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Original Research Article

A tertiary care centre profile of heart diseases among diagnosed cases of chronic kidney disease

Vijay Bakhtar[1], Niyati Bakhtar[2], Neha Pandey[3], Nikhil Bakhtar[4]*

[1]Department of Medicine, Dr. Panjabrao Deshmukh Memorial Medical College, Amravati, Maharashtra, India
[2]Intern Doctor, District Hospital, Amravati, Maharashtra, India
[3]Medical Officer, Military Hospital, Pulgaon, Maharashtra, India
[4]Consultant Physician, Bakhtar Hospital, Amravati, Maharashtra, India

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***Correspondence:**
Dr. Nikhil Bakhtar,
E-mail: drnikhilbakhtar@rediffmail.com

ABSTRACT

Background: Chronic Kidney Disease (CKD) is a risk factor for development of cardiovascular diseases. Cardiovascular diseases are the predominant cause of morbidity and mortality in patients with CKD. There is limited data on cardiovascular diseases among CKD patients from developing countries including India. With the present study, the prevalence and patterns of cardiac diseases among patients with CKD were profiled.
Methods: This was a cross sectional study in which 217 patients with CKD were studied over a period of two years and six months. Data on demographic characteristics and risk factors for cardiovascular diseases were collected using a standardized questionnaire. Cardiac evaluation was done using resting ECG and echocardiography.
Results: One hundred eighteen (54.4%) patients had either eccentric or concentric LVH. Patients with LVH were more likely to be hypertensive ($p<0.001$) or anemic ($p=0.034$). Up to 9.2% of study subjects had valvular heart disease (rheumatic or degenerative) and 22% had pericarditis. Patients with pericarditis were more likely to have a serum urea concentration greater than 60mg/dl ($p=0.327$). Forty-one patients (18.9%) had left ventricular systolic failure (EF<50%). There was a statistically insignificant higher prevalence of systolic failure in patients with LVH (21% vs. 16%), ($p=0.346$). Thirty-eight participants (17.5%) had diastolic failure while 2% had cardiac rhythm abnormalities.
Conclusions: Cardiac abnormalities are common in a relatively young Indian population with CKD. Clinicians should routinely screen and manage cardiovascular disease in CKD patients.

Keywords: Cardiac disease, Chronic kidney disease, Clinical profile, Screening

INTRODUCTION

Cardiovascular diseases are the primary cause of morbidity and premature mortality in patients with Chronic Kidney Disease (CKD).[1,2] The high risk of cardiovascular morbidity and mortality in End Stage Renal Disease (ESRD) is a well-established fact.[3] However a high rate of both fatal and non-fatal cardiovascular events has been observed in patients with earlier stages of chronic kidney disease.[4] Cardiac diseases have not been extensively studied among patients with CKD in India.

However, data drawn from more than 20000 subjects enrolled in landmark studies worldwide (Cardiovascular Health Study, Framingham Heart and others) showed association between CKD and a number of adverse cardiovascular outcomes. CKD was found to be an

independent risk factor for MI, stroke, and death after exclusion of patients with base line cardiovascular disease.[5]

The development of CKD is a risk factor for adverse cardiovascular events in patients with hypertension and normal base line renal function. This was demonstrated in a prospective cohort study involving 281 subjects with essential hypertension and normal base line kidney function in whom adverse cardiovascular events including Acute Myocardial Infarction (AMI), Heart failure, stroke, and/or death were more likely to occur in those who developed CKD (15%) in the 13 years of follow up (41% adverse events in CKD versus 13% in normal kidney function, HR 2.5, CI 95% 1.3-4.8).[6]

LVH has been reported in 30-45% of patients with CKD not on dialysis and the prevalence and severity of LVH was observed to increase with decreasing GFR/Renal function, with one study reporting LVH prevalence to be as high as 95.5% compared with 6.7% in controls.[7-10] With respect to cardiac arrhythmias; although their occurrence in patients with CKD can be secondary to hypertension, LVH, and heart failure; CKD is now recognized as an independent risk factor for cardiac arrhythmias especially Atrial Fibrillation (AF). A Japanese study that enrolled 1118 patients with hypertension showed that the development of CKD was a powerful predictor for new onset atrial fibrillation (p=0.009) independent of LVH and left atrial enlargement.[11] Patients with ESRD are at increased risk of tissue calcifications.[12,13] These calcifications may result in valvular stenosis and/or regurgitation. Further, pericardial diseases including pericarditis and pericardial effusion are relatively common in patients with renal failure. Uremic pericarditis has been observed in 6-10% of patients with advanced renal failure.[14] The pericarditis which affects both parietal and visceral pericardia is related to the level of azotemia, often occurring at BUN>60 mg/dL or 22 mmol/L.[14,15]

There is paucity of data on the occurrence of cardiovascular diseases among patients with CKD from central India. Further, the disease epidemiology has been observed to vary greatly across regions. Hence the present study was conducted with the objective of assessment of prevalence and patterns of cardiac diseases among patients with CKD at a tertiary care centre in central India.

METHODS

A cross sectional study was conducted at a tertiary care centre in central India between January 2017 to December 2018. All the patients coming to the tertiary care centre for kidney related complaints constituted the study population. A total of 258 patients were screened consecutively over a period of two years. Forty-one were excluded from the study on the basis of following criteria:

Inclusion criteria

- Age more than 18 years
- Confirmed case of CKD (defined as kidney damage for ≥3 months, as confirmed by markers of kidney damage, with or without decrease in glomerular filtration rate (GFR) or GFR<60 mL/min/1.73 m² for ≥3 months, with or without kidney damage).[1]

Exclusion criteria

- Patients who had any form of renal replacement therapy (Hemodialysis, peritoneal dialysis or renal transplant).
- Patients medically unfit to undergo evaluation.
- Patients refusing to give consent.

Ethical approval was obtained from the Institutional Ethics Committee. After due consent, a standardized pretested questionnaire was used to collect data on socio-demographic characteristics, medical history, and physical signs with emphasis on cardiovascular risk factors, laboratory test parameters, Electrocardiography (ECG) and Echocardiography variables. ECG was done primarily to evaluate cardiac rhythm with particular interest in atrial fibrillation (absent P waves). ECG changes suggestive of ischemic heart disease (Q waves, S-T and T wave changes) were also evaluated. Echocardiography was performed to evaluate cardiac structure and function. Left ventricular hypertrophy, ischemic heart disease, valvular heart disease, pericarditis, left ventricular systolic/diastolic failure and Pulmonary Artery Hypertension (PAH) were the key parameters studied at echocardiography.

Data was entered into MS excel and exported to STATA version 10 for analysis. Results were expressed as percentages with standard deviations. Chi-Square tests were used to determine associations. Results were considered statistically significant when the p value was <0.05.

RESULTS

A final sample of 217 patients were recruited in the study and were considered for analysis. One hundred and six participants (106, 49%) enrolled in the study were females. The mean age of study participants was 42.8 years (95% CI= 40.6- 44.9). About half of the patients had end stage renal disease (111, 51.2%) but were not on renal replacement therapy.

A total of 184 patients (84.8%) had proteinuria. One hundred sixty two patients (162, 74.65%) had a non-reactive HIV antibody test within the past three months of recruitment, thirty two patients (32, 14.75%) were HIV positive, while the remaining twenty three (23, 10.60%) had no evidence for the HIV test in the past three months. The patient characteristics are summarized in table 1.

Table 1: Demographic and clinical characteristics of study participants.

Characteristic		Frequency (n= 217)	(%)
Age	<45 years	124	57.1
	45-59 years	59	27.2
	≥60 years	34	15.7
Sex	Male	109	51.1
	Female	106	48.9
Stage of CKD	1 (GFR ≥90 ml/min/m²)	9	4.2
	2 (GFR 60-89 ml/min/m²)	12	5.5
	3 (GFR 30-59 ml/min/m²)	44	20.3
	4 (GFR 15-29 ml/min/m²)	41	18.9
	5 (GFR <15 ml/min/m²)	111	51.2
Proteinuria	Present	184	84.8
	Absent	33	15.2
HIV antibody test status	Non-reactive	162	74.7
	Reactive	32	14.8
	Not available	23	10.6

A total of 118 patients (54.4%) were found to have either concentric or eccentric LVH. Patients with LVH were more likely to be hypertensive (114, 96.6% vs. 4, 5.4%; p<0.001). Furthermore, patients with LVH were more likely to be anemic (92, 77.8% with Hb <11 g/dL vs. 26, 22.0% with Hb ≥11g/dL; p=0.034). Twenty patients (20, 9.2%) were found to have valvular heart disease. Three of the twenty patients had valvular abnormalities consistent with Rheumatic Heart Disease (RHD). The other seventeen patients had degenerative/atherosclerotic changes of cardiac valves involving mostly the aortic or mitral valve.

Forty-seven patients (47, 21.7%) had echocardiographic evidence of pericarditis suggested by pericardial effusion, pericardial thickening or both. Patients with pericarditis were more likely to have a serum urea concentration insignificantly greater than 60 mg/dL (85% with pericarditis had urea >60 mg/dL vs. 71% with normal pericardium and urea >60 mg/dL). None of the patients with pericarditis had evidence of cardiac tamponade. Forty-one patients (41, 18.9%) were found to be in left ventricular systolic failure ranging from mild to severe failure (i.e. left ventricular ejection fraction <50%). There was a higher prevalence of systolic failure among patients with LVH (25% vs. 16%) although this was not statistically significant, p=0.346. A small proportion of patients, thirty-eight (38, 17.5%) had Left Ventricular Diastolic Dysfunction (LVDD). Patients with LVDD were more likely to have LVH although this was not statistically significant. Four patients (4, 1.8%) were found to have cardiac rhythm disturbances with two having atrial fibrillation (Table 2).

Table 2: Distribution of cardiac diseases among study participants.

Variable	Number	Percentage
LVH	118	54.4
PAH	48	22.1
Pericarditis	47	21.7
LV systolic failure	41	18.9
LV diastolic failure	38	17.5
Valvular heart disease	20	9.2
Cardiac arrhythmias	4	1.8
Ischemic heart disease	1	0.5

The frequency of occurrence of cardiac diseases was observed not to vary much across the CKD stages, except LVH. The incidence of LVH went on increasing significantly with the progression of CKD from stage I to stage V (Table 3).

Table 3: Frequency of cardiac diseases across the different CKD stages.

Variable	CKD Stage					p- value
	I (N=9)	II (N=12)	III (N=44)	IV (N=41)	V (N=111)	
LVH N (%)	0(0.00)	4(33.3)	19(43.2)	24(58.5)	71(64)	0.001
IHD N (%)	0(0.00)	0(0.00)	1(2.3)	0(0.00)	0(0.00)	0.423
VHD N (%)	0(0.00)	0(0.00)	6(13.6)	1(2.4)	13(11.7)	0.182
Pericarditis N (%)	2(22.2)	0(0.00)	5(11.4)	11(26.8)	29(26.9)	0.091
LVSD N (%)	0(0.00)	1(8.3)	8(18.2)	8(19.5)	24(21.6)	0.473
LVDD N (%)	0(0.00)	3(25)	13(29.6)	6(14.6)	16(14.4)	0.101
Arrhythmias N (%)	1(11.1)	0(0.0)	1(2.3)	1(2.4)	1(0.9)	0.270

DISCUSSION

The present study focused on the incidence of cardiovascular diseases among patients with CKD. One

hundred eighteen patients accounting for 54.4% of study participants were found to have either eccentric or concentric left ventricular hypertrophy. This proportion is significantly lower than that found in other similar studies.[9,10,16,17] The reasons for this difference are not clear. Differences in determination of LVH where left ventricular wall thickness was used in this study as compared to left ventricular mass index in the Nigerian study may partly be accountable.[10] Age difference may have played a role as well, with few of the previous studies having had higher mean participant age.[16,17] Differences in the approach to treatment of hypertension including use of ACE inhibitors, which could probably account for this variation, need to be evaluated in further studies.

Anaemia and LVH are known causes of systolic failure or dysfunction. Both occur commonly among patients with CKD including those in this study. However, the association of LVH and anaemia with systolic failure was not statistically significant in this study most likely due to the relatively small sample size. With respect to the occurrence of systolic and diastolic failure, authors observations are corroborative of the observations of previous similar studies.[16-18] Despite the relatively small proportion of patients with evidence of ischemic heart disease, the development of CKD is a known risk factor for acute myocardial infarction.[6] Data from south east Asia about IHD in CKD are lacking and mostly unsubstantiated.

The finding of RHD in CKD with valvular lesions is suggestive of type 2 or chronic cardiorenal syndrome in which chronic cardiac dysfunction or failure results in renal dysfunction. However, there is also a possibility that renal and cardiac involvement is a consequence or complication of the same streptococcal infection. Available literature however suggests that valvular disease may result from extraosseous calcification involving cardiac valves in patients with uremia.[12]

Pericarditis presumed to be of uremic etiology was quite common among the study participants affecting up to 21.7%. Rostand et al, demonstrated a smaller proportion of pericarditis among patients with End Stage Renal Disease (ESRD) at 6-10%.[14] However consistent with findings in studies elsewhere is the fact that pericarditis is observed most often in patients with urea concentrations greater than 60 mg/dL. The relatively higher prevalence of pericarditis in this study could be explained by the high proportion of ESRD patients who are not on any renal replacement therapy. The most studied rhythm disturbance in CKD is atrial fibrillation. In this study, only two patients (0.9%) were found to have atrial fibrillation. A study done in the USA found a much higher atrial fibrillation prevalence of 21.2% in non-dialysis CKD patients.[19] This difference is probably due to age difference between the study populations. In the American study, the mean age of patients with atrial fibrillation was higher than that for patients with sinus rhythm (76±11 years vs. 63±15 years). These mean ages are both higher than the 42.8 years mean age for the subjects in this study.

The fact that worsening renal failure is associated with an increasing frequency of both cardiovascular risk factors and cardiac diseases is well established. However, the numbers were not adequate for observation of trends across the different stages of CKD. This study has demonstrated the common occurrence of abnormalities of cardiac structure and function among patients with CKD. The patients in this study are younger than western studies. The large number of patients with ESRD not on renal replacement therapy could partly account for the high burden of cardiac diseases in this relatively young patient population.

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