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Study of Cardiac Dysfunction in Patients of Chronic Kidney Disease

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Abstract
The present study was undertaken to assess the prevalence of systolic and diastolic dysfunction, to determine the prevalence of left ventricular hypertrophy (LVH) from left ventricular mass index (LVMI), to correlate the degree of cardiac dysfunction with severity of chronic kidney disease (CKD) by echocardiography in patients of CKD on conservative management. ***Material & method:*** *75 CKD patients were taken in the study which were divided into three groups - Group A → Age and sex matched healthy controls (n=20). Group B → Patients with mild to moderate CRF (n=45) (S. Creatinine =1.5-6.0 mg/dl). Group C → Patients with severe CRF (n=30) (S. Creatinine > 6.0 mg/dl).* ***Results:*** *The prevalence of LVH along with systolic dysfunction was 10.0% (p<0.2653) in severe CRF (group C), higher than mild/moderate CRF (group B) which was 2.2% (p<1.0). The prevalence of LVH along with diastolic dysfunction was 76.7% (p<0.0001) in group C, which was significantly higher than group B which was 44.4% (p<0.0001). 51.1% (p<0.0001) patients were found to have LVH in mild to moderate CRF (group B) and 76.7% (p<0.0001) of patients had LVH in severe CRF (group C). 48.9% patients had concentric LVH in group B and 73.3% had concentric LV hypertrophy in group C. In diabetic CRF patients LV dysfunction was predominantly diastolic irrespective of the degree of LV hypertrophy.* ***Conclusion:*** *Systolic dysfunction was well preserved in majority cases of CKD as found from the Ejection Fraction and Fractional Shortening parameter whereas diastolic dysfunction was more commonly found in CKD patients.* ***Key words:*** *chronic kidney disease, left ventricular hypertrophy, left ventricular mass index systolic dysfunction, diastolic dysfunction.*

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I. Introduction

Chronic kidney disease (CKD) is a state of irreversible impairment of renal function which is a public health problem worldwide, with adverse outcomes of renal failure, cardiovascular disease and premature death.[(1)] Cardiovascular disease is the foremost cause of morbidity and mortality in patients of chronic kidney disease at every stage. Advanced cardiovascular complications are already present in 30-45% of CKD patients reaching ESRD.[(2)]

It is now well recognised that chronic kidney disease (CKD), when present in patients with HF, independently predicts poor outcomes.[(3,4)] JNC-7 report has recognised CKD as an independent cardiovascular risk state.[(3, 5)] Cardiac disease is the leading cause of mortality in dialysis patients accounting for 40% of deaths in international registries.[(6, 7)]

Left ventricular hypertrophy is the most common finding in the cardiovascular system, but there is no clear data about the prevalence of left ventricular systolic and diastolic dysfunction.[(6,8)] LVH is common in moderate to severe CRF. Cardiac disease frequently predates the start of dialysis. Echocardiography if performed early in the course of CRF may be valuable in the monitoring of therapy of these patients.[(6, 9)] Cardiac disease is commonly found in patients around the time of beginning of dialysis, but there is little data on the prevalence and natural history of cardiac function in the indivisuals with milder degrees of chronic renal failure. Furthermore, early detection and management of cardiac dysfunction will improve outcome in patients of CKD.

Methods: - The study was undertaken at S.C.B. Medical College and Hospital, Cuttack, Odisha during the period from September 2011 to September 2012. All patients of Chronic Kidney Disease admitted to Postgraduate Department of Medicine and satisfying the following criteria were included in the study. Criteria for diagnosis of Chronic Kidney Disease was as given by- National kidney foundation: K/DOQI clinical practice guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification. [(1)]

CKD is defined as the presence, for at least 3 months, of evidence of kidney damage with an abnormal GFR or alternatively, by a GFR < 60 ml/min /1.73m^2 BSA. [(1)]

Kidney damage is evidenced by- proteinuria >300mg/day [9] or pathological abnormality found in histopathological study [9] or renal imaging study (USG) showing bilateral contracted kidneys < 9cm with thinned parenchyma and reduced corticomedullary differentiation.

Patients with CKD with the following diseases - valvular heart disease, coronary artery disease, congenital heart disease, cardiomyopathies, patients on haemodialysis, patients on treatment with erythropoietin, h/o of alcohol intake and smoking - were excluded from the study.

75 CKD patients were taken in the study which were divided into three groups - Group A → Age and sex matched healthy controls (n=20), Group B → Patients with mild to moderate CRF (n=45) (S. Creatinine =1.5-6.0 mg/dl), Group C → Patients with severe CRF (n=30) (S. Creatinine > 6.0 mg/dl).

II. Results

In group-B, maximum 22 cases (48.9%) were in the age group of 56-75 years and in group-C, maximum 14 cases (46.7%) were in the age group 36-55 years. In group-A, mean age was 43.9 + 17.4 years. In group-B, mean age was 57.7 + 14.6 years. In group-C, mean age was 53.5 + 13.2 years.

Fig – 1

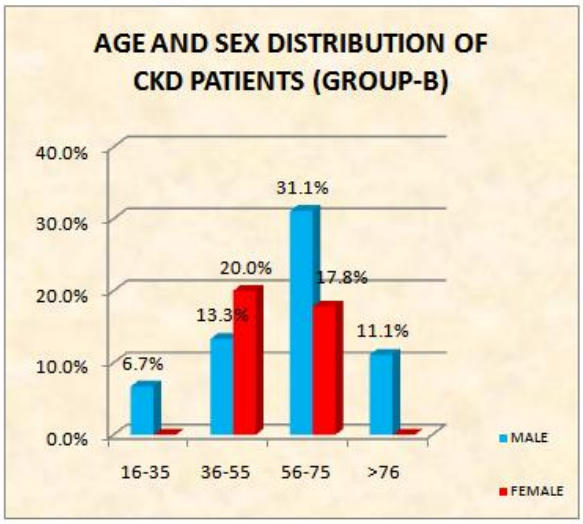
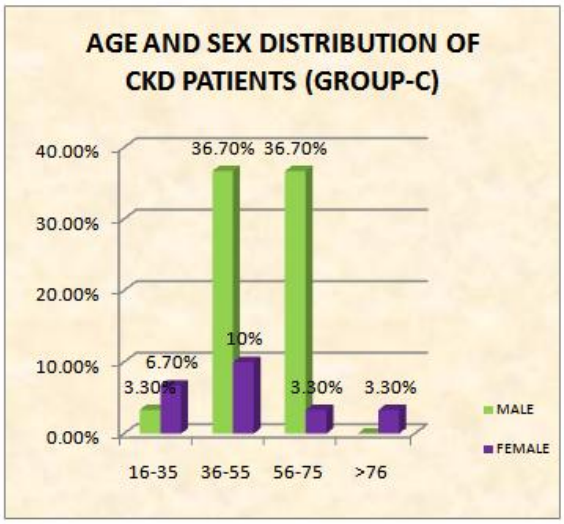


Fig – 2



In group-B, M = 28 cases (62.2%) and F = 17 cases (37.8%) with a M:F ratio of 1.6:1. In group-C, M = 23 cases (76.7%) and F = 7 cases (23.3%) with a M:F ratio of 3.3:1. In total, M = 51 cases (68%) and F = 24 cases (32%) with the M:F ratio of 2.1:1, showing male preponderance. Highest incidence of male CKD patients was in the age group of 56-75 years as compared to female CKD patients in the age group of 36-55 years. In group-B, 15 cases (33%) were found to be diabetic. In group-C, 7 cases (23.3%) were found to be diabetic. Overall in the study group 22 cases (29.3%) were diabetic and 53 cases (61.7%) were non-diabetic.

Both systolic and diastolic blood pressures were elevated in Group-B and Group-C patients with degree of elevation maximum in Group-C. Blood pressure was within normal range in the control population.

BMI and Hb values were significantly lower in Group-B and Group-C patients compared to normal controls, being lowest in Group-C. Blood urea and serum creatinine values showed increasing levels as severity of CKD patients increased. Patients in Group-C showed hyperkalemia. Lipid profile abnormalities were noted in all CKD patients with maximum abnormality found in patients having severe CKD (Group-C).

Table-1 BIOCHEMICAL PARAMETERS IN THREE GROUPS

	Group-A (n=20)	**Group-B (n=45)**	**Group-C (n=30)**
BMI	24.3 ± 3.4	20.1 ± 3.2	19.8 ± 3.5
HAEMOGLOBIN	12.9 ± 0.6	9.5 ± 1.7	7.4 ± 2.5
B. UREA	28.4 ± 10.5	72.3 ± 31.1	181.3 ± 75.1
S. CREATININE	0.7 ± 0.1	2.9 ± 1.1	9.6 ± 3.3
S. SODIUM	138.1 ± 6.0	131.1 ± 11.8	129.8 ± 9.8
S. POTASSIUM	4.1 ± 0.5	4.0 ± 1.2	5.1 ± 1.2
T. CHOLESTEROL	152.4 ± 19.0	180.6 ± 41.9	225.0 ± 29.1
TRIGLYCERIDE	84.1 ± 24.5	169.9 ± 51.1	199.3 ± 32.3
HDL	49.3 ± 7.8	42.5 ± 7.9	41.5 ± 6.3
LDL	84.1 ± 26.9	106.8 ± 29.9	135.7 ± 30.8
VLDL	25.1 ± 6.7	22.0 ± 9.9	34.3 ± 12.7

Ejection Fraction (EF) was significantly lower in CKD patients (p value <0.05) compared to controls, but was within normal range.

Table-2 ECHOCARDIOGRAPHIC PARAMETERS IN THREE GROUPS

	GROUP-A (n=20)	**GROUP-B (n=45)**	**GROUP-C (n=30)**
	MEAN+SD	**MEAN+SD**	**MEAN+SD**
LVID-d (cm)	4.2 ± 0.5	4.3 ± 0.5	4.5 ± 0.4
P value	Not significant		
LVID-s (cm)	2.73 ± 0.4	2.73 ± 0.5	3.0 ± 0.5
P value	A vs. B= >0.05, A vs. C= >0.05, B vs. C= >0.05		
EF (%)	67.0 ±6.1	62.2 ± 7.2	61.6 ± 8.3
P value	A vs. B= <0.05, A vs. C= <0.05 B vs. C= >0.05		
FS (%)	33.9 ± 3.4	32.7 ± 5.3	33.2 ± 6.2
P value	Not significant		
IVSd (cm)	1.0 ± 0.1	1.1 ± 0.2	1.2 ± 0.2
P value	A vs. B= >0.05, A vs. C= <0.001 B vs. C= >0.05		
LVPWd (cm)	0.9 ± 0.1	1.1 ± 0.2	1.2 ± 0.2
P value	A vs. B= <0.001, A vs. C= <0.001 B vs. C= >0.05		

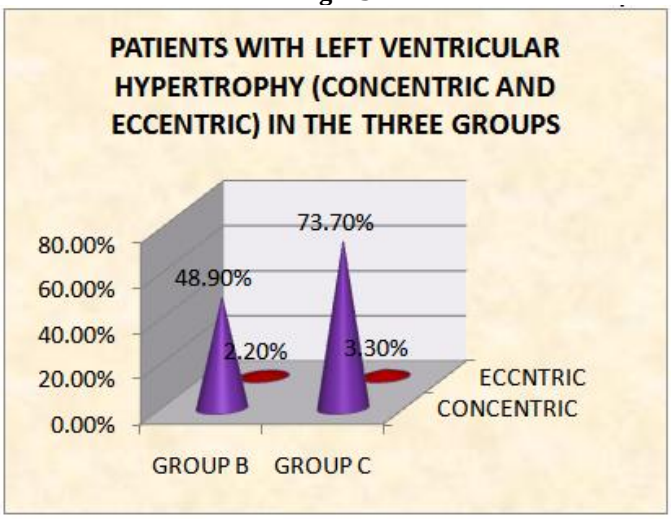
There was statistically significant increased Mean left ventricular mass index (LVMI) in CKD patients compared to controls.

Table-3 MEAN LEFT VENTRICULAR MASS INDEX AND ITS SEX-WISE DISTRIBUTION IN THREE GROUPS

LVMI	**GROUP-A (n=20)**	**GROUP-B (n=45)**	**GROUP-C (n=30)**
	MEAN+SD	**MEAN+SD**	**MEAN+SD**
TOTAL	88.0 ± 22.3	117.5 ± 38.8	140.0 ± 38.1
P value	A vs. B= <0.01, A vs. C= <0.001, B vs. C= <0.05		
MALE	94.3 ± 25.6	115.3 ± 39.8	138.5 ± 39.7
P value	A vs. B= >0.05, A vs. C= <0.001, B vs. C= <0.05		
FEMALE	79.4 ± 13.0	100.6 ± 40.8	153.9 ± 38.4
P value	A vs. B= >0.05, A vs. C= <0.001, B vs. C= <0.001		

Among the CKD patients in Group-B 23 cases (51.1%) had LVH, out of which 22 cases (48.9%) had concentric LVH and 1 case had eccentric LVH. In Group-C CKD cases 23 cases (76.7%) had LVH, out of which 22 cases (73.3%) had concentric LVH and 1 case had eccentric LVH. (p value A:B = < 0.0001, A:C = < 0.0001). Among CKD cases of Group-B 16 males (57.1%) had LVH and 7 females (41.2%) had LVH whereas Group-C 17 males (73.9%) had LVH and 6 females (85.7%) had LVH.

Fig – 3



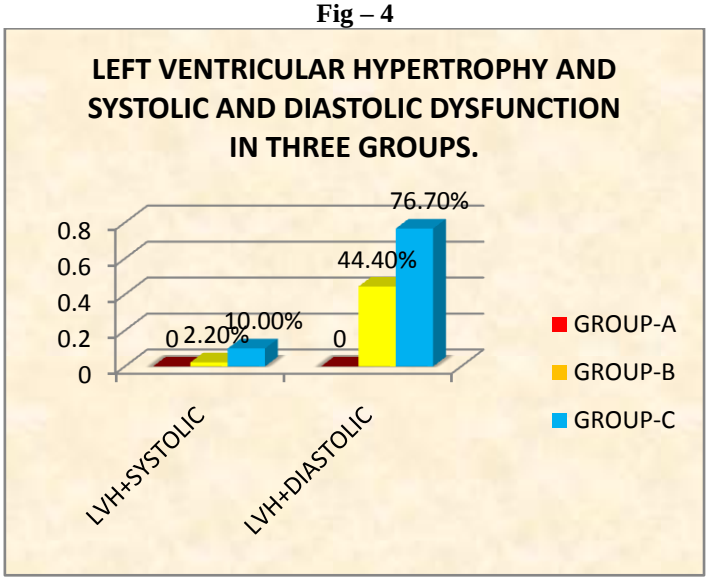
Ejection Fraction was lower in all CKD patients which was statistically significant (A vs.B= <0.05, A vs. C= <0.05, B vs. C= >0.05) as compared to controls, but was within normal range. No difference was observed among cases and controls in Fractional Shortening level.

Table-4 LEFT VENTRICULAR SYSTOLIC FUNCTIONS INDICES (EJECTION FRACTION AND FRACTIONAL SHORTENING) IN THE THREE GROUPS.

	Group-A (n=20)	**Group-B (n=45)**	**Group-C (n=30)**
EF (MEAN+SD)	67.0 ± 6.1	62.2 ± 7.2	61.6 ± 8.3
EF<50%	nil	1(2.2%)	3(10.0%)
FS (MEAN+SD)	33.9 ± 3.4	32.7 ± 5.3	33.2 ± 6.2
FS<25%	nil	1(2.2%)	3(10.0%)

In the CKD patients, 1 case (2.2%) (p<1.0) had systolic dysfunction whereas 20 cases (44.44%) had diastolic dysfunction in Group-B and in Group-C 3 case (10.0%) (p<0.2653) had systolic dysfunction whereas 23 cases (76.7%) had diastolic dysfunction. Diastolic dysfunction was the predominant abnormality noted in CKD patients.

Fig – 4



Diastolic dysfunction was noted in 33 (73.33%) cases of Group-B, out of which 22 (44.44%) (p<0.0001) cases had concentric LVH. In Group-C diastolic dysfunction was found in 26 (86.67%) cases, out of which 23 (76.67%) (p<0.0001) cases had concentric LVH.

In Group-B 38 (84.4%) cases had HTN and 23 (51.1%) (p<0.0001) cases had LVH. In Group-C 29 (96.7%) cases had HTN and 23 (76.7%) (p<0.0001) cases had LVH.

Both systolic and diastolic blood pressures were elevated in CKD cases. There was no significant difference between diabetic and non diabetic cases. In Group-B out of 30 non diabetic CKD cases 25 (83.3%) cases had HTN and out of 15 diabetic CKD cases 13(86.7%) cases had HTN. In Group-C out of 23 non diabetic CKD cases 22 (95.6%) cases had HTN and out of 7 diabetic CKD cases all 7(100.0%) cases had HTN. Among cases with diastolic dysfunction in Group-B 20 (66.7%) were non diabetic and 13 (86.7%) were diabetic whereas in Group-C 26 (86.7%) were non diabetic and 7 (100.0%) were diabetic.

III. Discussion

All the cases of CKD were in a wide age group range of 16 to 80 years. As per the second yearly report, CKD REGISTRY OF INDIA, INDIAN SOCIETY OF NEPHROLOGY, 2007 overall mean age for a CKD patient is 48.3 + 16.6 years. *(10)* In our study mean age of all CKD cases was 57.7±14.6yrs in group B and 53.5 ± 13.2 years in group C. In the study by P Dangri the mean age of the CKD cases was 37.9 ± 8.2 years in group B and 36.9 ± 9.7 years in group C. *(11)*

In total 51 cases (68%) were males and 24 cases (32%) were females. Males predominated with a M:F ratio of 2.1:1. As per the second yearly report, CKD REGISTRY OF INDIA, INDIAN SOCIETY OF NEPHROLOGY, 2007 among CKD patients 68.9% were males & 31.1% were females. *(10)* Males preponderance was probably due to higher incidence of Diabetes Mellitus and Hypertension in them. *(10)* The

study done by Dangri et al in 2003 also showed Male (17) to Female (13) ratio of 1.3:1.The mean age in male CKD cases was 59.0 ± 16.9 yrs and in female CKD cases was 55.5 ± 9.7 yrs in group-B. The mean age in male CKD cases was 54.8 ± 11.1 yrs and in female CKD cases was 41.4 ± 8.4 yrs in group-C.

As per the second yearly report, CKD REGISTRY OF INDIA, INDIAN SOCIETY OF NEPHROLOGY, 2007 30.3% CKD patients were due to diabetic nephropathy. [(10)] Overall in the study group 22 cases (29.3%) had diabetes mellitus. Hence our findings were consistent with that of CKD Registry of INDIA.

Premature cardiovascular disease is an important cause of morbidity and mortality among CRF patients. Systolic functions are usually well preserved in hypertensive and even diabetic patients with uraemia. [(6)] In our study, the mean ejection fraction (EF) in patients with mild/moderate CRF and severe CRF groups showed a descending trend but neither of the CRF groups had mean LVEF < 50%. These results are similar to the findings of Raj et al (1997). [(12)] In the present study, LVEF is well maintained in patients with CRF which was also found in these previous studies - Dangri et al (2003), [(11)] Ayus et al (1981), [(13)]. Only 1 (2.2%) patient had LVEF < 50% among patients in the mild/moderate CRF group, while 3 (10%) patients in severe CRF group had LVEF < 50% which was not significantly different from controls, as well as mild/moderate CRF population.

In our study, no noteworthy differentiation was found in the mean fractional shortening (FS) among the three groups; however, 1 case (2.2%) in mild/moderate CRF group and 3 cases (10.0%) in severe CRF group had FS ≤ 25%. In our present study we found mean FS in the controls 33.9 ± 3.4%, in group B CRF patients 32.7 ± 5.3%, and in group C CRF patients 33.2 ± 6.2. Dangri et al, [(11)] Raj et al, [(12)] Harnett et al (1995), [(14)] Colan et al (1987) [(15)] studies also found that FS as a function of left ventricular systolic function is well maintained in patients with CRF.

In our study, the number of cases with LVH and systolic dysfunction (EF < 50%) was 1 (2.2%) in mild/moderate CRF group and 3 (10%) in severe CRF group. Thus, in our study, systolic function was well preserved in patients with mild/moderate and severe CRF which is consistent with the prior studies done by Colan et al (1987), Greaves et al (1994), Harnett et al (1995) and P Dangri et al (2003).

In ESRD patients, Left ventricular diastolic dysfunction is the main cause of cardiac morbidity. Diastolic dysfunction appears to be the initial left ventricular dysfunction and might even precede LVH. London et al (1993) found a significant reduction in E/A ratio in CRF patients as compared to controls. [(16)] In the present study, the prevalence of diastolic dysfunction was found to be 73.33% (33 patients) in group B CRF and 86.67% (26 patients) in group C CRF.

In the present study the number of patients having both LVH and as well diastolic dysfunction was 20 (44.44%) in mild/moderate group, whereas it was 23 (76.67%) in severe CRF group. Thus in contrast to systolic function, diastolic function was deranged in more number of cases signifying that diastolic dysfunction is first to appear in CRF patients. Among the various factors that contribute to diastolic and systolic dysfunction, uncontrolled hypertension and anaemia, which are usually present in CRF, play a significant role. In this study, 89.3% had HTN and anaemia was present in all the patients, signifying that these factors might also have contributed towards development of diastolic and systolic dysfunction.

LVH is the single strongest independent forecaster of adverse cardiovascular events. [(17)] In our study, we observed that left ventricular mass index (LVMI) showed a progressive rise with increase in severity of renal failure. This finding is in concordance with the study done by Greaves et al. [(9)] In the present study, we found LVMI 88.0 + 22.3 in controls, 117.5 + 38.8 in group B CRF patients and 140.0 + 38.1 in group C CRF patients, which was significantly higher. In the present study, we found that 23 (51.1%) cases in group B CRF patients and 23 (76.7%) cases in group C CRF patients had LVH. These results match to prevalence of LVH in patients with ESRD from 40% to 80% in different studies. Raj et al [(12)] had also confirmed that the prevalence of LVH increases with progressive decline in renal function. In our study, concentric LVH was found in 48.9% of patients in mild/moderate CRF and 73.3% of patients in severe CRF group, while eccentric hypertrophy was seen in only 2.2% cases with mild/moderate CRF group and 3.3% cases with severe CRF group, signifying that concentric LVH is far more common than eccentric LVH in CRF patients. Huting et al study had found eccentric hypertrophy to be a major form of LVH in patients with CRF. [(18)] In ESRD patients, LVH combines features of concentric as well as eccentric hypertrophy which is also found in London et al study. [(19)]

In our study, 57.1% males had LVH in mild/moderate CRF group and 73.9% of males had LVH in severe CRF group. Conversely, 41.2% females in mild/ moderate CRF group and 85.7% females in severe CRF group had LVH, signifying that prevalence of LVH was more in females. In the study by P Dangri, in group B CRF patients, 23% males had LVH and in group C CRF patients, 94% of males had LVH. Conversely, 61% females in group B CRF patients and all females (100%) in group C CRF patients had LVH. [(11)] Deveroux et al had found that when sex specific criteria are used to find the prevalence of Left Ventricular Hypertrophy in hypertensive male and female populations, a higher proportion of female patients exhibited Left Ventricular Hypertrophy.[(20)] In our study, higher prevalence of Left Ventricular Hypertrophy in females as compared to males especially in mild/moderate CRF group may be because of sex specific criteria taken for Left Ventricular

Hypertrophy. High prevalence of anaemia and hypertension in CRF patients may also partly account for increased prevalence of LVH in CRF patients.

There was no statistically significant difference between the various Echocardiographic parameters among diabetic and non diabetic CKD cases. In diabetic CRF patients LV dysfunction was predominantly diastolic irrespective of the degree of LV hypertrophy.

IV. Conclusion

In conclusion, systolic dysfunction was well preserved in majority cases of CKD as found from the Ejection Fraction and Fractional Shortening parameter whereas diastolic dysfunction was more commonly found in CKD patients. In diabetic CRF patients LV dysfunction was predominantly diastolic irrespective of the degree of LV hypertrophy. Echocardiography should be performed early during course of chronic kidney disease to detect LV dysfunction and take necessary measures to prevent or delay further progression to reduce cardiovascular morbidity and mortality. Anaemia and hypertension, being major contributors of LVH, should also be treated adequately to prevent cardiovascular events.

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