RESEARCH PAPER | Medical Science | Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Prevalence of Cardiovascular Manifestations in patients of Chronic Kidney Disease at a tertiary hospital of Punjab

KEYWORDS: Chronic kidney disease, Left ventricular hypertrophy, Pericardial disease, Echocardiography, Systolic dysfunction, diastolic dysfunction

Dr Gian Chand	Dr Ajay Chhabra	Dr Abhishek Gupta
Associate Professor, Department of Medicine, Government Medical College, Amritsar	Assistant Professor,Department of Medicine, Government Medical College, Amritsar	Post-graduate Student,Department of Medicine, Government Medical College, Amritsar

ABSTRACT *Problem statement: Chronic kidney disease (CKD) is becoming a major global health problem. It increases patient mortality and morbidity and puts a major economic strain on the health care system. It is estimated that 1,00,000 new patients of end stage renal disease (ESRD) enter renal replacement programs annually in India. In the absence of any registry in our country these figures were based on estimates. CKD is an important cause of cardiovascular morbidity and mortality. Aims and objectives: Aim was to study the prevalence of cardiovascular dysfunction in patients of chronic kidney disease at a tertiary level hospital of North India. These include ischemic changes and arrhythmias on electrocardiographic evaluation, prevalence and pattern of left ventricular hypertrophy along with systolic and diastolic dysfunction on echocardiography. It was also intended to study the prevalence of pericardial disease in patients with chronic kidney disease. Materials and method: The present study was undertaken to study the pattern of cardiovascular dysfunction in the patients with chronic kidney disease in this part of the country. 100 consecutive patients of either sex attending OPD or admitted at Government Medical College, Amritsar, After informed consent and thorough history taking patients under went certain investigations which included blood urea, serum creatinine, glycosylated haemoglobin, electrocardiogram, 2-dimensional echocardiography with Doppler examination. The results were systematically collected and analysed. Results: Hypertension and dyslipidemia were seen in 78% and 35% patients of CKD. Atrial arrhythmias were found in 12% of patients and Ventricular arrhythmias were found in 21% patients in our study. LVH was found in 63% of our patients. Systolic dysfunction was found in 25% patients whereas diastolic dysfunction was seen in 55% patients. Echocardiographic evidence of pericardial disease was seen in 9% patients.*

Introduction

Chronic kidney disease (CKD) is emerging to be an important chronic disease globally.[1] India is no exception to this rule. Many parts of India are undergoing rapid epidemiological transition as a consequence of economic and social changes.[2] It has been recently estimated that the age-adjusted incidence rate of End Stage Renal Disease (ESRD) in India to be 229 per million population,[3] and >100,000 new patients enter renal replacement programs annually in India.[4] The exact incidence of chronic kidney disease is difficult to predict, because many patients are asymptomatic or its presence has not been easily recognised.

Globally, CKD is the 12th & 17th cause of death and disability, respectively. Data from the National Health and Nutrition Examination Surveys (NHANES) in the United States suggests that the prevalence of CKD has increased from 10% to 13% between 1988-1994 and 1999-2004.[5]

Chronic kidney disease (CKD) is a long term condition which can arise from damage to the kidneys from variety of diseases. In an important minority of people, CKD is progressive and results in ESRD. According to the Kidney Disease Outcomes Quality Initiative (K/DOQI) Clinical practice guidelines, to diagnose CKD, there must be:-

Kidney damage for >3months defined as either structural or functional abnormalities such as urinary sediment abnormalities or albuminuria.

Glomerular Filtration Rate (GFR) <60ml/min/1.73m^2 for >3months with or without evidence of structural damage.[6]

CKD is a heterogeneous condition, dependent upon cause and type of kidney disease, severity rate of progression and comorbid conditions. In order to stage CKD, it is necessary to estimate the GFR. Equation commonly used to estimate GFR is Cockcroft-Gault equation.[7]

Cockcroft-Gault equation

Estimated Creatinine clearance =

$$\frac{(140 - \text{Age}) \times \text{Body Weight (Kg) (Males) (ml/min)}}{72 \times \text{Serum Creatinine (mg/dl)}}$$

(Multiply by 0.85 in females)

Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines have classified CKD into five stages:-[6]

STAGE	DESCRIPTION	GFR(ml/min/1.73m^2)
1.	Slight kidney damage with normal or increased filtration	More than 90
2.	Mild decrease in kidney function	60-89
3.	Moderate decrease in kidney function	30-59
4.	Severe decrease in kidney function	15-29
5.	Kidney failure	Less than 15(or dialysis)

CKD leads to disturbances in the function of virtually every organ system and leads to fluid and electrolyte disturbances, abnormalities of metabolic and endocrine, gastrointestinal, neuromuscular, dermatological, hematological and immunological, cardiovascular and pulmonary systems.

Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Patients with CKD are at increased risk of developing Cardiovascular Disease (CVD).[8] Chronic kidney disease is an independent risk factor for cardiovascular disease.[9] Among patients with CKD, CVD is 2-4 times more prevalent and advances at twice the rate.[10] Mild to moderate loss of renal function is strongly associated with an increased risk of cardiovascular mortality.[11] Mortality from CVD in these patients is approximately 9% per year which is about 30 times the risk in the general population.[10] The incidence of cardiovascular disease increases with stage progression of CKD and is 0.7% in stage 1 chronic kidney disease and increases to 48.5% in stage 5 chronic kidney disease. [12]

Chronic heart failure (CHF) and chronic kidney disease (CKD) often coexist. Increasingly, the cardio-renal syndrome, defined as the confluence of cardiac and renal impairment, has been recognized as a known entity in which not only do cardiac and renal dysfunction coexist, but the failure of one system accelerates the decline of the other. Renal disease shares many of the same risk factors as cardiomyopathies. This confluence of cardiac and renal impairment may lead to an endless cycle of progressive concomitant functional decline.

CKD may also cause other cardiovascular problems such as heart failure in the absence of coronary artery disease. Most patients with CKD suffer frequently from left ventricular hypertrophy (LVH), left ventricular dilatation (LVD) or systolic dysfunction.[13] This cardiac disorder is called uremic cardiomyopathy. LVH is the most common cardiac alteration observed in CKD patients and is detected in approximately 74% of patients at the start of dialysis. LVH by demonstrating the presence of a high left ventricular mass index (LVMI) on echocardiography. Renal failure patients tend to have a higher LVMI. Diastolic dysfunction is very frequent in dialyzed patients. A low Left Ventricular Ejection Fraction (LVEF) was shown to be present in one-third of new dialysis patients.[14]

Both pressure and volume overload present in CKD contribute to these cardiac structural and functional abnormalities with progressive LV remodeling causing geometric and functional changes. Cardiac dilatation is considered to be a precursor of both LV dysfunction and clinical heart failure in patients with or without myocardial infarction.[14] Systemic hypertension, which is highly prevalent in the CKD population, is associated with LVH. Volume overload, anemia and arteriovenous fistulae are known to cause LVD.[15,16] Aoki et al showed that renal failure patients with dilated cardiomyopathy (DCM) display more severe myocyte hypertrophy and disarray than normal DCM subjects.[17] The ultrafiltrate and serum of uremic patients were shown to have negative inotropic and chronotropic effects.[18] Prolonged exposure to these uremic toxins can result in myocyte fibrosis and apoptosis.[19]

In CKD patients, plasma catecholamine concentrations were demonstrated to be increased by several fold.[20] Multiple lines of evidence indicate that both the increased cardiac adrenergic drive and the increase in circulating norepinephrine are ultimately damaging to the heart.

Thus CVD and CKD show intricate interactions and this confluence of cardiac and renal impairment may lead to an endless cycle of progressive concomitant functional decline.

MATERIALS AND METHODS

The study included one hundred diagnosed patients of chronic kidney disease of either sex attending OPD or admitted in various wards of Government Medical College, Amritsar.

The criteria for chronic kidney disease were taken to be as follows:

1. Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate, manifested by either pathological abnormalities; or markers of kidney damage, including abnormalities in composition of blood or urine, or abnormalities in imaging tests
2. Glomerular Filtration Rate <60ml/min/1.73m.sq for ≥ 3 months, which was calculated as per Cockcroft-Gault equation.[7]

The patients undergoing haemodialysis due to chronic kidney disease were also be included in the study.

Patients with congenital or rheumatic valvular heart disease, age less than 18 years, acute kidney injury or previous history of ischemic heart disease were excluded.

Patients after thorough history and clinical evaluation underwent following investigations: urine complete examination, 24 hr urine protein, haemoglobin, TLC, DLC, FBS/PPBS, blood urea, serum creatinine, total serum proteins, serum albumin, serum electrolytes (sodium, potassium), lipid profile, ultrasound abdomen, 12 lead, surface and resting electrocardiogram, X-ray chest PA view and transthoracic echocardiography.

Left ventricular dimensions (interventricular septal thickness [IVS], posterior wall thickness [PW], and left ventricular end-diastolic diameter [LVEDD]) were measured at end of diastole with M-mode by using the leading-edge–to–leading-edge convention. Left ventricular mass was determined by using the Troy formula according to the recommendations of the American Society of Echocardiography (ASE): left ventricular mass(g)=1.04[(LVEDD+IVS+PW)^{3}-LVEDD^{3}] x0.8+0.6.[21] Left ventricular mass was divided with body surface area to obtain the left ventricular mass index (LVMI). LVH was defined as LVMI ≥89 g/m^{2} in females and ≥103g/m^{2} in males. The term systolic dysfunction was used in patients with ejection fraction <55%. The diastolic dysfunction was measured and grading was done as per the grading given by American Society of Echocardiography. The results of the study were systematically recorded and statistically analyzed.

OBSERVATIONS

It was observed that the maximum number of patients were in the age group 55-64 years (39%). Out of the 100 cases included in our study, 49 individuals were males and 51 were females.

Only patients in stages III-V of CKD i.e. eGFR <60ml/min were included. We found the maximum patients in stage IV (42%) followed by stage III in which 34% patients were seen. 24% patients were in stage V. 24 were on haemodialysis.

40 percent patients were diabetics. However, the HbA1c levels >6.5 were seen in 27%. In the rest diabetes status was under control.

78 patients to be hypertensive. 20 out of 24 patients on dialysis were hypertensive. 58 out of 76 patients not undergoing dialysis were found to be hypertensive.

Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

Dyslipidemia was prevalent in 36% patients. Abnormalities in the serum triglyceride levels was the most commonly observed lipid abnormality and was found in 34% patients. Serum LDL levels were increased in 22% patients whereas total cholesterol was increased in 5% only.

Anaemia is a frequent association in patients with CKD. In the present study, we found anaemia (i.e. haemoglobin <10 gm/dl) in 70% patients. All the patients on haemodialysis had anaemia while 68% patients who were not undergoing dialysis had anaemia.

12 patients presented with atrial arrhythmias while ventricular rhythm abnormalities were seen in 21 patients.

Prevalence of Left Ventricular Hypertrophy (LVH) in patients with CKD:
LVH was found in 63% patients of CKD. LVH was found to increase in severity with decreasing eGFR. 13 CKD patients in stage III of the disease had LVH (i.e 38%) whereas out of the 66 patients in stage IV and V 50 had LVH on echocardiography (i.e 76%). The relation was found to statistically significant and the p value was found to be 0.004.

Systolic dysfunction in patients with CKD:
Ejection fraction was used as a marker of systolic dysfunction. Ejection fraction <55% was taken as abnormal in the present study. 21% patients had systolic dysfunction. 21 (31.8%) of the patients with eGFR <30 had systolic dysfunction whereas 4 (11.7%) of the patients with eGFR 30-60 had decreased ejection fraction. This increase with declining GFR was found to be statistically significant (p value- 0.03).

Prevalence of diastolic dysfunction in patients with CKD:
Diastolic dysfunction was found in 55% patients with CKD in our study. Diastolic dysfunction was found 11 out of 34 patients with Stage III CKD and 43 out of 66 patients of Stage IV and V. The p value for correlating diastolic dysfunction in moderate (stage 3) and severe (stage 4&5) was found to be very significant (p value- 0.003)

Prevalence of pericardial disease in patients with CKD:
Pericardial disease was a relatively frequent association with CKD and was seen only 9% patients. Pericardial involvement was seen in the form of pericardial effusion and pericardial thickening as a result of constrictive pericarditis.

Prevalence of valvular dysfunction in patients with CKD:
Valvular dysfunction was a less common association with CKD. Aortic valve was involved more commonly than the mitral valve. Aortic calcification/ stenosis was seen in 15% whereas mitral valve was involved in 5% patients only.

DISCUSSION
CKD leads to disturbances in the function of virtually every organ system and leads to fluid and electrolyte disturbances, abnormalities of metabolic and endocrine, gastrointestinal, neuromuscular, dermatological, hematological and immunological, cardiovascular and pulmonary systems. Chronic kidney disease is an independent risk factor for cardiovascular disease. The incidence of cardiovascular disease increases with stage progression of CKD and is 0.7% in stage 1 chronic kidney disease and increases to 48.5% in stage 5 chronic kidney disease.

In our study, we included the patients in stages III-V. We found the maximum patients in stage IV (42%) followed by stage III (34%) and stage V (24%). In our study a very large fraction of patients (24%) were in end stage renal disease. This finding was due to our study being conducted in a tertiary hospital care setting where many of the patients were admitted only in later stages of CKD.

This is because the majority of patients with stages I and II do not report to the medicine OPD due to lack of general awareness about the varied symptoms of the disease spectrum.

Diabetes is the most common causative risk factor for CKD in India and abroad. In the present study, there were 40 percent diabetics. However, the HbA1c levels >6.5 were seen in 27. In the rest patients, diabetes was controlled on regular medication. Modi et al also found Diabetic nephropathy as the commonest cause of ESRD though their prevalence was higher (44%) than our study (40%).[22]

In our study, 78% patients were found to be hypertensive. Twenty out of 24 patients on dialysis were hypertensive. Fifty eight out of 76 patients not undergoing dialysis were found to be hypertensive. Similar findings were obtained by Ridao et al.[23] Results showed the prevalence of HTN in the total group of patients with renal diseases was 60.5%.[14] The prevalence of hypertension in the CKD patients on dialysis was found to be 83%. Similar findings were observed by Agarwal et al who reported it to be about 86%.[24]

In our study, we found dyslipidemia in 35% patients. Serum triglyceride levels was the most commonly seen lipid abnormality found in 34% patients. Serum LDL levels were increased in 22% patients whereas total cholesterol was increased in 5% only. Vaziri et al similarly described the pattern of dyslipidemias in patients with CKD. It was found that these patients have increased serum triglyceride, VLDL, and LDL with unchanged Total Cholesterol and low HDL.25 Out of the 24 patients on haemodialysis, 12 (50%) were found to have dyslipidemia. The patients on Haemodialysis had normal TC and LDL levels with increased triglyceride levels in the present study. Our findings are also consistent with finding of Kasiske et al who found fifty percent of haemodialysis patients with dyslipidemia.26 Haemodialysis patients usually have normal TC and LDL levels.25

In our study 70% of the patients were found to be anaemic which was significantly higher than that in general population. However it was significantly higher than that in study conducted in US by McClellan et al which was perhaps due to lower socioeconomic status and superimposed nutritional anaemias being more prevalent in developing countries like India than in US.27

ECG changes were observed in every CKD patient included in our study. All the leads were looked for ST-T changes in all the patients. We found 23 patients with ST-T changes suggestive of ischemia. But as previously mentioned haemodialysis induce changes in serum electrolytes and volume status. These coupled with the presence of LVH and the effect of medications contribute to the changes in resting electrocardiogram. For these reasons, the ST segment depression on resting ECG is considered an unreliable marker of chronic ischemia in CKD patients. The prevalence of atrial fibrillation was 12% in our study which is consistent with the article by Salim et al which described its prevalence of 7-27%. The prevalence of ventricular arrhythmias and premature ventricular complexes was found to be 21% in our study which is less than that found in

Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

study conducted by Bonato et al in which its prevalence was found to be 35%.[29] This may be explained by the absence of inclusion of 24-hour ECG holter monitoring in our study.

In our study 63% of the total CKD patients have some degree of left ventricular hypertrophy. Similar results were obtained in study conducted by Levin et al and Foley et al in which the LVH found in 45-90% of patients in different stages of CKD patients.[30,31]

LVH was found to increase in severity with decreasing eGFR in our study. The relation was found to be statistically very significant as seen in a study done by Middleton et al.[32]

In the studies conducted by Agarwal et al and Collins et al, it was concluded that the prevalence of systolic dysfunction in CKD is more than that in general population.[33,34] In our study the overall prevalence of systolic dysfunction in CKD patients was found to be 25%.

In our study the prevalence of systolic dysfunction also increased significantly with decline in renal function and was about 31% in patients in patients with severe and end stage CKD. This was nearly similar to the results obtained in study conducted by Parfrey et al in which the systolic dysfunction was found in upto 28% of patients with severe CKD.[35]

Similar to systolic dysfunction, the prevalence of diastolic dysfunction is also increased in patients of CKD. Our study observed a 55% prevalence of diastolic dysfunction of various grades in patients of CKD. This finding was consistent with the study conducted by Kuntz et al which reported a prevalence of 50 to 65%.[36] In our study, prevalence of diastolic dysfunction with increasing stage of CKD was seen.

The prevalence of pericardial disease was found to be 9%. Similar results were observed by Gunukula et al.[37]

Aortic valve calcification was found in nearly 21% & 45% of non haemodialysed & haemodialysed CKD patients, respectively. The later result is slightly different from the study done by London et al who observed aortic valve calcification in 55% of the patients.[38]

We observed prevalence of mitral valve calcification in 15.7% of patients of CKD patients who were not on haemodialysis and in 33.3% of CKD patients on haemodialysis. These results are very similar to the study done by Mazzaferro et al.[39]

CONCLUSION

Thus, it has been found that CKD patients have more prevalence of cardiac abnormalities in one form or another. An element of this excess CVD risk in CKD is explained by the multifaceted range of myocardial and vascular insults, from malignant ventricular remodelling, LV conduction abnormalities, sequestered vasoprotective agents, low-grade inflammation, endothelial dysfunction, derangements in electrolytes and metabolic compounds, autonomic disorders, small and large arterial calcifications and loss of arterial compliance. However, we feel it is very likely that there are as yet undiscovered factors, and inter-relationships, which are of direct relevance.

CKD is silent epidemic of the 21st Cardiovascular disease is recognized as the predominant cause of death in Chronic kidney disease. Many cardiovascular implications of CKD are described in literature. There is enough data to support that patients with concurrent CKD and CVD likely benefit from many of the interventions implemented in individuals with CVD alone, including the same secondary measures employed in general population. Efforts to improve cardiovascular outcomes by single risk factor intervention have been unsuccessful and the approach should be global, multifaceted and multidisciplinary.

REFERENCES :

1. Ruggenenti P, Schieppati A, Remuzzi G. Progression, remission, regression of chronic renal diseases. Lancet. 2001; 357(9268):1601–8.
2. Prabahar MR, Chandrasekaran V, Soundarajan P. Renal Data from the Asia-Africa. Soudi Journal of Kidney Diseases and Transplantation. 2008; 19(5): 847-53.
3. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens 2004; 18(2):73–8.
4. Kher V. End-stage renal disease in developing countries. Kidney Int. 2002; 62(1): 350–62.
5. Harris K. Assessment of chronic kidney disease. In: Barratt J, Harris K, Topham P, editors. Oxford desk reference, Nephrology, Inc. Newyork. Oxford university press, 2009; 390.
6. National Kidney Foundation: K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, classification and stratification. Am J Kidney Dis 2000; 1: 39.
7. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum
8. creatinine. Nephron. 1976; 16: 31-41.
9. Collins AJ, Li S, Gilbertson DT, Liu J, Chen SC, Herzog CA. Chronic kidney disease and cardiovascular disease in the Medicare population. Kidney Int 2003:24–31.
10. Mann JFE, Gerstein HC, Pogue J: Renal insufficiency as a predictor of cardiovascular outcomes and the impact of ramipril: The HOPE Randomized Trial. Ann Intern Med 2001; 134:629-36.
11. Culleton BF, Larson MG, Wilson PW, et al. Cardiovascular disease and mortality in a community-based cohort with mild renal insufficiency. Kidney Int. 1999;56:2214-9
12. Collins AJ, Li S, Gilbertson DT, et al. Chronic kidney disease and cardiovascular disease in medicare population. Kidney Int Suppl. 2003;87:S34-31
13. Rajapurkar.M, Dabhi M, Burden of disease-prevalence and incidence of renal disease in India. Clinicl Nephropathy 2010:74;9-12.
14. Foley RN, Parfrey PS, Kent GM et al. Long-term evolution of cardiomyopathy in dialysis patients. Kidney Int 1998; 54: 1720–1725.
15. Vasan RS, Larson MG, Benjamin EJ et al. Left ventricular dilatation and the risk of congestive heart failure in people without myocardial infarction. N Engl J Med 1997; 336: 1350–1355.
16. London GM, Fabiani F, Marchais SJ et al. Uremic cardiomyopathy: An inadequate left ventricular hypertrophy. Kidney Int 1987; 31:973–980.
17. Weisensee D, Löw-Friedrich I, Riehle M et al. In vitro approach to "uremic cardiomyopathy. Nephron 1993; 65: 392–400.
18. Aoki J, Ikari Y, Nakajima H et al. Clinical and pathologic characteristics of dilated cardiomyopathy in hemodialysis patients. Kidney Int 2005; 67: 333–340.
19. Vanholder R, Glorieux G, Lameire N. Uremic toxins and cardiovascular disease. Nephrol Dial Transplant 2003; 18: 463–466.
20. Mall G, Huther W, Schneider J et al. Diffuse intermyocardiocytic fibrosis in uremic patients. Nephrol Dial Transplant 1990; 5: 39–44.
21. Converse RL, Jacobson TN, Toto RD et al. Sympathetic overactivity in patients with CRF. N Engl J Med 1992; 327: 1912–1918.
22. Troy BL, Pombo J, Rackley CE. Measurement of left ventricular wall thickness and mass by echocardiography. Circulation. 1972;45:602–611.
23. Modi GK, Jha V. The incidence of end-stage renal disease in India: A population-based study. International Society of Nephrology 2006;70;2131-3.
24. Ridao N, Luño J, García de Vinuesa S, Gómez F, Tejedor A, Valderrábano F. Prevalence of hypertension in renal disease. Nephrol Dial Transplant. 2001;16Suppl 1:70-3.
25. Agarwal R. Hypertension in chronic kidney disease and dialysis: patho-

Volume : 6 | Issue : 6 | June 2016 | ISSN - 2249-555X | IF : 3.919 | IC Value : 74.50

physiology & management. Cardio Clin. 2005 Aug;23(3):237-48.
26. Vaziri ND, Moradi H. Mechanisms of dyslipidemia of chronic renal failure. Hemodial Int. 2006;10:1–7. Salim et al., Int J Cardiovasc Res 2012, 1:3
27. Kasiske BL. Hyperlipidemia in patients with chronic renal disease. Am J Kidney Dis 1998; 32: S142–56.
28. McClellan W[1], Aronoff SL, Bolton WK, et al. The prevalence of anemia in patients with chronic kidney disease. Curr Med Res Opin. 2004 Sep;20(9):1501-10.
29. Salim I, Suwaidi JA, Gadhban W and Salam AM. Systematic Review of Atrial Fibrillation in Patients with Chronic Kidney Disease: Prevalence, Incidence, Morbidity and Mortality. Int J Cardiovasc Res. 2012;1:3
30. Bonato FOB, Lemos MM, Cassiolato JL, Canziani MEF (2013) Prevalence of Ventricular Arrhythmia and Its Associated Factors in Nondialyzed Chronic Kidney Disease Patients. PLoS ONE 8(6): e66036. doi:10.1371/journal.pone.0066036
31. Levin A, Thompson CR, Ethier J, et al. Left ventricular mass index increase in early renal disease: impact of decline in haemoglobin. Am J Kidney Dis. 1999;34:125-34.
32. Foley RN, Murray AM, Li S, et al. Chronic kidney disease and the risk for cardiovascular disease, renal replacement and death in the United States Medicare population, 1998 to 1999. J Am SocNephrol. 2005;16:489-95.
33. Middleton RJ, Parfrey PS, Foley RN. Left ventricular hypertrophy in the renal patient. J Am SocNephrol. 2001;12:1079-84.
34. Agarwal S, Dangri P, Kalra OP, et al. Echocardiographic Assessment of Cardiac Dysfunction in Patients of Chronic Renal Failure. JIACM 2003; 4(4): 296-303.
35. Collins AJ. Impact of congestive heart failure and other cardiac disease on patient outcomes. Kidney Int Suppl. 2002;81:S3-7.
36. Parfrey PS, Foley RN, Harnett JD, Kent GM, Murray DC, Barre PE: Outcome and risk factors for left ventricular disorders in chronic uraemia. Nephrol Dial Transplant 1996;11:1277–85.
37. Kuntz K, Dimitrov Y, Muller S, Chantrel F, Hannedouche T: Uraemic cardiomyopathy. Nephrol Dial Transplant 1998;13:39–43.
38. Gunkula SR, Spodick DH. Pericardial disease in renal patients. SeminNephrol. 2001;21:52-6.
39. London GM, Pannier B, Marchais SJ, et al. Calcification of aortic valve in dialysed patients. J Am SocNephrol. 2000;11778-83.
40. Mazzaferro S, Coen G, Bandini S, et al. Role of ageing chronic renal failure and dialysis in the calcification of mitral annulus. Nephrol Dial Transplant. 1993;8:335-40.