Transthoracic echocardiography in patients with chronic kidney disease

Shrestha B1, Gurung D2, Dhungel S3

1Balaram Shrestha, Professor; Department of Medicine, KIST Medical College Teaching Hospital, Lalitpur; 2Dhiraj Gurung, Lecturer; Department of Medicine, Karnali Academy of Health Sciences, Karnali; 3Sanjib Dhungel, Professor; Department of Medicine, Nepal Medical College Teaching Hospital, Attarkhel, Kathmandu, Nepal.

Abstract

Background: Evaluation of cardiac diseases in chronic kidney disease has been rarely investigated in Nepal.

Objectives: Objective of this study is to evaluate cardiac lesions in admitted chronic kidney disease patients.

Methodology: It is a prospective observational study of echocardiography of chronic kidney disease patients from April, 2007 to April, 2013 in Nepal Medical College Teaching Hospital.

Results: One hundred chronic kidney disease patients were evaluated. Male to Female ratio was 1.8:1 and age ± SD was 46.3 ± 17.2 years. Forty eight percent of the chronic kidney disease patients had left ventricular hypertrophy. Patients with chronic kidney disease with left ventricular hypertrophy group had interventricular septum of 1.5 ± 0.3 cm vs. 1.1 ± 0.1 cm (p<0.0001) and posterior wall of 1.1 ± 0.2cm vs. 1.0 ± 0.1cm (p< 0.01) in comparison to chronic kidney disease without left ventricular hypertrophy. Forty one percent had left ventricular systolic dysfunction with left ventricular ejection fraction of 39 ± 9.9 %. Pulmonary arterial hypertension was noticed in 39% patients. Valvular regurgitant lesions were quite common (241%) usually as multivalvular lesions (4.4 lesions per patient). Mitral regurgitation was the commonest regurgitant lesion (81%).

Conclusion: Echocardiographic cardiac evaluation is useful to diagnose concomitant cardiac lesions for standard care of chronic kidney disease patients.

Key words: Chronic kidney disease (CKD); Echocardiography; Left ventricular hypertrophy (LVH); Left ventricular systolic dysfunction (LVSD); Valvular lesions

INTRODUCTION

Worldwide prevalence of chronic kidney disease (CKD) has been estimated to be 8-16%1. Renal diseases are quite common in Nepal. With a population of 27 million people, the estimated incidence of end stage renal disease (ESRD) is around 2700 per year if we take 100 cases of ESRD/million population at par with India and Pakistan2, whereas the community based prevalence of CKD in eastern Nepal was found to be 10.6%3. The incidence of ESRD has increased gradually with 3.4 per million populations (pmp) in 1990 to 11.89 pmp in 1999 with an average annual incidence of 6 pmp and only 0.31% of expected ESRD patients received renal replacement therapy4.

Renal parenchymal disease is the most common cause of secondary hypertension5,6. Hypertension leads to hypertensive heart disease, which is the result of structural and functional adaptations leading to left ventricular hypertrophy (LVH), congestive heart failure, abnormalities of blood flow due to atherosclerotic coronary artery disease, microvascular disease and cardiac arrhythmias. Chronic kidney disease is associated with an eight to tenfold increase in cardiovascular mortality7. So, cardiac evaluation of CKD patients is important. Objective of this study is to evaluate the cardiac abnormalities in admitted CKD patients.

Echocardiography provides a non invasive assessment of left ventricular structure and function. Echocardiography based evaluation of cardiac...
abnormalities in CKD patients are available from various international centers\textsuperscript{8-15}, but it is quite rare in Nepal\textsuperscript{16}. Here, we present our prospective study of echocardiography based evaluation of cardiac abnormalities in admitted CKD patients.

**METHODOLOGY**

This is a prospective observational study of admitted CKD patients undergoing transthoracic echocardiography during six years period from 2007 to 2013 in Nepal Medical College Teaching Hospital Echocardiography laboratory (NMCTH echo lab). Diagnosis of different stages of CKD has been done as per previous recommendation\textsuperscript{5} with CKD stage I as estimated glomerular filtration rate >90 mL/min per 1.73 m\textsuperscript{2}, stage II as 60-89, stage III as 30-59, stage IV as 15-29 and stage V as < 15.

The decisions to do or not do echocardiography were as per the clinical judgments of the treating nephrologists/physicians. Patients >16 years to ≤ 80 years with CKD of various stages under hemodialysis or not under hemodialysis were included in the study. Patients with presence of pre-existing heart disease, e.g. Rheumatic heart disease, diagnosed valvular lesions, arrhythmias were excluded from the study.

Echocardiography machines used for this study were LOGIQ 400 MD MR3 Version 4.31 (GE, USA) and Toshiba Nemio XD (Tokyo, Japan). Evaluation of various cardiac parameters such as left ventricular ejection fraction (LVEF), left ventricular diastolic dysfunction (LVDD), left ventricular hypertrophy (LVH), valvular lesions and pericardial effusion were evaluated for this study. Echocardiographic findings were presented as one abnormality as one entity (e.g. one patient with 4 valvular regurgitant lesions, LVH, LVDD, PAH are collectively considered as 7 lesions) and one cardiac disease as one entity (e.g. one patient with 4 valvular regurgitant lesions, LVH, LVDD, PAH are collectively considered as one valvular lesion and not each lesion as one separate entity).

Teichholz method was used for calculation of LVEF per the local availability of this system in echocardiographic machines in NMCTH\textsuperscript{17}. With Teichholz formula\textsuperscript{18}, LVEF is calculated by dividing stroke volume (SV) in the LV outflow tract (LVOT), by end-diastolic volume (LVEDV)\textsuperscript{2}.

\[
SV = \pi \times (LVOT)^2 \times VTI_1 \div 2
\]

\[
LVEDV = \frac{7 \times LVEDD^3}{(2.4 + LVEDD)}
\]

Left ventricular wall thickness > 1.3 cm is unusual in physiological hypertrophy\textsuperscript{19}. Interventricular septum (IVS) and posterior wall (PW) thickness of 1.3 to 1.5 cm have been recommended as moderate hypertrophy in women and 1.4 to 1.6 cm as moderate hypertrophy (1.1 to 1.3 cm as mildly abnormal) in men\textsuperscript{20}.

LVEF less than 55\% was considered as low in this study\textsuperscript{21,22} sub-grouping ejection fraction of 45-54\% as mild systolic dysfunction, 30-44\% as moderate systolic dysfunction and less than 30\% as severe systolic dysfunction\textsuperscript{21,22}. The LVDD was diagnosed as previous criteria\textsuperscript{13,23}. We have used simple criteria of tall left ventricular inflow A wave in comparison to E wave to detect LVDD\textsuperscript{13,23}.

Estimated systolic pulmonary artery pressure (PAP) has been calculated with tricuspid regurgitation (TR) based trans-tricuspid pressure gradient [4 V\textsuperscript{2} of TR velocity (V)] + right atrial pressure (RAP). Right atrial pressure was empirically fixed as 10 mm Hg\textsuperscript{24,25}. The PAH was sub-grouped into mild PAH (36-45 mm Hg), moderate PAH (46-60 mm Hg) and severe PAH (>60 mm Hg)\textsuperscript{24,25}.

Data were presented as Mean ± SD. Unpaired t-test was performed where appropriate and p<0.05 was considered significant. Microsoft Excel 2007 was used for the calculations.

**RESULTS**

Altogether 100 admitted CKD patients underwent transthoracic echocardiography during the study period of six years. Out of them, male to female ratio was 1.8:1 and mean age ± SD was 46.3 ± 17.2 years.

Evaluation of echocardiography based cardiac lesions is shown in Figure 1. Valvular heart diseases were present in 60\% CKD patients in one disease one entity presentation. In one abnormality one entity presentation, altogether there were 440 cardiac lesions (440\%) detected in 100 CKD patients as shown in Figure 1. Regurgitant valvular lesions were the most common findings (241\%) in the echocardiography. Mitral regurgitation was the most common regurgitant lesion (81\%), followed by tricuspid regurgitation (76\%) and aortic regurgitation (38\%) as shown in Figure 1.
Comparison of presence or absence of LVH is shown in Table 1. Left ventricular hypertrophy was noticed in 48% of the CKD patients. Compared to the non-LVH group, the LVH group had IVS of 1.5 ± 0.3 cm vs. 1.0 ± 0.2 cm (p < 0.0001) and PW of 1.1 ± 0.2 cm vs. 0.9 ± 0.3 cm (p < 0.01).

LV wall thickness (Interventricular septum, IVS and Posterior wall, PW) in cm has been shown in Table 2, according to various grades of CKD. There were non-significant difference in IVS thickness (p = 0.18, non-significant) and PW thickness (p = 0.04, significant) when CKD IV and V were compared.

Comparison of presence or absence of low ejection fraction in CKD patients is shown in Table 3. Forty one percent had left ventricular systolic dysfunction (LVSD) with LVEF of 39.5 ± 9.9 % vs. 63.4± 6.4 % (p < 0.0001) in comparison to CKD patients without LVSD. Various grades of LVSDs are shown in Table 4 with 19% patients were having moderate LVSD.

LVEF according to various CKD grades are shown in Table 5. There were non-significant difference of LVEF between CKD stage IV (LVEF = 52.5±9.5%) and CKD stage V had LVEF of 50.9±18.1% (p=0.67, NS).

Pulmonary arterial hypertension (PAH) in CKD patients is shown in Table 6. Thirty nine percent of CKD patients had PAH out of which, 18% had mild PAH. Estimated pulmonary arterial hypertension in various grade of CKDs are shown in Table 7 with non-significant tendency of rising PAP with worsening grades of CKD.

(AR-aortic regurgitation; MR-mitral regurgitation; TR-tricuspid regurgitation; PR-pulmonary regurgitation; LVH-Left ventricular hypertrophy; PAH-Pulmonary arterial hypertension; PE-pericardial effusion; LVSD-Left ventricular systolic dysfunction; LVDD-Left ventricular diastolic dysfunction)

### Table 1: Left ventricular wall thickness in CKD patients with and without LVH

<table>
<thead>
<tr>
<th>LVH</th>
<th>IVS: Mean ± SD (Range)</th>
<th>PW: Mean ± SD (Range)</th>
<th>Frequency</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVH</td>
<td>1.5 ± 0.3 * (1.3 to 2.7 cm)</td>
<td>1.1 ± 0.2 # (0.8 to 1.8 cm)</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>No LVH</td>
<td>1.0 ± 0.2 * (0.7 to 1.2 cm)</td>
<td>0.9 ± 0.3 # (0.7 to 1.3 cm)</td>
<td>52</td>
<td>52</td>
</tr>
</tbody>
</table>

* p < 0.0001  
# p < 0.01  
(IVS: Interventricular septum; PW: Posterior wall).

![Figure 1: Echocardiographic findings in CKD patients](image-url)
Table 2: IVS and PW thickness according to various grades of CKD (n=100)

<table>
<thead>
<tr>
<th>CKD grades</th>
<th>IVS (Mean±SD) (Range)</th>
<th>PW (Mean±SD) (Range)</th>
<th>Frequency</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD V</td>
<td>1.3±0.3* (0.7 to 1.9 cm)</td>
<td>1.1±0.2# (0.7 to 1.6 cm)</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>CKD IV</td>
<td>1.5±0.6* (0.8 to 2.7 cm)</td>
<td>1.2±0.3# (1 to 1.8 cm)</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>CKD III</td>
<td>1.2 (1.1 to 1.2 cm)</td>
<td>1 (0.8 to 1.1 cm)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>CKD I</td>
<td>1 cm</td>
<td>1.1 cm</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

* p = 0.18 (NS)
# p=0.04
(IVS: Interventricular septum; PW: Posterior wall).

Table 3: Presence or absence of low ejection fraction in CKD patients

<table>
<thead>
<tr>
<th>LVEF</th>
<th>Mean ± SD (range)</th>
<th>Frequency</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low LVEF</td>
<td>39.5 ± 9.9 * (53.6 to 19.8%)</td>
<td>41</td>
<td>41</td>
</tr>
<tr>
<td>Good LVEF</td>
<td>63.4 ± 6.4 * (79.9 to 55 %)</td>
<td>59</td>
<td>59</td>
</tr>
</tbody>
</table>

*p< 0.0001

Table 4: Systolic dysfunction in CKD (n=100)

<table>
<thead>
<tr>
<th>Grades of LVEF</th>
<th>Grades of systolic dysfunction</th>
<th>Frequency</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;=55 %</td>
<td>Normal</td>
<td>59</td>
<td>59</td>
</tr>
<tr>
<td>45-54 %</td>
<td>Mild</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>30-44 %</td>
<td>Moderate</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>&lt;30 %</td>
<td>Severe</td>
<td>6</td>
<td>6</td>
</tr>
</tbody>
</table>

*p= 0.67 (NS)

Table 5: LVEF according to various CKD grades (n=100)

<table>
<thead>
<tr>
<th>CKD grades</th>
<th>LVEF (%) (Mean±SD) (Range)</th>
<th>Number</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD V</td>
<td>50.9±18.1* (25 to 79.9)</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>CKD IV</td>
<td>52.5±9.5* (43 to 65)</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>CKD III</td>
<td>65.5 (53.6 to 77.3)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>CKD I</td>
<td>61 (61)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*p= 0.67 (NS)

Table 6: Pulmonary arterial hypertension in CKD (n=100)

<table>
<thead>
<tr>
<th>Grades of PAH</th>
<th>PAH grades</th>
<th>Frequency</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>Normal</td>
<td>61</td>
<td>61</td>
</tr>
<tr>
<td>36-45</td>
<td>Mild PAH</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>46-60</td>
<td>Moderate PAH</td>
<td>13</td>
<td>13</td>
</tr>
<tr>
<td>&gt;60</td>
<td>Severe PAH</td>
<td>8</td>
<td>8</td>
</tr>
</tbody>
</table>

Table 7: Pulmonary arterial hypertension in various grades of CKD

<table>
<thead>
<tr>
<th>CKD grades</th>
<th>PAH (mm Hg) (Mean±SD) (Range)</th>
<th>Frequency</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CKD V</td>
<td>51.1±16.3 (28.6 to 90.4) *</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>CKD IV</td>
<td>43.9 (41.2 to 46.6) *</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>CKD III</td>
<td>46 (44 to 48)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>CKD I</td>
<td>32.3 (32.3)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*p= 0.17 (NS)
DISCUSSION

In this prospective study of a small group of admitted 100 CKD patients attending NMCTH-echo lab during six years period, male to female ratio was 1.8:1. Similar male predominance in Nepalese population has been reported by several other authors as well 26,27 reporting approximately 65% male patients. In our male dominated society, males get more treatment especially when it is expensive27. In one study, one- third of the CKD patients (37%) had to sell their property for the treatment 27.

Poverty and lack of female awareness may have contributed to less female referral to tertiary care centres for better CKD management. Mean age (age± SD, 46.3 ± 17.2 years) of CKD patients was similar to previous study28. Echocardiography provides a non-invasive assessment of systolic and diastolic function of left ventricle. It is also very useful in evaluation of the presence of LVH and its severity9, 12, 14, 15.

The incidence of LVH increases with progressive decline in renal function29. It was noticed in 48% of the CKD patients undergoing echocardiography. Patients with CKD with LVH group had IVS of 1.5 ± 0.3 cm vs. 1.0 ± 0.2 cm, p<0.0001) and PW of 1.1 ± 0.2 cm vs. 0.9 ± 0.3 cm, p< 0.01) in comparison to CKD without LVH. There was non-significant difference in degree of hypertrophy in CKD IV (1.5±0.6 vs 1.3±0.3 (p=0.18, NS) as compared to CKD V (1.2 ±0.3 vs 1.1 ± 0.2 (p=0.04, Significant) as shown in Table 2.

Individuals with LVH are at increased risk for coronary heart disease (CHD), stroke, congestive heart failure, and sudden death. Aggressive control of hypertension can regress or reverse LVH and reduce the risk of cardiovascular disease 3.

Good BP control in general Nepalese hypertensive was noted (19.0%)30 and in CKD patients, it was noted in 31.4%. The control of BP in these CKD patients had been poor. In comparison to intensive BP controlled group, uncontrolled group received more antihypertensive agents (3.0 ± 1.3 vs. 2.0 ± 0.8, p< 0.05)31.

Echocardiography is a very valuable noninvasive tool found to be extremely useful in the evaluation of left ventricular systolic function (LVSD). In this study, 41% of the patients had LVSD. This finding is higher than previous report of 13.2%16. One cause for it may be inclusion of LVEF <55% as LV systolic dysfunction. However, our data is similar to pre-transplant data reported elsewhere12.

Patients with CKD with LVSD had LVEF of 39.5 ± 9.9 % vs. 63.4 ± 6.4 % (p<0.0001) in comparison to CKD without LVSD. Left ventricular ejection fraction, in CKD stage IV 52.5±9.5 vs 50.9±18.1 % (p=0.67, NS), as compared with CKD stage V, was not statistically significant.

Valvular lesions were present in 60% CKD patients in one disease one entity presentation. In one disease one entity presentation, regurgitant valvular lesion were common findings (241%) in the echocardiography. Mitral regurgitation being the most common (81%) lesion, was followed by TR (76%) and AR (38%). Cause for having excessive regurgitant lesion may be due to the inclusion of trivial or minimal regurgitant lesions. These trivial regurgitant lesions may be normal findings. This higher proportion of valvular lesions may also be due to selection bias, selecting clinically more symptomatic patients with the higher probability of having various cardiac lesions inclusive of regurgitant lesions for echocardiographic evaluation. All of these valvular lesions are unlikely to be directly related to CKD. Causes like hypervolemic status in CKD, chamber dilation, annular dilation and mitral annular calcification may have at least partly contributed to regurgitant lesions such as MR and AR. Presence of significant regurgitant lesions in CKD may have contributed to the significant left ventricular systolic dysfunction in this study. When meticulously searched in general population, MR can be detected in 70-80%, TR in 80-90% and PR in 70-80% without clarifying whether it is trivial or mild regurgitation33. Aortic regurgitation is rare in normal individuals that is present in 5% in young individuals with increasing prevalence of AR with age.

The left ventricular diastolic dysfunction (LVDD) was noticed in 25 patients (25%) in this study. This finding is less than the other report of left ventricular diastolic dysfunction in 58.5%16. They may have used various techniques to better detect LVDD without elaboration. We have used simple technique to detect LVDD which may pick up LVDD stage I and miss equivocal cases and LVDD stage III. This may have resulted in less LVDD.

The PAH is highly prevalent in end-stage renal disease. Several observational studies based on an echocardiographic diagnosis of PAH, have suggested a prevalence of 30-60% and an association with increased mortality and poorer outcome following renal transplantation34. In this study, PAH was noticed in about one third of patients (39%). In CKD patients under hemodialysis, usually have hypervolemic state, resulting in increased stroke volume, increased right ventricular output and increased pulmonary artery pressure.
hypertension is very common comorbid condition, it may have resulted in deterioration in left ventricular systolic dysfunction and pulmonary arterial pressure. In our study, there was non-significant but rising trend in pulmonary arterial hypertension in severe CKD stage as compared to milder CKD stages. Further study is necessary with more patients to achieve the statistically significant interpretation.

Data related to distribution of various grades of PAH were a bit higher than the report of 2351 Chinese CKD patients35, with mild (12.1%) and moderate PAH (4.9%). The cause of this discrepancy is not known. The difference in ethnicity may have played a role. They have reported pulmonary hypertension, PAH in CKD being associated with cardiac morbidity and stated as increasing cardiac morbidity were seen with increasing PH severity35.

In this study, pericardial effusion was detected in 25% of CKD patients. In comparison to one previous study, out of 50 end stage renal disease patients16, 32.1% were reported to have pericardial effusion. This data is nominally higher than our findings. In asymptomatic CKD patients (35 ERSD patients), 11% had pericardial effusion with 6% having effusion > 100 ml. However, in symptomatic ERSD patients with symptoms of pericarditis, 51% had pericardial effusion16. As our study did not discriminate for symptomatic or non-symptomatic CKD patients, our effusion data is reasonable. In another paper, 32.1% patients were reported to have pericardial effusion14.

Conclusion

The high prevalence of left ventricular systolic dysfunction, left ventricular hypertrophy, pulmonary arterial hypertension and regurgitant valvular lesions in this study with CKD patients is important and useful information while dealing with the clinical problems in CKD patients. It is recommended for CKD patients to undergo echocardiographic evaluation of co-morbid cardiac conditions such as LVSD, LVDD and LVH.

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