Original Research Article

Asymptomatic cardiac manifestations in CKD

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ABSTRACT

Background: Chronic kidney disease is recognised as health concern globally with more than 40 percent of morbididty and mortality. CKD is one of the independent risk factor for cardiovascular diseases and its unfavourable health outcomes. The risk factors like smoking, hypertension, dyslipidemia and diabetes which are highly prevalent in CKD. The therapeutic interventions in CKD patients to reduce CVD events does not hold a desired effect and has bad prognosis in end stage renal disease. The initial evidence indicating a relationship between CKD and CVD is more apparent in patient with dialysis. The aim of the study was to evaluate the asymptomatic cardiac manifestations in 2-4 stages of CKD through non-invasive methods like ECG and Echocardiography.
Methods: It is a cross sectional study investigated on 250 CKD patients receiving care in JSS hospital, Mysore. For the primary objective, correlational analysis were performed to evaluate the association of renal functional parameters like serum creatinine, urine albumin, eGFR with cardiac parameters through ECG and Echocardiographic changes.
Results: ECG revealed LVH with pressure overload pattern in 36%. 25% patients had ST-T changes. Echocardiography revealed LVH and diastolic dysfunction as abnormalities. LVH has significant p value.
Conclusions: CVD is a leading cause of morbidity and mortality in patients of CKD who succumb to Cardio vascular deaths before reaching the end stage renal disease. Thus, focus of patient care in early CKD stages should be directed to prevention of cardiovascular complications through early ECG and Echocardiography.

Keywords: Cardiovascular disease, Chronic kidney disease

INTRODUCTION

Patients with chronic kidney disease (CKD) carry a high cardiovascular risk. An abundance of evidence has emerged in recent years establishing minor reductions in estimated glomerular filtration rate as an independent risk factor for cardiovascular mortality. Additionally, cardiac changes, such as left ventricular hypertrophy and impaired left ventricular systolic function, have been associated with an unfavorable prognosis. Despite the significant prevalence of underlying cardiac abnormalities, symptoms may not manifest in many patients with CKD. A range of available and emerging echocardiographic modalities may assist with diagnosing heart disease in CKD.[1]

The definition and classification of CKD have evolved over time, but current international guidelines define CKD as decreased kidney function shown by GFR of less than 60 mL/min per $1\cdot73m^2$, or markers of kidney damage, or both, of at least 3 months duration, regardless of underlying cause.[2]

Early detection of cardiovascular abnormalities in CKD helps in reducing morbidity and mortality and improving the quality of life.

This study was undertaken in view of lack of adequate studies in this aspect till date.

The aim of the study was to evaluate the asymptomatic cardiac manifestations in 2-4 stages of CKD. To study the ECG and Echocardiographic changes in Patients with CKD.

METHODS

The study is a cross sectional study which was conducted in 250 patients with chronic kidney disease on OPD basis and who were admitted in medicine and nephrology department in JSS Hospital Mysore during the period of October 2015 to September 2017.

Inclusion criteria

The following criteria were used in selection of cases

- All documented cases of CKD.
- All cases with eGFR <60ml/min/1.73m^2.
- Patients with persistent albuminuria.

Exclusion criteria

- Patients who were known valvular heart disease, coronary heart disease,
- Patients who were known hypertensive before the onset of chronic kidney disease.
- Patients on peritoneal or hemodialysis.
- Chronic alcoholics.
- Patients with acute illness, recent surgery, trauma.

Statistical methods

Summary statistics was done by measuring mean, SD, proportions. Inferential statistics was done using Chi-square test, independent t test, Pearson correlation. Graphical representation was done using Microsoft Excel. $P<0.05$ considered as significant. SPSS version 21.0 is used for calculations.

Procedure

Creatinine clearance had been calculated in all patients using the CockCroft-Gault equation:

Estimated Creatinine: (140 – age) x body weight (kg) ÷72 x serum creatinine (mg/dl) Clearance(ml/min)

This equation is for men. It is multiplied by 0.85 for women.

RESULTS

The study included a total of 250 patients which included 168(67.2%) males and 82(32.8%) females.

Age distribution

The mean age of the patients included in the study was 59 varied from 47 to 73 years.

Table 1 represents the age and sex distribution of the patients in study.

Table 1: Age and sex distribution.

		SEX			
		Male		Female	
		Count	Column N %	Count	Column N %
Age category	<40	17	10.2	9	11.0
	41-60	62	37.3	32	39.0
	61-80	76	45.8	40	48.8
	>80	11	6.6	1	1.2

Table 2: Mean systolic and diastolic pressures.

	Mean/ n	SD/ %
Systolic	146	13
diastolic	82.24	5.43
SBP >140 mm of Hg	205	82.7%
DBP >90 mm of Hg	65	26.2%

Blood pressure

229 patients had high blood pressure. The systolic BP varied from 132to 160 mm of Hg and the diastolic BP

from70 to 90 mm of Hg. Table 2 represents the mean systolic and diastolic pressures.

Hemoglobin

Haemoglobin ranged from 7.5 to 11.5 in both males and females. The mean haemoglobin was 9.86 with standard deviation of 1.69.

Table 3 represents the mean hemoglobin levels with respect to CKD stages.

Table 3: Mean hemoglobin in respect to CKD stages.

		HB		
		n	Mean	SD
CKD	Stage 3	136	9.87	1.64
	Stage 4	112	9.85	1.74

P=0.9

Chest radiograph

Chest radiography showed cardiomegaly in 75 patients and others were grossly normal.

Electrocardiography

- LVH with pressure overload pattern – 90(36%) cases.

- Low voltage QRS complexes – 43(17.2%) cases.
- Sinus tachycardia- 135(54%)

Ejection fraction

The mean ejection fraction as found to be 55.21 with standard deviation of 6.13

LVH (left ventricular hypertrophy)

106(42.4%) patients had LVH in echocardiography and ECG. Table 4 represents the stages of LVH in CKD. Table 5 shows graph representation of LVH in CKD stages.

Table 4: LVH in various stages of CKD.

		CKD							
		Stage 1		Stage 2		Stage 3		Stage 4	
		Count	Column N %	Count	Column N %	Count	Column N %	Count	Column N %
LVH	Yes	0	.0	0	0.0	45	33.1	61	54.5
	No	1	100.0	1	100.0	91	66.9	51	45.5

P=0.005

Table 5: LVDD grading in CKD stages.

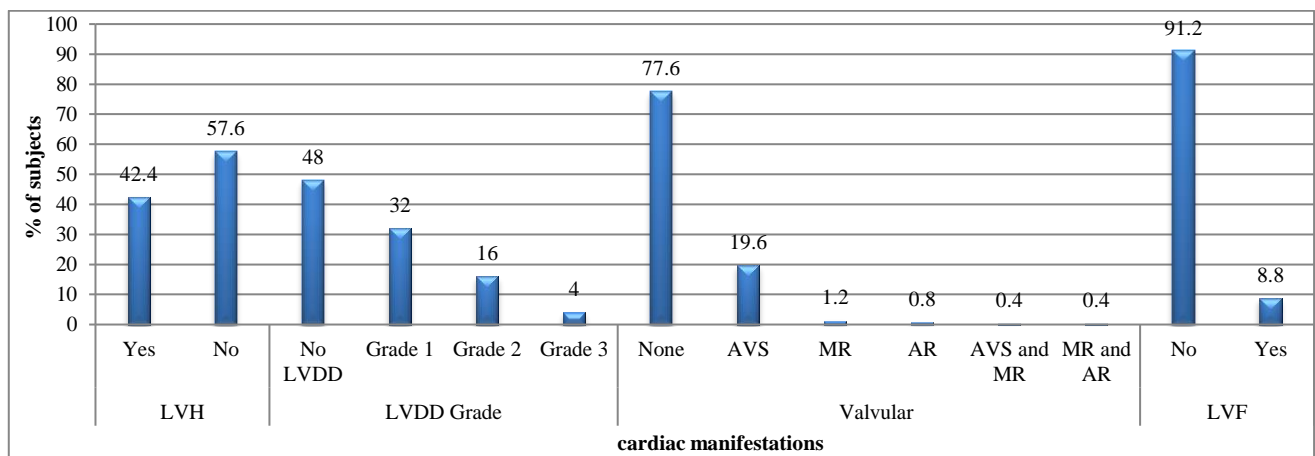|		CKD							
		Stage 1		Stage 2		Stage 3		Stage 4	
		Count	Column N %	Count	Column N %	Count	Column N %	Count	Column N %
LVDD_GRD	Normal	1	100.0	1	100.0	65	47.8	53	47.3
	Grade 1	0	0.0	0	0.0	45	33.1	35	31.3
	Grade 2	0	0.0	0	0.0	22	16.2	18	16.1
	Grade 3	0	0.0	0	0.0	4	2.9	6	5.4

p=0.9

Figure 1: Cardiac manifestations.

LVDD (left ventricular diastolic dysfunction)

130 (52%) patients had left ventricular diastolic dysfunction out of which 80(32%) had grade 1,40(16%) had grade 2 and 10(4%) had grade 3 LVDD. Table 6 represents the gradining off LVDD according to the stages of CKD.

Left ventricular failure

22 (8.8%) patients had left ventricular failure in both males and females.

Table 5 depicts the overall cardiac manifestations in CKD stages.

Co-morbodities

Most of the patients had diabetes in our study, 161(64.4%). 229(91.6%) patients had high BP at the time of examination.

All the patients had hypertension in our study.

Table 6: correlation between blood pressure, EF with creatinine and GFR.

Correlations		Systolic	DIAS	CREAT	GFR	EF
CREAT	Pearson correlation(r)	-0.011	0.078	1	-0.663[**]	-0.050
	P	0.864	0.220		0.000	0.435
	N	250	250	250	250	250
GFR	Pearson correlation®	-0.035	-0.011	-0.663[**]	1	-0.013
	P	0.583	0.859	0.000		0.832
	N	250	250	250	250	250

No significant correlation was observed between levels of Creatinine, and GFR with blood pressure and EF. The same has been shown in Table 6 representing the correlation between blood pressure, creatinine Ejection Fraction and Egfr.

DISCUSSION

This hospital based cross-sectional observational study demonstrates various ECG and echocardiographic manifestations in patients with CKD stages 2-4.

Although a longitudinal study would be preferable, progression of renal disease is too slow to permit this approach in a single center.

Age and sex distribution

The study included a total of 250 patients. Of these 250 patients, 168(67.2%)were males and 82 (32.8%) were females. The age of the patients varied from 47 to73 years. The mean age was 59 years.

In a study done by Laddha M et al in D.Y Patil Hospital Pune, out of 70 patients there were 53 males (75.7%) and 17 females (24.3%). Maximum number of patients belonged to age group of 51-60 years (26 patients). Mean age of ESRD patients was 53.[3]

In NHANES III, the distribution of estimated GFRs for the chronic kidney disease stages was similar in both sexes. The USRDS 2004 Annual Data Report reveals that the incident rate of renal failure cases is higher for males compared to females (409 vs 276 per million population). The sex distribution of renal disease in present study was in parallel with above studies. According to Framingham Heart Study, CVD prevalence in renal failure patients was 17.9% in men and 20.4% in women. According to Neugarten J, Golestaneh L in a study Gender and the prevalence and progression of renal disease concluded that males progress faster to renal failure than females.[4]

Symptoms

The duration of symptoms varied from 3 months to 3 years. Easy fatiguability was the most common symptom which was present in all the patients. On investigations they were found to have elevated renal parameters and subsequent work up confirmed the presence of Chronic Kidney Disease.

Blood pressure

Almost all patients had high blood pressure. The mean systolic BP was146 mm of Hg and the mean diastolic BP was around 82 mm of Hg. About 17.3% of patients had moderate hypertension.82% patients had BP more than 140mmhg.73.8%patients had normal diastolic

pressure.26% had more than 90mmhg. One patient had severe hypertension. All were receiving anti hypertensives during the study.

According to Kramer et al factors contributing to development of congestive heart failure in patient with CKD are volume over load, valvular heart disease, negative inotropic effects of Calcium, cardiac arrhythmias, pressure overload, myocardial damage and anemia.[5]

CKD patients have higher mortality, when compared to the general population, which is mainly attributed to cardiovascular events. Deaths due to cardiovascular events are far more common than progressing to ESRD and the need of renal replacement therapy.[6]

Proteinuria, whether considered as a marker of systemic endothelial dysfunction or a result of renal damage, has been associated with increased cardiovascular mortality.[7] In repeated studies, the presence of micro- and macroalbuminuria and GFR reduction were independent predictors of increased overall and cardiovascular mortality in both diabetic patients and non-diabetic patients.[8,9]

Irrespective of the presence of proteinuria, decline in GFR has been associated with increased cardiovascular morbidity and mortality. An inverse relationship between GFR and the severity of coronary artery stenosis was found as well as increased probability of having triple vessel disease with decreasing GFR.[10]

Investigations

Almost all patients in the study had Hemoglobin less than 12g/dl. The lowest value was 7g/dl and the highest was 12g/dl. Mean hemoglobin of 9.8g/dl. In Laddha M et al Mean haemoglobin percentage was 7.78 ± 1.84gm%. 22(44%) patients had severe anemia defined by Hemoglobin less than 7g/dl. 32(64%) patients had Hemoglobin between 7 to 10g/dl. Anemia is an independent risk factor for cardiac abnormalities. For every 1g/dl drop in mean hemoglobin, risk of cardiac failure increases by 25%.

P value was calculated for hemoglobin with reference to duration of symptoms. Which shows no statistical significance. Mean creatinine was 2.44. Creatinine clearance evaluated by Cockcroft Gault formula, varied from 22 to 44ml/min/1.73m². 2 patients had Creatinine clearance more than 50 ml/min. Mean creatinine as 32.39. In Laddha M et al, Mean blood urea level was 151.7 ± 51.37 mg%. Mean serum creatinine level was 10.35 ± 5.56 gm%.

P value was calculated for blood urea and serum Creatinine with reference to duration of symptoms which shows no statistical significance.

ECG showed evidence of Left ventricular hypertrophy with pressure overload pattern 90(36%).43(17.3%) patients had low voltages complexes. The diagnosis of left ventricular hypertrophy in ECG was made by using Sokolow-Lyon criteria.

Many patients had non-specific ST-T changes. 25(10%) patients had atrial fibrillation, LBBB appears in 20(8%)patients. However, sinus tachycardia being most common seen in67 (26.8%) patients.

In a study done by Laddha M et al ECG changes occurs as ECG changes in decreasing order of frequency were sinus tachycardia in 48.6%, LVH in 45.7%, ST – Tchanges in 30%, ventricular ectopics and Tall 'T' wave in 7.1%, QT prolongation and low voltage pattern in5.7%, ventricular tachycardia in 2.9% and complete heart block in 1.4% was noted. Kimura et al concluded that arrhythmias are due to acid base and electrolyte disturbances and underlying ischemic heart disease

In cardiovascular health study early-stage CKD was associated with only modest differences in ECG measurements of atrial conduction, ventricular depolarization, and ventricular repolarization.[6] These differences were explained by cardiovascular risk factors and medication use. According to same study longer QRS and corrected QT intervals were independently associated with incident heart failure, coronary artery disease and mortality among individuals with CKD. Same study also stated that the strength of association between ECG markers and cardiovascular events seemed qualitatively stronger for participants with CKD. However, these differences were not statistically significant.

LVH

left ventricular hypertrophy is the most common abnormality detected. It was found in 106(42.3%) patients.

In a study done by Parfrey PS et al in Division of Nephrology, Salvation Army Grace General Hospital, Canada, 41% of patients had concentric left ventricular hypertrophy.[11]

Dai Y et al has reported an incidence of LVH in 52% of patients.[12] Gruppen MP et al has reported LVH in 47% of male patients and 39% of female patients.[13] The study by Gruppen et al was a Dutch cohort study done in young adult patients with end-stage renal disease since childhood.

Echocardiography showed concentric left ventricular hypertrophy in 69(27.6%) patients. About 118(47.2%) patients had normal ECG but proved to have left ventricular hypertrophy by Echocardiography. this signifies the role of Echocardiography in diagnosing left ventricular hypertrophy. Increasing age, hypertension, anemia were the causes of concentric left ventricular

hypertrophy in uremia. Hyperparathyroidism can also cause left ventricular hypertrophy.

Foley et. al, reported that prevalence of LVH in patients with ESRD was found in 74% patients of which 44.3% had concentric hypertrophy and 29.6% had eccentric hypertrophy.[14] In a study by McGregor et al found prevalence of LVH in 64-70% of males and 63-65% of females.[15] High prevalence of anemia and hypertension in patients with CKD may also partly account for increased prevalence of LVH in patients with CKD. This high prevalence of LVH contrasts with a prevalence of less than 20% in Framingham Heart Study participants.

Limitations of study: Following were the limitations of the present study

- Small sample size
- Hospital based study
- Cross sectional study
- Study done for a shorter duration
- Non-randomized study

This study showed that, in all patients with CKD, early screening with ECG and Echocardiography is helpful to reduce morbidity and mortality due to cardiac diseases.

CONCLUSION

- Higher proportion of cardiac abnormalities were observed in our study which were similar to other studies.
- Echocardiography is easily performed, non-invasive, safe, reproducible and accurate in assessment of cardiac function in chronic kidney disease.
- left ventricular hypertrophy is the commonest abnormality in chronic kidney disease. Hence, ECHO should be done for all individuals with CKD.
- Echocardiography is more sensitive in diagnosing left ventricular hypertrophy than by X-Ray and ECG.
- Echocardiographically detectable LVH and concentric left ventricular hypertrophy were present in asymptomatic patients. Hence this necessitates screening of patients without cardiac symptoms for cardiac abnormalities immediately after the diagnosis of chronic kidney disease has been made.
- ECG is a simple bedside method to detect the earliest cardiac manifestations in individuals with CKD.
- ECG and ECHO will detect cardiac manifestations in early stages so that early intervention and appropriate medications will reduce cardiac complication and increase the quality of life.

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