting from the decreased concentration of red blood cells. Other is diminished delivery of oxygen to the tissues because of the decreased Hb which causes vasodilatation. In present study patients with anemia had higher percentage of diastolic dysfunction (85.33%), LVH (82%), RWMA (54%) and Pericardial Effusion (44.67%) as compared to patients who were not having hypertension. The comparison was insignificant (p>0.05). Balananda *et al*. [19] estimated the levels of serum creatinine and blood urea to identify the ESRD and to assess the levels of LV function and detect pericardial abnormalities in patients with advanced renal insufficiency by Echo and reported that the reduce in GFR causes decrease in renal excretion of water and solutes and many of the waste products of metabolism such as urea and creatinine accumulate largely due to reduction in functional nephrons. As a result, there is an increase in the levels of urea and creatinine, similar findings were supported by the studies of Dangri.P *et al*. (2003) [20]. As indicated in the results Hb levels are much less in CRF patients. Maximum patients were suffering from anemia.

In present study non diabetes patients had higher percentage of diastolic dysfunction (29.33%) and LVH (60%) as compared to diabetes whereas RWMA (40.67%) and Pericardial Effusion (32.67%) were higher among diabetes as compared to patients who were not having hypertension. The comparison was insignificant (p>0.05).

Cross sectional nature of the study was the main drawback of the study hence, present study findings cannot be applied to larger populations, a large randomized clinical trial is needed to strengthen the present study results. Another limitation was that we cannot included hyperthyroidism, hyper homocysteine and other invasive methods in present study.

Conclusion

Based on the findings of present study we can conclude that cardiovascular abnormalities in chronic kidney disease were observed in maximum no of patients and left ventricular dysfunction was the commonest cardiovascular abnormality. LVH was the most common echocardiographic abnormality in chronic kidney disease cases. Diastolic function was deranged in more number of patients. Major contributing factors for left ventricular hypertrophy and diastolic dysfunction were diabetes, hypertension and anaemia. Echocardiography was more sensitive for detecting LVH and minimal pericardial effusion prior to clinical detection. Early identification of factors involved is necessary to prevent this devastating process.

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