A STUDY OF CARDIAC DISEASES IN PATIENTS WITH CHRONIC KIDNEY DISEASE
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ABSTRACT

BACKGROUND
The heart and the kidneys are tightly interlinked with each other. So, primary disorder of one of these organs often results in the secondary dysfunction of other. The patients with CKD most of the times die from cardiovascular diseases than progressing to End-Stage Renal Disease (ESRD). Cardiovascular diseases such as CAD (Coronary Artery Disease), HF (Heart Failure), arrhythmia and sudden cardiac death represent the leading causes of morbidity and mortality in the patients with CKD, increasing sharply as the patients approach ESRD.

The aim of the is to study the–
1. Cardiac changes and complications in patients with chronic kidney disease;
2. Incidence of left ventricular dysfunction, concentric left ventricular hypertrophy and pericardial effusion in chronic kidney disease patients using echocardiography.

MATERIALS AND METHODS
Study was conducted among 54 patients with chronic kidney disease, admitted in Basaveshwara Teaching and General Hospital attached to Mahadevappa Rampure Medical College from January 2011 to August 2012.

RESULTS
There were 40 males and 14 females. Pedal oedema, dyspnoea and chest pain were the common symptoms. 75 had symptoms for more than 6 months. Severe anaemia occurred in 40%. About 94.5% had serum creatinine more than 5 mg/dL. About 68.5% had stage 5 chronic kidney disease (creatinine clearance < 15 mL/min). Normal chest x-ray finding was present in 72.3%. ECG revealed LVH with pressure overload pattern in 18.5%. Low voltage complexes was seen in 3.7%. Echocardiography - pericardial effusion (46.3%) and concentric LVH (44.4%) were the common abnormalities. Dilated LV occurred in 25.9%, diastolic dysfunction in 27.8% and systolic dysfunction in 20.4%.

CONCLUSION
Pericardial effusion followed by concentric left ventricular hypertrophy were the commonest abnormalities in chronic kidney disease. Echocardiographically, it was better to detect the mild pericardial effusion and concentric left ventricular hypertrophy compared to x-ray and ECG. Hence, this necessitates screening of patients without cardiac symptoms for cardiac abnormalities immediately after the diagnosis of chronic kidney disease has been made.

KEYWORDS
Chronic Kidney Disease, Pericardial Effusion, LV Dysfunction, Left Ventricular Hypertrophy.


BACKGROUND
Cardiovascular disease is emerging as the most common cause of death in patients with end-stage renal disease. The age adjusted cardiovascular complications and mortality is about 30 times higher in end-stage renal disease than in general population.1 Pre-transplant cardiovascular disease is also a risk factor for post-transplant cardiovascular disease. Besides the traditional risk factors like age, gender, etc., there are many risk factors specific to chronic kidney disease like anaemia, hyperparathyroidism, hyperhomocysteinaemia, proteinuria, hypoalbuminaemia, activated renin-angiotensin system which contribute to cardiovascular disease. Angina pectoris, myocardial infarction, dysrhythmia, cardiac failure, stroke and peripheral vascular disease are common in end-stage renal disease.2

Cardiomyopathy, whether clinically silent or not, is an independent predictor of cardiac morbidity and mortality.3 Natural history studies suggests that2,6

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Cardiomyopathy predisposes to cardiac failure and death.

Ischaemic heart disease results from and predisposes to cardiomyopathy, cardiac failure and death.

An understanding of the pathophysiology of cardiovascular diseases in chronic kidney disease enables prevention, early diagnosis and prompt interventions to control the complications. This study was done at MR Medical College, Gulbarga.

Aims and Objectives
1. To study the cardiac changes and complications in patients with chronic kidney disease.
2. To study the incidence of left ventricular dysfunction, concentric left ventricular hypertrophy, pericardial effusion in chronic kidney disease patients using echocardiography.

MATERIALS AND METHODS
A Cross-Sectional study was conducted in patients with chronic kidney disease admitted in Basaveshwara Teaching and General Hospital attached to Mahadevappa Rampure Medical College from January 2011 to August 2012.

Sample Size- Study was conducted in 54 chronic kidney disease patients admitted to BTGH. Cases were selected by random sampling method.

Study Subjects- Patients with chronic kidney disease.

Inclusion Criteria
The following criteria were used in selection of cases-
1. Patients who were known chronic kidney disease patients between ages 15 - 80 years.
2. Patients who were symptomatic for 3 months or more.
3. Patients with serum creatinine more than 3 mg% and creatinine clearance < 30 mL/min.
4. Patients with bilateral contracted kidneys on abdominal ultrasonogram with poor corticomedullary differentiation and type 2 or type 3 parenchymal changes.

Exclusion Criteria
1. Patients who were known valvular heart disease, coronary heart disease, diabetes mellitus, etc.
2. Patients who were known hypertensive for years before the onset of chronic kidney disease.
3. Patients who underwent dialysis after admission.
4. Patients who were alcoholics.

In all patients, a detailed history was taken with special interest to the duration of symptoms was noted. Cardiovascular symptoms like dyspnoea, chest pain, pedal oedema and pallor were noted. Blood pressure was measured thrice and the average was taken. Cardiovascular examination was done. Complete haemogram, blood urea, serum creatinine, serum electrolytes, serum calcium, phosphorus and uric acid, and serum lipid profile were measured.

Patients were also subjected to abdominal ultrasonogram and chest x-ray. Creatinine clearance was calculated in all patients using the Cockcroft-Gault equation:

\[
\text{Estimated Creatinine Clearance (ml/min) - } \frac{(140 - \text{age}) \times \text{body weight (kg)}}{72 \times \text{serum creatinine (mg/dl)}}
\]

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

Presence of cardiomegaly, pulmonary interstitial oedema and pleural effusion were looked for on chest x-ray postero-anterior view.

Evidence of left ventricular hypertrophy, low-voltage complexes and ischaemic changes were looked for in electrocardiogram.

Finally, 2D Echocardiography was done. The following parameters were looked for-

Chamber Size- In the 2D, the patients with interventricular septal thickness and left ventricular posterior wall thickness in diastole more than 1.1 cm represents concentric left ventricular hypertrophy. It is difficult to differentiate physiologic hypertrophy and pathologic hypertrophy. To avoid this, relative wall thickness was calculated in all patients using the following equation:

\[
\text{Relative Wall Thickness} = \frac{\text{IVS (D)} \times \text{LVPW (D)}}{\text{LVID (D)}}
\]

Relative wall thickness > 0.45 cannot occur in physiologic hypertrophy and it signifies pathologic hypertrophy.7

In the parasternal long axis view, left ventricular internal diameter in diastole more than 5.6 cm represents dilated left ventricle. Left atrial antero-posterior diameter of more than 3.8 cm represents dilated left atrium.

Systolic Function- The systolic function was assessed mainly by M-mode measurements. The Ejection Fraction is defined as the ratio of stroke volume to end-diastolic volume. Normal values of ejection fraction are 55 to 75.7

Grading of Systolic Dysfunction
i) Mild 45 to 55%.
ii) Moderate 35 to 45%.
iii) Severe < 35%.

Fractional shortening is calculated by the following equation:

\[
\text{Fractional Shortening} = \frac{\text{LVID (D)} - \text{LVID(S)}}{\text{LVID (D)}} \times 100
\]
Diastolic Function
Diastolic function was assessed by Pulsed Wave Doppler using the E/A measurements. E (m/s) indicate mitral flow, which causes ventricular filling following opening of the mitral valve. An (m/s) indicates ventricular filling due to atrial systole. E/A is normally more than 1. Less than 1 indicates diastolic dysfunction.
Diastolic dysfunction can be graded as follows-
Grade 1 = Impaired relaxation.
Grade 2 = Pseudonormalised pattern.
Grade 3 = Reversible restrictive pattern.
Grade 4 = Reversable restrictive pattern.

Left Ventricular Wall Motion Abnormalities-
Left ventricular wall was divided into a number of segments. Determining the motion of each segment provides the wall motion score.

Pericardial Effusion-
The pericardial effusion is quantified by the amount of echo-free space surrounding the heart. The pericardial effusion can be graded as-
Minimal pericardial effusion- Posterior atrioventricular groove shows echo free space. This is seen in systolic phase only. It represents normal pericardial fluid.
Mild pericardial effusion- Echo free space < 1 cm
Moderate pericardial effusion- Echo free space 1 – 2 cm
Large pericardial effusion- Echo free space > 2 cm

Valvular Abnormalities-
The valves were looked for stenotic lesions, regurgitant lesions, calcifications or vegetations.
All values were expressed as means with Standard Deviation (SD) or number. All the observations and particulars of each patient were recorded in a proforma.

RESULTS
The study included a total of 54 patients, which included 40 (74%) males and 14 (26%) females.

<table>
<thead>
<tr>
<th>Males</th>
<th>Females</th>
<th>Total</th>
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<tbody>
<tr>
<td>40 (74%)</td>
<td>14 (26%)</td>
<td>54</td>
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</table>

Table 1. Sex Distribution of CKD Patients

Age Distribution-
Age of the patients in the study varied from 13 to 48 years.
In the study, mean age of males was 29.72 ± 8.64 yrs. and mean age of females was 29.57 ± 9.44. Total mean age was 29.46 ± 8.77.

Duration of Symptoms-
Duration of symptoms varied from 3 months to 3 years.

<table>
<thead>
<tr>
<th>Duration</th>
<th>Number of Patients</th>
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<tbody>
<tr>
<td>Less than 6 months</td>
<td>13 (24.1%)</td>
</tr>
<tr>
<td>6 months - 1 yr.</td>
<td>22 (40.7%)</td>
</tr>
<tr>
<td>More than 1 yr.</td>
<td>19 (35.2%)</td>
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Table 2. Duration of Symptoms in CKD Patients

Symptoms-
Easy fatigability was present in all patients. Pedal oedema and dyspnoea were the other common symptoms present.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pedal oedema</td>
<td>50 (92.6%)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>38 (70.4%)</td>
</tr>
<tr>
<td>Chest pain</td>
<td>10 (18.5%)</td>
</tr>
<tr>
<td>Palpitation</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7 (13%)</td>
</tr>
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</table>

Table 3. Frequency of Symptoms in CKD Patients

Pallor-
Pallor was present in 52 (96.3%) cases. It was absent in 2 (3.7%) cases.

Jugular Venous Pulse-
Jugular venous pulse was normal in 35 (64.8%) cases. It was elevated in 19 (35.2%) cases.

Blood Pressure-
Almost all patients had high blood pressure. The systolic BP varied from 130 to 190 mmHg and the diastolic BP from 80 to 116 mmHg. The mean systolic BP was 152.55 ± 14.58 mmHg. The mean diastolic BP was 94.55 ± 8.93 mmHg.
Cardiovascular System
1. Apical impulse shifted down and out - 2 cases.
2. Pansystolic murmur in mitral area - 2 cases.
3. Ejection systolic murmur in the aortic area - 5 cases.
4. Muffled heart sounds - 2 cases.
5. Only 1 patient had pericardial rub.

Haemoglobin- Haemoglobin levels varied from 5 to 11 gm/dL with the mean being 7.50 ± 1.31 g/dL. Haemoglobin (g/dL), Number of patients.

<table>
<thead>
<tr>
<th>Haemoglobin</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 7</td>
<td>22 (40.7%)</td>
</tr>
<tr>
<td>7 to 10</td>
<td>30 (55.6%)</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>2 (3.7%)</td>
</tr>
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</table>

Table 4. Haemoglobin Concentration (g/dL) in CKD Patients

Creatinine- The range of Creatinine 3.5 to 16.5 mg/dL and the mean was 9.80 ± 3.17 mg/dL.

<table>
<thead>
<tr>
<th>Serum Creatinine (mg/dL)</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 5</td>
<td>3 (5.5%)</td>
</tr>
<tr>
<td>5 to 10</td>
<td>31 (57.4%)</td>
</tr>
<tr>
<td>More than 10</td>
<td>20 (37.1%)</td>
</tr>
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</table>

Table 5. Serum Creatinine Concentration (mg/dL) in CKD Patients

Creatinine Clearance- Creatinine clearance varied from 7 to 27 mL/min, and the mean value was 12.6 ± 4.68 mL/min.

<table>
<thead>
<tr>
<th>Creatinine Clearance (mL/min)</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 15</td>
<td>37 (68.5%)</td>
</tr>
<tr>
<td>15 to 30</td>
<td>17 (31.5%)</td>
</tr>
<tr>
<td>More than 30</td>
<td>Nil</td>
</tr>
</tbody>
</table>

Table 6. Creatinine Clearance (mL/min) in CKD Patients

Causes- The most common cause of chronic kidney disease in the study was chronic glomerulonephritis.
DISCUSSION

Chronic kidney disease is a pathophysiological process with multiple aetiologies, resulting in inexorable attrition of nephron number and function leading to end-stage renal disease. End-stage renal disease is a clinical condition in which there has been an irreversible loss of endogenous renal function, of a degree sufficient to render the patient permanently dependent upon renal replacement therapy.

Easy fatigability was the most common symptom, which was present in all the patients. The next common symptom was pedal oedema. Dyspnoea on exertion was present in 38 patients. Dyspnoea may be due to anaemia, volume overload or pulmonary congestion due to failing left ventricle. Chest pain was found in 10 patients. Of these 10 patients, 7 were found to have concentric hypertrophy and rest 3 had dilated left ventricle. The cause of chest pain in concentric LVH group could be due to increased demand by the hypertrophied muscle mass or constriction of the smaller coronary vessels by the muscular contraction during systole. Chest pain can also be due to pericarditis, in which the pain is more on lying down posture and alleviated by sitting up and leaning forward. History of palpitation was obtained from 7 patients.

Clinical Findings- Bilateral pedal oedema was present in 52 patients. The remaining 2 patients who did not have pedal oedema presented with vomiting, dyspnoea, easy fatigability to the general medical outpatient department, and on investigations they were found to have elevated renal parameters and subsequent workup confirmed the presence of Chronic Kidney Disease. Pallor was present in 52 patients. JVP was normal in 35 patients and elevated in 19 patients. The patients with elevated JVP showed other features of volume overload like facial puffiness, ascites, etc.

Almost all patients had high blood pressure. The mean systolic BP was 152 mmHg and the mean diastolic BP was around 94 mmHg. About 39% of patients had moderate hypertension. One patient had severe hypertension. All the patients were receiving antihypertensives after admission during the study.

Anaemia is an independent risk factor for cardiac abnormalities. For every 1 g/dl drop in mean haemoglobin, risk of cardiac failure increases by 25%, echocardiographically demonstrable left ventricular hypertrophy in 42% and the risk of death increases by 14%.8

Echocardiographic Profile

Pericardial Effusion- It is the most common abnormality in the study. Frommer JP et al has reported an incidence of pericardial effusion in 18 out of 50 (36%) patients.9 Gupta et al reported an incidence of 8.8% in patients on maintenance haemodialysis.10

Patients with mild effusion had only non-specific ST-T changes in the ECG. This shows that echocardiography is sensitive in diagnosing mild pericardial effusion.

Concentric LVH- In a study done by Parfrey PS et al4 in Division of Nephrology, Salvation Army Grace General Hospital, Canada, 41% of patients had concentric left ventricular hypertrophy. Dai Y et al has reported an incidence of LVH in 52% of patients.11 Gruppen MP et al has reported LVH in 47% of male patients and 39% of female patients.12

The study by Gruppen et al was a Dutch cohort study done in young adult patients with end-stage renal disease since childhood. Echocardiographically proved left ventricular hypertrophy is an independent risk factor for cardiovascular morbidity and mortality.13

Lowering of cardiac size and increase in fractional shortening were both associated with reduced subsequent likelihood of cardiac failure.13

These associations were independent of baseline age, diabetes mellitus, ischaemic heart disease, baseline echocardiographic parameters. The mean duration of illness in patients with concentric hypertrophy was 11 months. The mean age of patients with concentric hypertrophy was 29.6 years. The mean BP in patients who had concentric hypertrophy was 152 mmHg (systolic) and 94 mmHg (diastolic).

About 14 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 and anaemia were the causes of concentric left ventricular hypertrophy in uraemia.4 Hyperparathyroidism can also cause left ventricular hypertrophy.7

Dilated Left Ventricle- Dilated left ventricle is defined as the left ventricular internal diameter in diastole more than 5.6 cm. About 14 (25.9%) patients in the study had dilated left ventricle. This was similar to the study done by Parfrey PS et al, which had dilated left ventricle in 28%.4 Of the 14 patients with dilated left ventricle, 10 had cardiomegaly and 2 patients had cardiomegaly and pulmonary interstitial oedema on chest x-ray; 4 out of 14 patients with dilated left ventricle had systolic dysfunction. The risk factors for dilated left ventricle includes anaemia, hypertension and hypoalbuminaemia.

Dilated Left Atrium- Dilated left atrium was present in 4 cases, out of which 3 had dilated left ventricle and systolic dysfunction.
Systolic Dysfunction - Systolic dysfunction defined as Ejection fraction less than 55% or Fractional shortening less than 25% was found in 11 (20.4%) patients. The incidence of systolic dysfunction in the study by Parfrey PS et al was 16%. This shows that dilated left ventricle is an independent risk for systolic dysfunction. Two patients had global hypokinesia of left ventricle with systolic and diastolic dysfunction. One of these patients had dilated left ventricle and left atrium and had the criteria fulfilled for dilated cardiomyopathy.

Other Abnormalities - Aortic valve calcification can occur in End-stage Renal Disease due to secondary hyperparathyroidism and increased calcium phosphorus product. Age is also an important risk factor for aortic valve calcification. Raine AEG has reported an incidence of 28% to 55% of Aortic valve calcification in End-stage Renal Disease, with 3% to 13% having aortic stenosis.

Results of this study done in MR Medical College and the study done by Parfrey et al in Division of Nephrology, Salvation Army Grace General Hospital, Canada can be summarised as follows:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Present Study</th>
<th>Parfrey et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentric LVH</td>
<td>44.4%</td>
<td>41%</td>
</tr>
<tr>
<td>Dilated LV</td>
<td>25.9%</td>
<td>28%</td>
</tr>
<tr>
<td>Systolic Dysfunction</td>
<td>20.4%</td>
<td>16%</td>
</tr>
<tr>
<td>Normal</td>
<td>14.8%</td>
<td>16%</td>
</tr>
</tbody>
</table>

Table 8. Parameters

Blood pressure, Anemia, Calcium Phosphate, Sodium retention, Hypoalbuminemia, Angiotensin II, Aldosterone, Depression and sleep disorders

Table 9. Chronic Kidney Disease related Risk Factors Specific to CKD Emerging Risk Factors

CONCLUSION
1. Echocardiography is easily performed, non-invasive, safe, reproducible and accurate in assessment of cardiac function in chronic kidney disease.
2. Pericardial effusion followed by concentric left ventricular hypertrophy were the commonest abnormalities in chronic kidney disease.
3. In Echocardiography pericardial effusion occurred in 46.3%, concentric LVH in 44.4%, dilated LV in 25.9%,
diastolic dysfunction in 27.8% and systolic dysfunction in 20.4%.
4. Echocardiography is more sensitive in diagnosing pericardial effusion and left ventricular hypertrophy than by X-ray and ECG.
5. Echocardiographically detectable mild pericardial effusion 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.

REFERENCES