ORIGINAL RESEARCH ARTICLE

Assessment of Lest Ventricular Hypertrophy and Left Ventricular Diastolic Dysfunction Cardiovascular in Patients of Chronic Renal Failure by Echocardiography

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ABSTRACT

Introduction: Chronic renal failure, regardless of the cause, is the presence of kidney damage or a reduced level of kidney function for three months or longer. It is a group of signs and symptoms brought on by slow and long-term renal damage. The most frequent cardiovascular finding in people on dialysis is LVH.

Objective: The study was conducted to estimate the prevalence of left ventricular hypertrophy and left ventricular diastolic dysfunction by echocardiography in patients with chronic renal failure.

Method: This was an observational cross-sectional study at the Department of General Medicine among IPD patients, Tertiary Care Hospital, Surat.

Result: Left ventricular hypertrophy out of 34 cases 22 (64.71%) cases were show left ventricular hypertrophy with an odd ratio of 3.208 (1.049, 9.81) and a p-value 0.0378 which was statically significant. prevalence of diastolic dysfunction was 79%. comparison of renal function test and echocardiographic change of chronic renal failure. In the renal function test serum, creatinine and EGFR were show a p-value < 0.001 which was statistically significant.

Conclusion: Cardiac dysfunction and LVH are frequently noted in individuals with chronic renal failure at the time of commencement of dialysis. cardiovascular abnormalities in the form of LVH and diastolic dysfunction which antedate severe systolic dysfunction are frequently observed in milder degrees of chronic renal failure

Key words: Left ventricular hypertrophy, Left ventricular diastolic dysfunction, Chronic renal failure, Echocardiography

INTRODUCTION

The existence of kidney damage or a diminished degree of kidney function for three months or more, regardless of the reason, is referred to as chronic renal failure. It is a collection of symptoms and indicators brought on by gradual and permanent kidney impairment.[1]

LVH is the most common cardiovascular finding in the dialysis population [2]. Patients with end-stage renal illness frequently experience left ventricular hypertrophy, which is a significant negative prognostic indication.

In fact, 60–75% of patients beginning renal replacement therapy were found to have left ventricular hypertrophy as shown by echocardiography.[3] Of these, 40% of patients beginning dialysis already had signs of CAD, and only 15% were considered to have normal left ventricular structure and function.

Because chronic renal failure affects a younger population in India and 2/3 of those affected had end-stage renal disease at the time of diagnosis [4], it is important to assess cardiovascular health early on when chronic renal failure is present. The frequency of dilated Between 50% and 65% of patients with chronic renal insufficiency have left ventricular dysfunction.[1] The mechanistic definition of left ventricular dysfunction is impaired LV relaxation and increased LV stiffness.[5] Despite typical systolic left ventricular dysfunction, diastolic dysfunction might result in left ventricular failure. Systolic dysfunction, on the other hand, can be managed but not fully treated, whereas diastolic dysfunction can be restored to normal on medication.[1] Diastolic dysfunction detection prevents the development or advancement of systolic dysfunction.

Co-morbid disorders like CRF provide a hemodynamic and metabolic load that activates the sympathetic nervous system and the RAAS while suppressing the parasympathetic nervous system [6]. These factors produce a pro-inflammatory and profibrotic signalling that attracts circulating hematopoietic progenitor cells, changes endothelial function, and increases ROS (reactive oxygen species). These changes in ROS and ROS levels change the extracellular matrix, which promotes fibrosis and cardiomyocytic mechanisms like calcium and energy regulation, myofilament structure and function, and intracellular signalling. Diastolic dysfunction is the end outcome of these ECM and cardiomyocyte alterations taken collectively.

METHODOLOGY

Patients with Chronic Renal Failure admitted in medicine ward were included in the study. Patients were provided with all information about the study in the form of PIS (Patient Information Sheet) in their local language. Those

patients who gave written informed consent were formally enrolled in the study. Patients were subjected to symptom analysis, clinical examination, and laboratory investigations. A structured clinical proforma was used for data collection in which all pertinent details of the patients were recorded. Study was conducted at Department of General Medicine among IPD patients, Tertiary Care Hospital, Surat. After taking ethical approval patients were include in the study till 15 months of duration. This was observational cross-sectional study. Patients were including in the study based on following criteria

Patient with kidney damage of more than or equal to 3 months, GFR< 60ml/min/1. 73m for >3 months with evidence of kidney damage, age >18 years, serum creatinine value of >1. 5mg%, patients on haemodialysis with or without arterio - venous fistula and abnormalities like decrease kidney size and loss of cortico- medullary differentiation detected by USG was included in the study.

We also excluded those patients who had kidney damage of less than or equal to 3 months or age <18years or unilateral and bilateral renal artery stenosis or nephrectomy of 1 kidney

During the study period, all patients satisfying the inclusion criteria were invited to participate in the study. Patients were provided with all information about the study in the form of PIS (Patient Information Sheet) in their local language. Those patients who gave written informed consent were formally enrolled in the study. A structured clinical proforma was used for data collection in which all pertinent details of the patients were recorded. Information regarding chief complaints, history of present illness, personal history etc. was recorded. The demographic variables collected were age, gender, occupation, etc. General physical examination was done to record variables like pulse rate, blood pressure, respiratory rate, temperature, pallor, icterus etc. All routine investigations like CBC, LFT, RFT, Urine routine micro, RBS, ESR, Lipid profile, Chest X-Ray and USG abdomen were done in all the patients. Electrocardiography and echocardiography were performed subsequently.

Sample size calculated by considering the proportion of LV dysfunction among CRF patient and that is 48% (24/50) from previous study [5] Taking p as 48%, q as 1-p, L Allowable error 10%, Zα/2 as 95% level of significance the calculated sample was 96 using sample size formula n = $Z^2\alpha_{/2}pq/L^2$ which was rounded to 100.

Data was entered in MS EXCEL Spread sheet and analysed with the help of Open- epi version 3. 01 updated 2013/04/06 and SPSS software the statistical analysis was done by appropriate Statistical method. Descriptive statistics was explained by frequency and percentage. Test of significance using ANOVA test and Chi-square test. Confidence interval was set as 95 %. Thus, p value less than 0. 05 was considered as statistically significant. Informed written consent for allowing the clinical data of the patients to be used for study purpose was obtained from all the patients. Method of blood collection as well as advantage and disadvantage of study was explained to the patients. The personal identification of the patients like name, address etc. we're not entered during the preparation of the data spread sheet. Unique identifiers were allotted to all the patients and only the unique ID was entered during data entry and analysis. All the patient's proforma were kept securely under lock and key with the principal investigator. Patient were educated about clinical features of chronic renal disease. Patient were explained about results of cardiac manifestations in Chronic Renal Failure and appropriate management was advised.

Equation from the Modification Diet in Renal Disease study: MDRD Study equation provides a clinically useful estimate of GFR up to approximately 90 mL/min/1. 73 m^2

Estimated GFR (mL/min per 1. 73 m^2) = 186x $(S.Cr)^{-1.154}$x $(age)^{-0.203}$ multiply by 0. 742 for women Multiply by 1.21 for man.

Cockcroft-Gault equation is Estimated creatinine clearance (ml/min) = (140-age) x body weight (kg)/72 x S. Cr (mg/dL) Multiply by 0. 85 for women

The CKD-EPI Creatinine Equation

The CRF-EPI (Chronic Renal Failure Epidemiology Collaboration) creatinine equation is based on the same four variables as the MDRD Study equation but uses a 2-slope "spline" to model the relationship between estimated GFR and serum creatinine, and a different relationship for age, sex and race. The equation was reported to perform better and with less bias than the MDRD Study equation, especially in patients with higher GFR.

GFR = 141 x min $(scr/\varkappa, 1)^{\alpha}$ x max $(scr/\varkappa, 1)^{-1.209}$ x 0. 993Age×1.018 (if female) x1. 159 (if black) where, SCr (standardized serum creatinine) = mg/dL

Where $\varkappa$ = 0. 7 (females) or 0.9 (males), α = -0. 329 (females) or -0.411 (males), Min = indicates the minimum of SCr/$\varkappa$ or 1, Max = indicates the maximum of SCr/$\varkappa$ or 1 and Age in years

Based on the above investigational profile the study population was divided in following groups:

Stage 1: Kidney damage with normal or increased GFR (>90 mL/min/1. 73 m^2)
Stage 2: Mild reduction in GFR (60-89 mL/min/1. 73 m^2)
Stage 3a: Moderate reduction in GFR (45-59 mL/min/1. 73 m^2)
Stage 3b: Moderate reduction in GFR (30-44 mL/min/1. 73 m^2)
Stage 4: Severe reduction in GFR (15-29 mL/min/1. 73 m^2)
Stage 5: Kidney failure (GFR < 15 mL/min/1. 73 m^2 or dialysis)

Echocardiography

Echocardiography was performed on a GE VIVD 56 ECHO machine with a 2. 5 to 3.5 MHTZ transducer on 2-D M mode and Doppler ultrasound.

M-Mode echocardiography: M-mode recording was done by method of Sahn et al. Left ventricular internal diameter (LVID) at systole (LVIDS) and end diastole (LVIDd) which gives a reliable index of LV chamber size and are most reproducible, was calculated by 2D directed M mode echo at the level of papillary muscle.

Interventricular septal thickness (IVS) was measured at end'

of systole (IVSS) and end diastole (IVSd) by Leading Edge metho d (American college of echocardiography 1978).

LV posterior wall thickness (LVPWT) was also measured at end systole (LVPWTS) and end diastole (LVPWTd)by Leading Edge method. LV diameters, IVS and PWT were all measured at the level of chordae tendinae.

The ratio of interventricular septum (IVSd) and posterior wall thickness (PWTd) at end diastole were calculated. A ratio greater than 1.3 was taken as evidence of asymmetrical septal hypertrophy. Left atrial diameter was calculated as described by Sahn. A diameter of greater than 4.0 cm was taken as evidence of left atrial dilatation. Percent fractional shortening (% FS). It is a demonstrable echo parameter but can be calculated as %FS = LVIDA-LVIDSs ×100% LVIDA. It is a useful index of LV contractile state, but usually in absence of regional wall motion abnormality.

2-D Echocardiography: Left ventricular volumes at end systole [LVESV] and end diastole [LVEDV] were measured by apical 4 chamber view. LV ejection fraction [LVEF] is the most useful single index of LV function because it correlates best with patient's clinical outcome.

It can be calculated as: LVEF= LVEDV-LVESV x 100% LVEDV

The left ventricular ejection fraction (LVEF) and fractional shortening (FS%) were taken as measures of LV systolic function. EF was considered decreased if it was <50 % and FS of < 25% was taken as index of systolic dysfunction

Diastolic function was determined by Ratio of peak early diastole velocity [E] divided by peak atrial filling velocity [A] of LV, measured by spectral Doppler LV inflow velocity with sample volume at the level of mitral valves. LV diastolic dysfunction was considered if E/A velocity was found to be <0. 8, Left ventricular mass was determined by M-mode echo using formula, LVM (gm) 0.8 x 1. 04 $[(LVIDd+PWT+IVS)^3- (LVIDd)^3] +0.6$, LVM was indexed per square meter of body surface area (BSA) and LV hypertrophy was denned in absolute terms as more than 134gm /m^2 in men & > 110gm/m^2 in women.

RESULT

In table 1 show that distribution of chronic renal failure according to their age gender and stages of chronic renal failure, further as per age group distribution 34 cases were belong from 41 to 50 years group, out of 34 cases 22 (64.71%) cases were show left ventricular hypertrophy with odd ratio 3.208 (1.049, 9.81) and p value 0.0378 which was statically significant.

While as per gender distribution male patients were contribute 70 cases and out of 70 cases 40(57.14) cases were show left ventricular hypertrophy with odd ratio 1.75(0.7752, 3.951) and p value 0.175 which was statically significant.

Table 1 Comparison of Demographic variables with Left ventricular hypertrophy

Variables	Cases	Left ventricular hypertrophy (%)	Odd ratio (95%CI)	P value
Age group (in years)				
21-30	22	8 (36.36)	Ref	
31-40	18	9 (50.00)	1.75 (0.4924, 6.22)	0.3854
41-50	34	22 (64.71)	3.208 (1.049, 9.81)	0.0378
51-60	12	5 (41.67)	1.25(0.2964,5.272	0.7611
61-70	10	7 (70.00)	4.083 (0.8184, 20.37)	0.07718
71-80	4	4 (100.00)	-	0.0188
Gender				
Female	30	15 (50.00)	Ref	
Male	70	40 (57.14)	1.75(0.7752, 3.951)	0.175
CRF Stage				
3	14	6 (42.86)	1.39 (0.3429, 5.657)	0.6427
4	20	7 (35.00)	Ref	
5	66	42 (63.64)	3.25 (1.141, 9.257)	0.02345

CI – Confidence interval; *CRF - chronic renal failure

Table 2: Comparison of Demographic variables with Diastolic disfunction

Variables	Cases	Diastolic disfunction (%)	Odd ratio	P value
Age group (in years)				
21-30	22	13 (59.09)	Ref	
31-40	18	16 (88.89)	5.53(1.014, 30.25)	0.03575
41-50	34	28 (82.35)	3.23(0.9495, 10.99)	0.05489
51-60	12	12 (100.00)		
61-70	10	6 (60.00)	1.038(0.2262, 4.767)	0.9613
71-80	4	4 (100.00)		
Gender				
Female	30	26 (86.66)	2.085(0.6369, 6.825)	0.2183
Male	70	53 (75.71)	Ref	
CRF Stage				
3	14	12 (85.71)	2.57 (0.4353, 15.19)	0.2892
4	20	14 (70.00)	Ref	
5	66	53 (80.30)	1.74 (0.563, 5.422)	0.3306

CI – Confidence interval; *CRF - chronic renal failure

Table 3 Comparison of Renal function and Echocardiographic variables with Stages of CRF

Variables	Stages of CRF			P value
	3	4	5	
S. Creatinine	2.06±0.40	4.6±0.85	8.54±2.99	<0.001
EGFR	34.54±2.84	18.96±3.15	18.96±3.15	<0.001
Echocardiographic findings				
LA (mm)	36.85 ±8.79	35 ± 7.85	33.53 ± 6.78	0.273
LVESD (mm)	30.14 ± 5.12	29.3 ± 3.97	31.09 ± 5.66	0.395
LVESD (mm)	47.85 ± 4.16	44.2 ± 4.95	45 .33 ± 7.90	0.295
IVS thickness(mm)	3.14 ± 0.53	5 ± 0	4.68 ± 0.46	-
LVPWT (mm)	10.85 ± 2.45	10.9 ± 2.35	12.48 ± 2.92	0.0261
EF%	45 ± 12.70	48.5 ± 12.15	50.66 ± 10.99	0.230
FS%	23.57 ± 6.77	24.8 ±6.15	25.98 ± 4.81	0.270

S. CREAT – serum creatinine; EGFR - Estimated Glomerular Filtration Rate; LA – Left atrium; LVESD – Left ventricular end-systolic diameter; LVPWT – Left ventricular posterior wall thickness; IVS - Interventricular septal thickness; EF - Ejection fraction; FS - Fractional shortening

Furthermore, stages of chronic renal failure distribution stage 5 were contributed 66 cases, out of 66 cases 42 (63.64%) patients were show left ventricular hypertrophy with odd ratio 3.25 (1.141, 9.257) and p value 0.02345 which was statically significant.

Table 2 show that distribution of chronic renal failure according to their age gender and stages of chronic renal failure, further as per age group distribution 34 cases were belong from 41 to 50 years group, out of 34 cases 28 (82.35%) cases were show diastolic disfunction with odd ratio 3.23(0.9495, 10.99) and p value 0.05489 which was statically significant.

While as per gender distribution male patients were contribute 70 cases and out of 70 cases 53(75.71%). with odd ratio 2.085(0.6369, 6.825) and p value 0.2183 which was not statically significant.

Furthermore, stages of chronic renal failure distribution stage 3 were contributed 14 cases, out of 14 cases 12 (85.71%) patients were show diastolic disfunction with odd ratio 2.57 (0.4353, 15.19) and p value 0.2892 which was statically significant.

Table 3 show that comparison of renal function test and echocardiographic change of chronic renal failure. In renal function test serum creatinine and EGFR were show p value < 0.001 which was statistically significant. While comparison of echocardiographic changes and stages of chronic renal failure were not show any statistically significant expect LVPWT.

DISCUSSION

Left ventricular hypertrophy as per age group distribution 34 cases were belong from 41 to 50 group, out of 34 cases 22 (64.71%) cases were show left ventricular hypertrophy with odd ratio 3.208 (1.049, 9.81) and p value 0.0378 which was statically significant. In the metanalysis of various international studies done by Nathan R. Hill et al; 13.7% patients were of age group 31-40 years, 12% patients were between 41-50 years, 16% patients were between 51-60 years, 27.6% patients were between 61 to 70 years and 34.3% were older than 70 years.[7]

In comparison to metanalysis done by Nathan R. Hill, we have 47.6% less patients with age of >60 years and 13% more patients in 41-60 years age group. This difference may be due to age distribution of general population of India, it is quite younger with only 6.4% of population is older than 65 years.

Increasing age is a risk factor for LVH. In the present study, LVH was more prevalent in41- 50years age group with mean age of 47.42 years. While in a study by Abdou Elhendy et al [8] the age group with maximum prevalence of LVH was 50-70 years with mean age being 66 years. In another study by Saxena S. et al. mean age of patients in the study was 37.5 years. Shutov AM. et al from Russia showed in their study of CRF patients that the mean age of patients was 51 years 40-60 years.

While as per gender distribution male patients were contribute 70 cases and out of 70 cases 40(57.14) cases were show left ventricular hypertrophy with odd ratio 1.75(0.7752, 3.951) and p value 0.175 which was statically significant. In a study done by Bikbov B. et al. the male to female ratio of CRF prevalence across 195 countries were found to be 0.8 against the general population's sex ratio [M:F] of 1.01.[9] Where as in our study the male to female ratio of CRF was 2.33 against the Surat population's sex ratio [M:F] of 1.35. So, in our study male proportion was higher in comparison to general population, while in study done by Bikbov et al. female proportion was higher in comparison to general population. This gender disparity is partly contributed by the sex ratio [M: F] of Surat city which is 1.35. This sex ratio is also because most of Surat city's population is migratory and is mainly formed by migratory males from different parts of India.

In present study, prevalence of LVH was more in males compared to females and the result is consistent with CRIC study while in a study by IT Murkamilov, there is a trend towards a worse prognosis among women with baseline LVH compared with men[10] Furthermore, stages of chronic renal failure distribution stage 5 were contributed 66 cases, out of 66 cases 42 patients were show left ventricular hypertrophy with odd ratio 3.25 (1.141, 9.257) and p value 0.02345 which was statically significant.

In the metanalysis of around 100 global studies done by Nathan R. Hill et al [7] the stage wise prevalence out of total CRF prevalence in general population was 24% in stage 1, 23% in stage 2, 49% in stage 3, 3% in stage 4 and 1% in stage 5. In comparison to metanalysis done by Nathan R. Hill, we have 47% less patients with CRF Stage 1 and 2 while 82% more patients in CRF Stage 4 and 5. Thus our study had a greater proportion of severely affected patients than the study done by Nathan R. Hill. This difference may

be due to metanalysis had study subjects from general population, while current study was carried out in patients admitted at tertiary care center of South Gujarat There is increased chance of left ventricular hypertrophy in CRF patients. With respect to category of Chronic Renal Failure, the LVH prevalence progressively increases with increasing severity of CRF (Chronic Renal Failure) as seen in present study as well as in Vankayala et al study. [11]

In our study as per age group distribution 34 cases were belong from 41 to 50 group, out of 34 cases 28 (82.35%) cases were show diastolic disfunction with odd ratio 3.23(0.9495, 10.99) and p value 0.05489 which was statically significant. While as per gender distribution male patients were contribute 70 cases and out of 70 cases 53(75.71).

In our study, prevalence of diastolic dysfunction was 79% and the results were consistent with other studies like Tarun Rao et al [12] and P. Chillo et al [13] with 67.20% and 68.60% prevalence respectively. Furthermore, stages of chronic renal failure distribution stage 3 were contributed 14 cases, out of 14 cases 12 patients were show diastolic disfunction with odd ratio 2.57 (0.4353, 15.19) and p value 0.2892 which was statically significant. In the present study, the prevalence of diastolic dysfunction was maximum in stage 5 that is 67.09% and in a study by Tarun Rao, the results were like our study with 77.8% prevalence.

In our present study, in stage 3 both LVH and Diastolic dysfunction was present in 9.30% patients (4 out of 43), 22.22% (8 out of 36) patients had only diastolic dysfunction without LVH. In stage 4, both LVH and diastolic dysfunction was present in 11.63% patients (5 out of 43), 25.0% patients (9 out of 36) had only diastolic dysfunction without LVH.

In stage 5, both LVH and Diastolic dysfunction was present in 79.90% patients (34 out of 43),52.78% (19 out of 36) patients had only diastolic dysfunction without LVH and the results were significant (P value=0.04620).

In the study by S.Agarwal et al [14], LVH and diastolic dysfunction was present in 30% patients of mild to moderate CRF stage and 53.2%patients of severe CRF stage which is in concordance with previous study done by Rathod Nitin et al in which , LVH and diastolic dysfunction was present in 11.1% patients of mild to moderate CRF stage and 56.52%patients of severe CRF stage and the results were significant showing P value =0.0018.

In our study comparison of renal function test and echocardiographic change of chronic renal failure. In renal function test serum creatinine and EGFR were show p value < 0.001 which was statistically significant.

While comparison of echocardiographic changes and stages of chronic renal failure were not show any statistically significant expect LVPWT

LIMITATION OF STUDY

The sample size of our study was relatively low. The results which we found can be more accurate with larger sample size. The cross-sectional nature of the study makes it impossible to confirm a casual relationship between CRF and LV dysfunction as LV dysfunction may have developed before CRF and other risk factors seen in study population.

CONCLUSION

Cardiac dysfunction and LVH are frequently noted in individuals of chronic renal failure at the time of commencement of dialysis. cardiovascular abnormalities in the form of LVH, diastolic dysfunction which antedate severe systolic dysfunction are frequently observed in milder degrees of chronic renal failure. therefore, echocardiography should be performed early in the course of chronic renal failure (CRF) and early detection of cardiovascular disease enables reduction in cardiovascular mortality and morbidity and will help in providing better quality of life of CRF patients.

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