A STUDY OF ECHOCARDIOGRAPHIC CHANGES IN CKD PATIENTS ON MAINTENANCE HEMODIALYSIS: A SINGLE CENTRE STUDY
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HOW TO CITE THIS ARTICLE:
Rajaram Barde, Himanshu V. Patel, Pankaj R. Shah. "A Study of Echocardiographic Changes in CKD Patients on Maintenance Hemodialysis: A Single Centre Study". Journal of Evidence Based Medicine and Healthcare; Volume 2, Issue 40, October 05, 2015; Page: 6626-6634, DOI: 10.18410/jebmh/2015/904

ABSTRACT: OBJECTIVES: The Aim of this study to assess and analyze the echocardiographic changes in chronic kidney disease patients on maintenance hemodialysis. MATERIAL AND METHODS: We performed Prospective study of echocardiographic changes in chronic kidney disease (CKD) patients undergoing on maintenance hemodialysis at our institute. We performed M-mode echocardiography in 100 CKD patients without obvious clinical evidence of coronary artery disease, Valvular heart disease, congenital heart disease. RESULTS: 100 Patients Undergoing Hemodialysis were included in our study. Of them Echocardiography finding shown LV dilation and diastolic dysfunction in 49(49%), left ventricular hypertrophy (LVH) in 57 (57%), systolic dysfunction and pericardial effusion in 28(28%) and 13(13%) patients respectively. RWMA was present in 10% and Valvular calcification was seen in 5 patient. In sub-group of patients with Hb<10 gm%, LVH was present in 77.41% (48) vs 23.68% (9) in patient group with Hb ≥ 10 gm% (p <0.01). Other Sub Group of Patients with BP > 140/90mmhg, LVH Was Present in 64.47 % (49) vs 33.33 % (8) in patients group with BP< 140/90 mm hg (p=0.02). In both sub group p value for systolic dysfunction, RWMA & pericardial effusion is statistically not significant. CONCLUSION: LV diastolic dysfunction and hypertrophy were most common echocardiographic findings. There was statistically significant correlation between anemia and presence of LVH and positive correlation between presence of hypertension and LVH. KEYWORDS: CKD; HB%; Echocardiography: MHD; LVH: Diastolic dysfunction.

INTRODUCTION: Chronic Kidney Disease is a prevalent worldwide condition in both developed and developing countries. In India alone there are about 55,000 patients on dialysis and this number going at the rate of 10-20%. Each year.[¹] Chronic Kidney Disease is associated with significantly increased morbidity and mortality. Chronic Kidney Disease affects almost every system of the body and results in various functional and structural abnormalities. Among the various causes, infections and cardiovascular causes contribute towards the large proportion of increased morbidity and mortality. Cardiac disease is the major cause of death in dialysis population accounting for 40% of deaths in international registries.[²]

In the cardiovascular system, left ventricular hypertrophy (LVH) is the most frequent finding.[³] The prevalence of left ventricular systolic and diastolic dysfunction is less clear. Cardiac disease frequently predates is less clear. Cardiac disease frequently predates the start of dialysis and LVH is common in moderate to severe chronic renal failure. Echocardiography should be performed early in the course of CKD and may be valuable in the monitoring of therapy of these patients.[⁴]
Diabetes (DM) and hypertension (Htn) are the leading cause of CKD worldwide, whereas hypertension is a cause as well as effects of CKD. Recently genetic background of hypertension is gaining importance in pathophysiology of hypertension. G protein coupled and Ca2+ dependent kinases are responsible for control of blood pressure.\[^5\] Even lots of mutation may cause changes in the receptors, which in turn raise blood pressure.\[^6\] CKD is risk factor for cardiovascular event and complications increases as CKD progress to end stage renal disease (ESRD).\[^7\] Cardiovascular (CV) mortality is 10-20 times more common in ESRD patients on renal replacement therapy as compared to general population. One of the major structural cardiac anomalies in patients with CKD is left ventricular hypertrophy (LVH) and is associated with increase the risk for cardiac ischemia, congestive heart failure, as well as a very strong independent predictor of cardiovascular mortality.\[^8\] Majority patients with CKD die due to cardiovascular events before reaching ESRD due to both traditional and nontraditional risk factors.\[^9\] Whether CV events differ in patients with and without CKD is poorly defined and also whether differences in cardiovascular disease in CKD patients suggest preventive or therapeutic strategies unique to this population is unclear.

Anemia and hypertension are most consistently associated with cardiac failure, a pre lethal occurrence that predated two thirds of all dialysis patients’ death.\[^10\] 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.

Hemodialysis is one form of renal replacement therapy, during which metabolic waste products including creatinine, urea, excess water and salt are removed. It also maintained the nutritional status, mental and physical wellbeing if done on regular basis. Noor ul Amin et al had shown that hemodialysis is an effective means of removing metabolic waste products.\[^11\]

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

**MATERIAL AND METHODS:** This is a prospective cross sectional in which 100 Hemodialysis CKD patients irrespective of underlying etiology were included in this study, who attended Dialysis units of Department of Nephrology, at Smt. G. R. doshi & Smt. K. M. Mehta, IKDRC, DR H. L. Trivedi ITS Ahmedabad (India). A person was labeled as stage 5 CKD if his or her GFR was less than 15 ml/1,7 m² as per CKD-EPI formula and who were on MHD. Patient with obvious clinical evidence of coronary artery disease, Valvular heart disease, rheumatic heart disease, congenital heart disease and primary cardiomyopathies 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 and 2-D echocardiography. 2D-Echocardiography machine SIEMENS MODEL ACCUSON was used with 3.5 MHz transducer probe. The M. mode recording perpendicular to the long axis of and through the center of the left ventricle at the papillary muscle level was taken as standard measurements of the systolic and diastolic wall thickness and chamber dimensions. The left ventricular ejection fraction (LVEF) and fractional shortening (FS) were taken as measure of left ventricular systolic dysfunction and ejection fraction <55% 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. LVH was diagnosed when inter ventricular septum thickness or left ventricular posterior wall thickness was ≥12mm. Hypertension was defined as BP ≥ 140/90 mmHg in right arm supine position and anemia was diagnosed with hemoglobin < 13.5 gm/dl in male and 12.5 gm/dl in female.

**STATISTICAL ANALYSIS:** All collected data entered into the SPSS V20 Software and analysis has been conducted and using chi square test and fisher exact test has been used to calculate statistically significant value. A 'p value less than 0.05 were considered significant.

**RESULTS:** This study included 100 patients of CKD on MHD Clinical examination, suggested laboratory test and echocardiography were performed in every patient.

Out of 100 patients, 77% (77) male and 23% (23) were female. Maximum patients were in age group between 41-50 yrs. (34%) (Figure 1).

Mean age of the patients was 42.33 ± 12.48 (Figure.2).
Basic demographic and clinical characteristic were shown in Table 1. Hypertension was present in 76 (76%) mainly in age group more than 40 years.

| Parameters          | Range     | Mean±SD       |
|---------------------|-----------|---------------|
| Age(Years)          | 20-68     | 42.33±12.48   |
| Calcium (mg/dl)     | 6.8-13.5  | 9.87±1.72     |
| Phosphorus (mg/dl)  | 3.5-12    | 7.72±2.01     |
| Urea (mg/dl)        | 43-189    | 108.14±32.83  |
| Creatinine (mg/.dl) | 2.8-10.2  | 5.52±1.65     |
| Hemoglobin % (gm/dl)| 4.2-11.4  | 7.89±0.96     |
| Serum albumin (gm/dl)| 2.2-5    | 3.64±0.53     |
| Total cholesterol(mg./dl)| 111-268 | 160.32±27.56 |

Table 1: Basic demographic profile and laboratory parameters of study population

Most common cause of CKD was diabetes 44(44%) followed by hypertension, chronic glomerulonephritis (CGN) and chronic tubulointerstitial nephritis (CTIN) in 29(29%), 14(14%) and 9(9%) cases respectively (Figure 3) & 4 (4%) were with unknown etiology.

Anemia was observed in all patients and hemoglobin of less than 10 gm% was seen in 62 (62%) patient. Echocardiographic parameter analyzed in our study were left ventricular internal diameter in diastole (LVIDd), left ventricular internal diameter in systole (LVIDs). Interventricular septal diameter in systole, E/A ratio, fractional shortening, ejection fraction and size of left atrium (Table 2).

Mean echocardiography parameters in cases of ESRD on MHD

| Parameters                                    | No. of cases | %  |
|-----------------------------------------------|--------------|----|
| Left ventricular hypertrophy                  | 57           | 57%|
| Ejection fraction (<55%) Systolic dysfunction | 28           | 28%|
| E/A ratio (<0.75 or >1.8) Diastolic dysfunction | 49           | 49%|

Figure: 3 bar diagram showing basic disease of the study population
Regional wall motion abnormality | 10 | 10%  
Pericardial effusion (<10 mm) | 13 | 13%  
Valvular calcification | 5 | 5%  
Table 2: Echocardiographic parameters in CKD patients on MHD  

On comparing the echocardiographic findings in patients with Hb <10 gm% vs patients with Hb ≥ 10 gm%, statistically significant number of patients had LVH: 77.41% vs 23.68% (Table 3).

| Echocardiographic Findings | Hb level | P-value |
|---------------------------|----------|---------|
|                           | <10gm/.dl | ≥10gm/dl |
|                           | N(62) 62% | N(38) 38% |
| LVH                       |          |         |
| Absent                    | 14 22.58 | 29 76.31 |
| Present                   | 48 77.41 | 9 23.68  | <0.01*  
| Decreased (<55%)          |          |         |
| Absent                    | 41 66.12 | 31 81.57 |
| Present                   | 21 33.97 | 7 18.42  | 0.09(NS)  
| RWMA                      |          |         |
| Absent                    | 54 87.09 | 36 94.73 |
| Present                   | 8 12.9  | 2 5.26   | 0.31(NS)  
| Pericardial Effusion      |          |         |
| Absent                    | 57 91.93 | 30 78.94 |
| Present                   | 5 8.06  | 8 21.05  | 0.07(NS)  
Table 3: Hemoglobin level and echocardiographic parameters of study patients  

Similarly majority patients with LVH had hypertension (64.47%) compared to normotensives (37.5%) and it was statistically significant (P=0.02) (Table 4.) RWMA was present in 12.9% patients with hemoglobin of <10gm% and 5.26% in patients with HB ≥10gm%, although it was statistically not significant.

| Echocardiographic Findings | Hypertension | P-Value |
|---------------------------|--------------|---------|
|                           | <140/90 mmHg | ≥ 140/90 mmHg |
|                           | N(24) 24% | N(76) 76% |
| LVH                       |          |         |
| Absent                    | 16 66.66 | 27 35.52 |
| Present                   | 8 33.33  | 49 64.47 |
| Decreased EF (<55%)       |          |         |
| Absent                    | 20 83.33 | 52 68.42 |
| Present                   | 4 16.66  | 24 31.57 |
|                           | 0.16(NS)    |         |
DISCUSSION: Cardiovascular disease is the major cause of death in patients with end stage renal disease. The detection of echocardiographic abnormalities with subclinical cardiac disease is considered to be an important step for characterization of individual risk for heart failure in the general population as well as in patients of CKD [9]. 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.

In our study LVH was present in 57%, systolic dysfunction in 28% and diastolic dysfunction in 49% of patients. Echocardiographic findings in other studies have also observed presence of systolic dysfunction in 20% and diastolic dysfunction in 50% patients.[12,13] Agarwal S. et al had observed diastolic dysfunction in 53.2% and systolic dysfunction in 30%, patients with severe CKD (S.Cr.>6mg %).[14] we observed pericardial effusion and RWMA in 17.14%, 8.5% case respectively. In a study conducted by Laddha M et al. in 2014, reported LVH in 74%, systolic dysfunction in 24.3% diastolic dysfunction in 61.4% and pericardial effusion in 14.35% of ESRD patients on hemodialysis.[15] Zoccall C et al. had reported incidence of IVH and systolic dysfunction of 77% and 22% respectively in ESRD population on hemodialysis.[16] Valvular calcification are four times more common in dialysis patients compared to general population.[17] Shivendra s et al had observed LVH in 48%, Diastolic dysfunction in 51.42% and systolic dysfunction in 28.57% in CKD Patients on Hemodialysis.[18] Valvular calcifications are four times more common in dialysis patients compared to general population.[19] None of our patients had Valvular calcification probably because of small study population.

Majority (76%) patients had hypertension. In hypertensive group LVH was present in 64.47% vs 33.33% in normotensive group. In subgroup of patients with hemoglobin level <10gm%, LVH was seen in 77.41% compared to 23.68% in patients with hemoglobin of ≥10gm% (P<0.01). Patrick et al. had showed that rise in mean arterial pressure was associated with increased incidence of IVH in ESRD population on hemodialysis [20]. Levin et al also reported association between elevated systolic blood pressure and low hemoglobin level with IVH in predialysis patients.[21,22] Anemia is a strong predictor of development of LVH and mortality and morbidity in ESRD.[10] Data et al observed severity of anemia correlated to LVH in patients with CKD.[20] In ESRD patients on dialysis it has been observed that decrease in Hb level of 1 gm% increased LVH by = 50% and mortality by 18-25%.[23]

CONCLUSION: Cardiac structural as well as functional abnormalities are common in patients with CKD on MHD, more so in those with hypertension and anemia. LVH is the commonest
cardiac abnormality in ESRD patients, followed by diastolic dysfunction. Both conditions are more marked in hypertensive and anemic populations. LVH has got prognostic implications, because this group of ESRD patients will die of diastolic dysfunction or sudden cardiac death.[24] 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 both therapeutic and prognostic implications. All asymptomatic ESRD patients especially anemic and hypertensive CKD Patients should undergo a routine echocardiographic evaluation. In our study we also observed young adult patients age between 21-30 years (24%). It shows increased prevalence CKD in young adult population. So further Studies required for confirmation.

Limitations of our Study: Impact of hyperlipidemia, secondary hyperparathyroidism, homocysteine levels, and markers of inflammation and duration of MHD were not studied in our patient population.

REFERENCES:
1. Jha, V, et al. Current status of end stage renal disease core in India. Kidney international Supplements (2013), 3, 157-60.
2. Fassbinder W, Brunner FP, Brynger H et al. Combined report on regular dialysis and transplant in Europe XX1989. Nephrol Dial Transpl 1991; 6(Suppl 1): 5-35.
3. Bullock RE, Hassem AA, Simpson I et al. Cardiac abnormalities and exercise tolerance in patients receiving renal replacement therapy. BMJ 1984; 28: 1479-84.
4. Greaves SC, Gamble GD, Collins JF et al. Determinants of left ventricular hypertrophy and systolic dysfunction in chronic renal failure. Am J Kidney Dis 1994; 24: 768-76.
5. Santulli G. Trimarco B. Iaccarino G (2013) G-protein-coupled receptor kinase 2 and hypertension: molecular insights and pathophysiological mechanisms. High Blood Press Cardiovasc Prev 20. 5-12.
6. Santulli G, Cipolletta E, Sorriento D, Del Gludice C, Anastasio A, et al. (2012) CaMK4 Gene Deletion Induces Hypertension. J Am Heart Assoc. 1: e001081.
7. Agodoa LY, Eggers PW (1995) renal replacement therapy in the United States Renal Data System. Am J Kidney Dis 25: 119-133.
8. Parfrey PS, Foley RN, Harnett JD, Kent GM, Murray DC et. al (1996) Outcome and risk factors for left ventricular disorders in chronic uremia. Nephrol Dial Transplant 11: 1277-1285.
9. Foley RN, Parfrey PS, Harnett JD. Kent GM, Martin CJ, et al. (1995) Clinical and echocardiographic disease in patients starting end-stage renal disease therapy. Kidney Int 47: 186-192.
10. Foley RN, Parfrey PS, Harnett JD. Kent GM, Murray DC et al (1996) the impact of anemia on cardiomyopathy, morbidity and mortality in end-stage renal disease. Am J Kidney Dis 28: 53-61.
11. Noor ul Amin, Raja Tahir Mahmood, M. Javaid Asad, Mudassar Zafar, Asad Mehmood Raja (2014) Evaluating urea and creatinine levels in chronic renal failure pre and post dialysis. A prospective study JCVD, 2014 in press.

12. Mcmurray JV, McDonagh TA, Davle AP, Cleland JG, Francis CM, et al (1998) Should we screen for asymptomatic left ventricular dysfunction to prevent heart failure? Eur Heart 19: 842-846.

13. Kunz K. Dimitrow Y. Muller S. Chantrel F, Hannedouche T (1998) Uremic cardiomyopathy,. Nephrol Dial Transplant 13 Suppl 4: 39-43.

14. S. Agarwal, P. Dangri, OP Karla, S Rzjpal (2003) Echocardiographic assessment of cardiac dysfunction in patient of chronic renal failure JIACM 4: 296-303.

15. Laddha M, V Sachdeva, PM Diggikar, PK Sapathy, AL Kakrani (2014) Echocardiographic assessment of cardiac dysfunction in patients of end stage renal disease on hemodialysis. JAPI 62: 28-32.

16. Zocall C. Benedetto FA, Mallamac F. Tripepi G. Giacone G, et al. (2004) Prognostic value of echocardiographic indicators of left ventricular systolic function in asymptomatic dialysis patients. J Am Soc Nephrol 15: 1029-1037.

17. Shivendra S, Doley PK, Pragya P, Shivasankar M, Singh VP, et al. (2014). Echocardiographic Changes in Patients with ESRD on Maintenance Hemodialysis-A Single Centre Study. J Cardiovasc Dis Diagn 2: 165.

18. Lekinen Y. Paana T, Saha H. Groundstroem K. Lehtimaki T, et al (2009) Valvular calcification and its relationship to atherosclerosis in chronic kidney disease,. J Heart Valve Dis 18: 429-438.

19. Parfrey PS. Foley RN (1999) the clinical epidemiology of cardiac disease in chronic renal failure J Am Soc Nephrol JO: 1606-1615.

20. Levin A. Thompson CR, Ethier,m J. Carlisle EJ, Tobe S, et al (1999) left ventricular mass index increase in early renal disease impact of decline in hemoglobin. Am J Kidney Dis: 34 125-134.

21. Levin A, Singer J, Thompson CR, Ross H. Lew3is M (1996) Prevalent left ventricular hypertrophy in the predialysis population identifying opportunities for intervention. Am J Kidney Dis 27: 347-354.

22. Data S. Abraham G. Mathew M. Somasundaran H. Muralidharan TR et al (2006) Correlation of anemia, secondary hyperparathyroidism with left ventricular hypertrophy in Chronic Kidney Disease patients. J Assoic Physicians India 54 699-703.

23. Harnett JD, Kent GM, Foley RN, Parfrey FS (1995) cardiac function and hematocrit level. Am J Kidney Dis 25-3-7.

24. Pecoits-Filho R, Barberato SH (2010) Echocardiography in chronic kidney disease diagnostic and prognostic implications. Nephrone Clin Pract 114: 242-247.
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Date of Submission: 18/09/2015.
Date of Peer Review: 19/09/2015.
Date of Acceptance: 21/09/2015.
Date of Publishing: 29/09/2015.