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ORIGINAL RESEARCH

To study the Echocardiographic abnormalities in patients of Chronic Kidney Disease who have undergone haemodialysis

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***ABSTRACT*:**
Aims and objectives: To evaluate and analyse the echocardiographic abnormalities in patients of chronic kidney disease who have undergone haemodialysis. **Material and methods:** About 50 patients of ESRD who were on maintenance haemodialysis in GNDH hospital, Amritsar were taken into study. M mode Echocardiography was performed in the interdialytic period at least after 18 hours post dialysis in those patients without any obvious clinical evidence of coronary heart disease, congenital or valvular heart disease or pericardial effusion. **Results:** Echocardiography revealed Diastolic dysfunction in 64% patients and LVH in 62% patients, systolic dysfunction in 30% patients, RWMA in 18% patients, pericardial effusion in 8% patients and valvular calcification in 16% patients. In a subgroup of patients with Hb<10 g/dL, Diastolic dysfunction was present in 72.5% patients vs 30% in the patient group with Hb≥10g/dL (p=0.012). Similarly Diastolic dysfunction was significantly higher in hypertensive group compared to normotensive group (p=0.03). **Conclusions:** Diastolic dysfunction and LVH were the most common echocardiographic abnormalities noted. There is a significant correlation between anemia and presence of diastolic dysfunction, Similarly significant positive correlation exist between hypertension and diastolic dysfunction in ESRD patients.
Keywords: ESRD; Echocardiography; MHD; LVH ; Diastolic dysfunction; anemia.

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INTRODUCTION:
Chronic Kidney Disease (CKD) is a worldwide public health problem, with increasing incidence and prevalence, high costs, and poor outcomes.[1] End stage renal disease (ESRD) is the irreversible deterioration of renal function which results into impairment of excretory, metabolic and endocrine functions leading to development of the clinical syndrome of uraemia.[2] Haemodialysis is a form of renal replacement therapy, during which metabolic waste products including creatinine, urea, excess water and salt are removed.[3] This is an easily available life-saving treatment modality for ESRD patients compared to renal transplant. Cardiovascular Disease (CVD) is the single most important cause of death among patients receiving long-term dialysis; accounting for 44% of overall mortality. The high burden of CVD mortality is well illustrated by comparing CVD mortality in dialysis population to general population which is 10-30 times higher.[4]
ESRD patients do have myriads of structural and functional cardiac abnormalities which includes LVH, depressed LV function, regional wall motion abnormality, pericardial effusion and valvular calcification. LVH is one of the major structural cardiac abnormalities in patients with CKD and is a very strong independent predictor of cardiovascular mortality.[5] In ESRD patients, hypertension is the leading cause of LVH.Structural LV changes and myocardial fibrosis may also be due to non-hemodynamic factors like angiotensinogen II, parathormone, endothelin, aldosterone and increased sympathetic discharge.[6]

Anemia and hypertension are most consistently associated with cardiac failure, a pre-lethal occurrence that predated two thirds of all dialysis patients' death.[7]. Anemia has an independent impact on the development of congestive heart failure and mortality.[8] Anaemia may contribute to cardiac dysfunction by increasing cardiac output and thereby exacerbate LVH.[9] For every 1 g/dl drop in mean hemoglobin, the risk of cardiac failure increases by 25%, echocardiographically demonstrable LVH by 42%, and risk of death by 14%.[10]

There is progressive increase in LVH with loss of renal function, so that 80% of patients on renal replacement therapy have LVH. The prevalence of diastolic dysfunction increased in parallel with changes in left ventricular mass.[11] Impairment of diastolic function in patients with CKD may occur very early, even in the absence of LVH and it is suggested that early detection of diastolic dysfunction could yield an improvement in the adverse cardiovascular outcomes.[12] Zoccali et al found that LV systolic dysfunction is frequent in asymptomatic dialysis patients. Independent of other risk factors, it carries prognostic value for incident CV complications. The presence of systolic dysfunction interacts with LVH in the prediction of incident CV events.[13]

In this study we evaluated the cardiovascular abnormalities by performing 2-D echocardiography in CKD patients on maintenance hemodialysis (MHD).

MATERIALS AND METHODS:

Fifty ESRD patients irrespective of underlying etiology were included in this study. A person was labelled as ESRD if his or her GFR was less than 15 ml/1.7 m^2 as per Modified Diet in Renal Disease (MDRD) equation and who were on MHD for atleast 3 months. Patient with obvious clinical evidence of coronary artery disease, valvular heart disease and pericardial effusion, rheumatic heart disease, congenital heart disease, primary cardiomyopathies and age less than 18 years were excluded from the study. All patients were clinically evaluated thoroughly and subjected for complete blood count, renal function test, serum cholesterol, calcium, and phosphate. Echocardiography was performed in the inter-dialytic period atleast 18 hours post dialysis.

Transthoracic echocardiography was done in each individual using M Mode 2D-echocardiography-PHILIPS IE33 machine, in the department of Medicine in Govt. Medical College, Amritsar and the parameters like Left Ventricular Hypertrophy, Systolic Dysfunction, Diastolic Dysfunction, Regional Wall Motion Abnormality (RWMA), pericardial effusion and valvular Calcification were recorded

The M. mode recording perpendicular to the long axis of and through the centre of the left ventricle at the papillary muscle level was taken as standard measurements of the systolic and diastolic wall thickness and chamber dimensions. LVH was diagnosed when inter ventricular septum thickness or Left ventricular posterior wall thickness at systole is ≥ 12 mm. Ejection Fraction (EF) is measured using modified Simpson method. EF<55% was considered as systolic dysfunction.

Diastolic function is 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 is considered as diastolic dysfunction. Regional wall motion abnormality (RWMA), pericardial effusion and valvular calcification was recorded by direct visualization using 2D echocardiography.

The data were collected systematically and analysed statistically according to the standard statistical methods using SPSS software. Chi square test was used and 'p' value less than 0.05 was considered significant.

RESULTS:

This study included 50 patients of ESRD on MHD. Clinical examination, suggested laboratory tests and echocardiography were performed in every patient. The mean age of the patients is 57.18±12.8 yrs. Maximum number of patients 27 (54%) belong to the age group of 41-60 yrs. Out of 50 patients, 26(52%) were males and 24(20%) were females.

The Etiology of CKD were Diabetes in 27(54%) patients, Hypertension in 16(32%) patients, Chronic Glomerulonephritis (CGN) in 6(12%) patients and Chronic tubulointerstitial disease(CTID) in 1(2%) patient. Diabetes (54%) is the major contributor to CKD followed by hypertension. Distribution of patients according to duration of MHD is shown in figure 1.The basic demographic and biochemical characteristics of the study population is shown in table 1.

The most common echocardiographic abnormality observed in our study is diastolic dysfunction (64%) followed by LVH (62%). The least noticed abnormality is pericardial effusion (8%) as shown in table 2.

The mean haemoglobin (Hb) of patients in our study is 7.79 g/dL. Most patients (54%) had Hb between 5-9 mg/dL. Except for 1 patient, all other patients had anemia (as per KDIGO criteria). Based on the Hb levels, we divided the study patients into 2 groups, one group has patients with Hb ≥10 g/dL and other group has patients with Hb <10 g/dL (significant anemia group). 40 patients belong to the "significant anemia" group and 10 patients fall in the other group.

Table 3 shows the echocardiographic findings in these two groups as compared in our study. 29(72.5%) patients had diastolic dysfunction in the group with Hb<10 g/dL compared to 4(30%) patients in the group with Hb≥10 g/dL. This was statistically significant with p=0.012**.**

In this study, 45(90%) patients were hypertensive (BP ≥140/90) and 5 (10%) patients were normotensive. The ratio of hypertensive to normotensive patients in this study is 9:1. Echo findings in the two groups are

compared as shown in table 4. Hypertensive group has LVH in 64% patients compared to 35% in normotensive group. But this was not statistically significant. (p value=0.28). 68.89% patients in Hypertensive group and 20% patients in normotensive group had Diastolic dysfunction. This was statistically significant (p value=0.03). Valvular calcification is found only in the patients with maintenance hemodialysis duration of 10-12 months.

FIGURE 1: DISTRIBUTION OF PATIENTS ACCORDING TO DURATION OF MHD

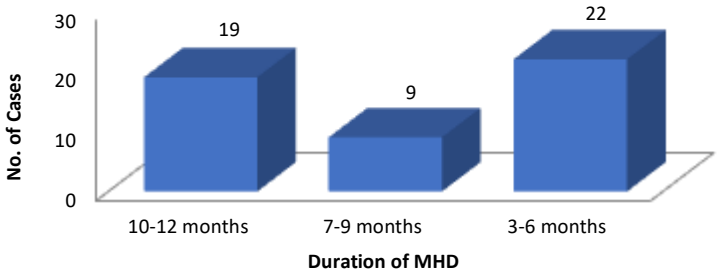

TABLE 1: DISTRIBUTION OF PARAMETERS

Parameters	Mean	SD	Minimum	Maximum
Age in years	57.18	12.81	50	80
Hb (g/dL)	7.79	2.377	3.5	13.6
Urea (mg/dL)	174.64	72.46	74	470
Creatinine (mg/dL)	8.15	2.250	3.7	16
Sodium (mEq/dL)	132.44	1.44	111	146
Potassium (mEq/dL)	4.60	0.13	2.5	8
Calcium (mg/dL)	9.85	.814	8.3	11.2
Phosphorus (mg/dL)	5.88	.80	4.6	7.3
Calcium Phosphate Product	57.95	9.43	41.40	79.57
Serum albumin (g/dL)	4.18	3.49	2.6	4.8
Total cholesterol (mg/dL)	220.7	42.25	151	292

TABLE 2: ECHOCARDIOGRAPHIC CHANGES IN CKD PATIENTS ON MHD

No.	Echo Parameters	No. of Cases	Percentage
1	Left ventricular hypertrophy (LVH)	31	62%
2	Systolic dysfunction / Ejection fraction <55%	15	30%
3.	E/A ratio <0.75 or >1.8 / diastolic dysfunction	32	64%
4	Regional wall motion abnormality (RWMA)	9	18%
5	Pericardial effusion (<11 mm)	4	8%
6	Valvular calcification	8	16%

TABLE 3: RELATIONSHIP BETWEEN SIGNIFICANT ANEMIA AND ECHO CHANGES

Sr. No	Echo parameters	Significant Anemia (Hb<10)				Total	'p' value
		Present (n=40)		Absent (n=10)			
		No. of cases	% age	No. of cases	% age		
1	Left Ventricular Hypertrophy	24	60	7	70	31	0.56
2	Ejection fraction (<55%) Systolic Dysfunction	13	32.5	2	20	15	0.44
3	E/a Ratio (<0.75 or >1.8) Diastolic Dysfunction	29	72.5	3	30	32	0.01*
4	Regional Wall Motion Abnormality	6	15	3	30	9	0.26
5	Pericardial Effusion	2	12.5	2	20	4	0.11
6	Valvular Calcification	6	15	2	20	8	0.69

TABLE 4: RELATIOSHIP BETWEEN PRESENCE/ABSENCE OF HYPERTENSION AND ECHOCARDIOGRAPHIC CHANGES:

Sr. No.	Echo parameters	Hypertension				Total	'p' value
		Present (n=45)		Absent (n=5)			
		No. of cases	%age	No. of cases	%age		
1	Left ventricular hypertrophy	29	64.44	2	40	31	0.28
2	Ejection fraction (<55%) systolic dysfunction	12	26.67	3	60	15	0.12
3	E/a ratio (<.75 or >1.8) diastolic dysfunction	31	68.89	1	20	32	0.03*
4	Regional wall motion abnormality	9	20	0	0	9	0.26
5	Pericardial effusion	3	6.6	1	20	4	0.29
6	Valvular calcification	6	13.33	2	40	8	0.12

TABLE 5: PREVALANCE (IN PERCENTAGES) OF ECHOCARDIOGRAPHIC ABNORMALITIES AMONG ESRD PATIENTS IN VARIOUS STUDIES.

	LVH	Diastolic dysfunction	Systolic dysfunction	RWMA	Pericardial effusion	Valvular calcification
Agarwal S et al (2003)[97]		53.2	30			
Zoccoli et al (2004)[60]	77		22			
Laddha M et al (2014)[98]	74.3	61.4	24.3	12.9	14.35	
Shivendra et al (2017)[27]	48	51.42	28.57	8.5	17.14	0
Sachdeva et al (2017)[99]	65.21	43.47	21.7	2.83	21.73	
This Study	62	64	30	18	8	16

DISCUSSION:

Cardiovascular disease is the major cause of death in patients with end stage renal disease. The common cardiac abnormalities in CKD patients are LVH, systolic and diastolic dysfunction due to myocardial fibrosis, myocardial calcification and changes in the vascular structure, leading to adverse cardiovascular events.

The prevalence of various echo findings in ESRD patients in similar studies is summarised in Table 5 . In this study, prevalence of LVH was observed in 62% patients. Zocalli et al[13] found LVH in 77% patients. Laddha M et al[14] observed LVH in 74% of his patients. Also Damija et al[15] & Shivendra et al[16] both observed LVH in a consistent 48% of patients in their study group. Harnett et al[17] observed LVH in 74% of patients. Our observation of LVH is not consistent with any of these studies. In fact it is higher than in Shivendra et al[16] and Dhamija et al[15] and less when compared to Zocalli et al[13] and Laddha M et al[14]

Diastolic dysfunction was observed in 33(66%) patients in our study. While similar studies by Laddha M et al[14], Agarwal et al[18] and Shivendra et al[16] found diastolic dysfunction in 61.4%, 53.2%, and 51.42% patients respectively, Our study had higher prevalence of diastolic dysfunction comparatively. This study is most consistent with Laddha M et al.[14]

Systolic dysfunction was observed in 15 (30%) patients in our study. while Zoccali et al[13], Laddha M et al[14], Agarwal S et al[18], Shivendra et al[16] found systolic dysfunction in 22%, 24.3%, 30%, 28.57% of their patients respectively. With respect to prevalence of systolic dysfunction, our study is consistent with Agarwal et al[18]

RWMA is seen in 18% patients and pericardial effusion is seen in 8% patients in our study. Valvular calcification is found in 8(16%) patients in our study. Parfrey[19] et al showed that Valvular calcifications are four times more common in dialysis patients compared to general population. In our study we have no comparative cohort of non dialysed CKD patients to compare. Other similar studies of Shivendra et al[16] and Dhamija et al[15] and many others[14,18] found no patients with valvular calcification probably because of lesser duration of maintenance hemodialysis and inter-observer variability.

In this study, we divided the patients into 2 groups based on Hb levels. 20% of patients had Hb ≥10 g/dL and 80% of patients had Hb <10 g/dL (significant anemia). LVH is seen in 60% of patients in significant anemia group compared to 70% of patients in the

group with Hb≥10 g/dL. This was statistically insignificant (p=0.58). But laddha M et al[14], Shivendra et al[16], Dhamija et al[15] showed a significant correlation between LVH and anemia by similar grouping methods and cut offs. On a similar note, our study is also in contrast to Datta et al[20] who observed severity of anemia in correlation to LVH in patients with CKD. This study is also not consistent with Foley et al[7] who showed that Anemia is a strong predictor of development of LVH.

Diastolic dysfunction was seen in 72.50% of patients in significant anemia group compared to 30% of patients in group with Hb>10 g/dL. This was statistically significant with p value of 0.01. This observation is not consistent with Shivendra et al[16] and Dhamija et al[15], as their studies failed to show such correlation.

In our study, Hypertension is seen in 90% of patients. 64% of the patients in hypertensive group had LVH compared to 40% in normotensive group. This was not statistically significant. (p=0.28). This finding is not consistent with Shivendra et al[16], Dhamija et al[15] and Laddha M et al[14] who showed significant correlation between presence of hypertension and LVH.

Diastolic dysfunction was seen in 68.8% of patients in hypertensive group compared to 20% of patients in normotensive group. This was statistically significant with p value of 0.02. This finding is consistent with Laddha M et al[14] who found significant correlation between Hypertension and diastolic dysfunction (p<0.05). But Shivendra et al[16] and Dhamija et al[15] couldn't find such correlation.

Levin et al showed association between elevated systolic blood pressure and low hemoglobin level with LVH in predialysis patients.[21,22]

CONCLUSION:

Cardiac structural as well as functional abnormalities are common in patients with ESRD, more so in those with hypertension and anemia. Diastolic dysfunction is the commonest cardiac abnormality in ESRD patients, followed by LVH. Diastolic Dysfunction is more marked in hypertensive and anemic populations. The frequency of echocardiographic abnormalities had no correlation with the duration of maintenance hemodialysis except for valvular calcification which was found only in patients of long-term maintenance hemodialysis. It's a prevalence study, and hence no follow up was done to comment on prognostic significance of the echo parameters. Echocardiography is a cost effective noninvasive diagnostic test which can detect early changes in the cardiac parameters. This is important for risk stratification and early preventive measures. Thus echocardiographic screening of ESRD patients has therapeutic implications. All asymptomatic ESRD patients especially anemic and hypertensive should undergo a routine echocardiographic evaluation.

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