EVALUATION OF CARDIAC ABNORMALITIES IN CHRONIC KIDNEY DISEASE UTILISING ECHOCARDIOGRAPHY – A STUDY OF 54 PATIENTS

Dissertation Submitted to

THE TAMIL NADU DR. M.G.R MEDICAL UNIVERSITY

In partial fulfillment of the regulations
for the award of the degree of

M.D. BRANCH – I
GENERAL MEDICINE

GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL
THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA.

MARCH 2007

CERTIFICATE

This is to certify that the dissertation titled **"EVALUATION OF CARDIAC ABNORMALITIES IN CHRONIC KIDNEY DISEASE UTILISING ECHOCARDIOGRAPHY – A STUDY OF 54 PATIENTS"** is the bonafide original work of **DR. P. MUTHU KUMAR** in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamilnadu DR. M.G.R Medical University to be held in March 2007. The Period of study was from August 2005 to September 2006.

PROF. S. NATARAJAN, M.D. Professor and Head of the Dept. of Medicine, Govt. Stanley Medical College and Hospital Chennai-600 001.	**PROF. T. VENKATAKRISHNAN** Addl. Professor of Medicine Govt. Stanley Medical College and Hospital Chennai-600 001.

DEAN
Govt. Stanley Medical College & Hospital,
Chennai – 600 001.

DECLARATION

I, **DR. P. MUTHU KUMAR,** solemnly declare that dissertation titled **"EVALUATION OF CARDIAC ABNORMALITIES IN CHRONIC KIDNEY DISEASE UTILISING ECHOCARDIOGRAPHY – A STUDY OF 54 PATIENTS"** is a bonafide work done by me at Govt. Stanley Medical College and Hospital during August 2005 to September 2006 under guidance and supervision of my unit chief **Prof. T. VENKATAKRISHNAN**., **M.D**.,Addl. Professor of Medicine.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University, towards partial fulfillment of requirement for the award of **M.D. Degree (Branch – I) in General Medicine.**

Place : Chennai.

Date :

(DR. P. MUTHU KUMAR)

ACKNOWLEDGEMENT

I owe my thanks to the Dean, Govt. Stanley Medical College and Hospital, **Dr. D. R. GUNASEKARAN, M.S., FICS** for allowing me to avail the facilities needed for my dissertation work.

I am grateful to **Prof. S. NATARAJAN, M.D.,** Professor and Head of the Department of Medicine, Govt. Stanley Medical College and Hospital for permitting me to do the study and for his encouragement.

I express my gratitude to **Prof. T. VENKATAKRISHNAN, M.D.,** Addl. Professor of Medicine, Chief of Medical Unit V, Govt. Stanley Medical College and Hospital for his valuable assistance and guidance.

I am extremely thankful to **Prof. SHIVAKUMAR, M.D.,** Professor of Therapeutics, Govt. Stanley Medical College and Hospital for his valuable assistance and guidance.

I am grateful to **Prof. R. SUBRAMANIAM, M.D, D.M.**, Professor and Head of the Dept of Cardiology, Govt. Stanley Medical College and Hospital for permitting me to use the facilities of the Department.

I express my gratitude to **Prof. R. VIJAYA KUMAR, M.D, D.M.,** Professor and Head of the Dept of Nephrology, Govt. Stanley Medical College and Hospital for his valuable guidance and encouragement.

I am extremely thankful to my Assistant Professors **Dr. G. VASUMATHY, M.D**., and **Dr. S. PASUPATHY M.D.,** for their guidance and encouragement.

I owe my thanks to **DR. GOPALAKRISHNAN. M.D, D.M**., Assistant Professor of Nephrology, Govt. Stanley Medical College and Hospital for his support and guidance .

I express my gratitude to **DR. KANNAN M.D, D.M.,** and **DR. ASHOK VICTOR M.D, D.M.,** Assistant Professors of Cardiology, Govt. Stanley Medical College and Hospital for their guidance and encouragement.

I am extremely thankful to **DR. S. SOCRATES** and **DR. S. JEYABOOPATHY,** Postgraduates in Cardiology for their immense help and guidance.

I am also thankful to my colleagues for their full cooperation in this study.

Last but not the least, my sincere thanks to all the patients who co-operated for this study, without whom this study would have been impossible.

CONTENTS

INTRODUCTION

In health the volume and composition of body fluids vary within normal limits and the kidneys are largely responsible for maintaining this state. The kidneys also subserve a host of metabolic and endocrine functions. Chronic kidney disease is a pathophysiological process with multiple etiologies, 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.

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 anemia, hyperparathyroidism, hyperhomocysteinemia, proteinuria, hypoalbuminemia, 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[3-7] suggests that (1) cardiomyopathy predisposes to cardiac failure and death, and (2) ischemic 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 done at Stanley Medical College, Chennai identifies the cardiovascular changes and complications found in patients with chronic kidney disease.

AIM OF THE STUDY

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.

REVIEW OF LITERATURE

Review of literature is discussed under the following headings:

1. Chronic kidney disease.
2. Stages of chronic kidney disease.
3. Pathophysiology of uremia.
4. Cardiovascular complications of chronic kidney disease.
5. Pathophysiology of cardiovascular diseases in chronic kidney disease.
6. Uremic cardiomyopathy.
7. Heart failure.
8. Ischemic heart disease.
9. Pericardial diseases.
10. Heart murmurs and valvular abnormalities.
11. Cardiac arrhythmias.
12. Echocardiography.

CHRONIC KIDNEY DISEASE:

The kidney has such considerable functional reserves that in healthy men reduction of renal mass by half cause no disturbances of clinical importance. However when renal mass is reduced further, excretion of waste products of metabolism cannot be achieved without their levels rising in serum and when sufficient nephron loss occurs, control of many physiological processes become inadequate and symptoms and abnormal physical signs results.

Chronic kidney disease is a pathophysiological process with multiple etiologies, 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 (dialysis or transplantation) in order to avoid life threatening uremia. Uremia is the clinical and laboratory syndrome, reflecting dysfunction of all organ systems as a result of untreated or undertreated chronic renal failure.

STAGES OF CHRONIC KIDNEY DISEASE[8].

A widely accepted international classification divides chronic kidney disease into a number of stages defined by clinical estimation of glomerular filtration rate.

STAGES OF CHRONIC KIDNEY DISEASE

Stage	Description	GFR in ml/min per 1.73 cm^2
	At increased risk	90(with CKD risk factors)
1	Kidney damage with normal or increased GFR	90
2	Kidney damage with mildly decreased GFR	60-89
3	Moderately decreased GFR	30-59
4	Severely decreased GFR	15-29
5	Renal failure	<15 (or dialysis)

PATHOPHYSIOLOGY OF UREMIA:

The finding that sera from patients with uremia exert toxic effects in a variety of biologic test systems has motivated a diligent search to identify the responsible toxins. The most likely candidates as toxins in uremia are the by

products of protein and amino acid metabolism. Unlike fats and carbohydrates, which are eventually metabolized to carbon dioxide and water, substances that are easily excreted even in uremic subjects in lungs and skin, the products of protein and amino acid metabolism depend largely on the kidneys for excretion. Urea represents some 80 percent or more of the total nitrogenous end products of protein metabolism and others include substances such as guanidine, methyl and dimethyl guanidine, Creatinine and guanidino succinic acid. As with urea, guanidines are derived at least in part from urea cycle.

Uremic symptoms correlate only in a rough and inconsistent way with the concentration of urea in blood. Urea may account for some of the clinical abnormalities including anorexia, malaise, vomiting, and headache. On the other hand, elevated levels of plasma guanidino succinic acid acts by interfering with the activation of platelet factor III by adenosine diphosphate, and contributes to the impaired platelet function seen in chronic kidney disease. Creatinine may cause adverse effects following conversion to metabolites such as methyl guanidine.

Nitrogenous compounds of larger molecular weight are also retained in chronic kidney disease. A toxic role for these substances has been suggested because of the impression that patients treated with intermittent peritoneal dialysis are less troubled with neuropathy than patients maintained on chronic hemodialysis, despite higher levels of urea and Creatinine in blood in the former group. Since the clearance of small molecules depends mainly on blood and

dialysate flow rates which are higher with hemodialysis, whereas clearance of larger molecules depend more on membrane surface area and time, which are greater with peritoneal dialysis this latter therapy may be more effective in removing substances of larger molecular weight.

The role of ‘middle molecules’ in the uremic syndrome remains speculative. Not all middle sized molecules accumulate in uremic plasma because of decreased renal excretion alone. The kidney normally catabolises a number of circulating plasma proteins and polypeptides, with reduced renal mass this capacity may be impaired greatly. Furthermore plasma levels of many polypeptide hormones (including parathyroid hormone, insulin, glucagon, growth hormone, leutinising hormone and prolactin) rise with chronic renal failure. Of these excessive parathyroid hormone may be important because of its adverse effects on several organ systems.

In chronic renal failure, compensatory and adaptive mechanisms remain within acceptable limits until the glomerular filtration rate is about 10-15 ml/min. The popular explanation for continuing function is the ‘intact nephron hypothesis’ which states that when most nephrons are non-functioning, the remaining few function normally and they produce an increased volume of filtrate and then tubules also respond by excreting fluid and solutes in amounts which maintain external balance.

CARDIOVASCULAR COMPLICATIONS OF END-STAGE RENAL DISEASE:

End-stage renal disease and cardiac disease seem to be inextricably linked. Approximately half of all deaths seen in end-stage renal disease patients are attributed to cardiovascular disease; this figure is remarkably similar throughout the world[9-14]. Cardiovascular disease is frequently present in patients starting end-stage renal disease therapy and undoubtedly contributes to the excessive cardiovascular morbidity and mortality seen in patients on renal replacement therapy. Pre clinical cardiovascular abnormalities are even commoner. Non-invasive studies, principally using echocardiography have consistently shown that upto 80 percent of patients starting on renal replacement therapy have structural or functional abnormalities of the left ventricle[3,15-18]. In the Canadian hemodialysis morbidity study, the annual incidence of myocardial infarction or angina requiring hospitalization was 10 percent per year[19]. A similar incidence was observed for pulmonary edema[19].

PATHOPHYSIOLOGY OF CARDIOVASCULAR DISEASES IN CHRONIC KIDNEY DISEASE:

In addition to traditional risk factors which are frequently present in patients with chronic kidney disease, there are few more risk factors specific to chronic kidney disease which contributes to the increased burden of cardiovascular diseases.

TRADITIONAL RISK FACTORS FOR CARDIOVASCULAR DISEASES

Hypertension	Older age
Diabetes mellitus	Male gender
High LDL	Physical inactivity
Low HDL	
Smoking	
Left ventricular hypertrophy	

CHRONIC KIDNEY DISEASE RELATED RISK FACTORS

SPECIFIC TO CKD	EMERGING RISK FACTORS
Blood pressure	↑ Homocysteine
Anemia	↑ Nitric oxide synthesis
Calcium phosphate	↑ Lipoprotein (a)
Sodium retention	↑ Insulin resistance
Hypervolemia	
Hypoalbuminemia	
Angiotensin II	
Aldosterone	
Depression and sleep disorders	

For every increase of systolic blood pressure by 5 mm of Hg and every 10 year rise in age, there is an increase in the risk of left ventricular hypertrophy by 11 and 25 percent respectively[20]. The male gender has an increased risk by 40 percent[20].

ANALYSIS OF RISK FACTORS:

1. HYPERTENSION:

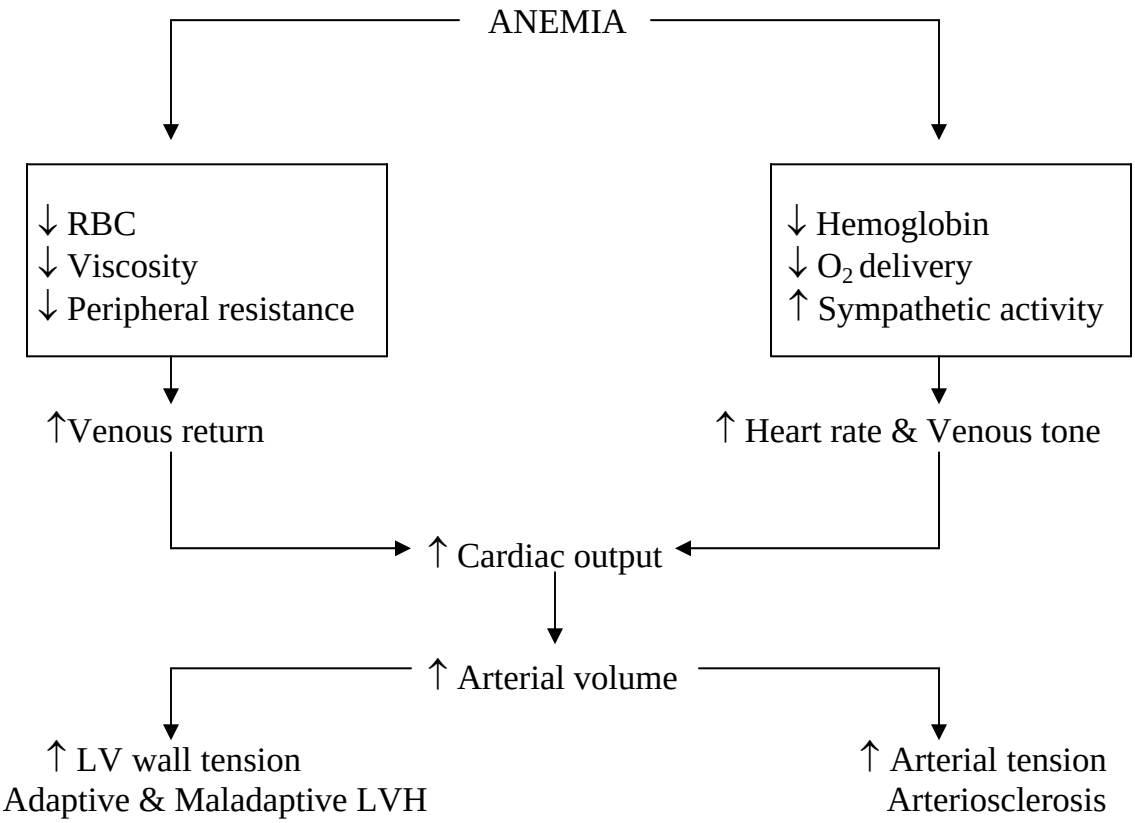
Hypertension is a strong predictor for left ventricular hypertrophy, cardiac dilatation, cardiac failure, ischemic heart disease and worsening of atherosclerosis. Blood pressure is an important determinant of left ventricular mass more so in uremics. There is a blunting of nocturnal dip in blood pressure in uremics. Whether the non-dipping leads to left ventricular hypertrophy or left ventricular hypertrophy is the cause of the blunted nocturnal dip, this puts the patients at higher risk for vascular disease[21]. Aggressive control of blood pressure reduces the rate of nephron loss in progressive renal impairment in the pre dialysis phase. It is not just hypertension; even hypotension is associated with increased cardiovascular morbidity and mortality. Impairment of cardiac perfusion during diastole particularly in the presence of left ventricular hypertrophy or decreased aortic compliance leads to ischemic myocardial damage. Increase in age, hypertension, increase in vessel wall calcium leads to stiff arteries which in turn leads to high systolic and low diastolic pressures. While high systolic blood pressure leads to increased myocardial work, low diastolic blood pressure impairs the myocardial circulation in diastole. For any given systolic pressure a greater

pulse pressure correlated with increased risk of death. A pulse pressure of greater than 50 mm of Hg carries a higher risk[22].

2. ANEMIA:

The kidney being main source of erythropoietin, anemia is apparently an integral part of advancing renal failure. Anemia exerts an independent effect on the cardiovascular system. For every 1 g/dl drop in mean hemoglobin, the risk of cardiac failure increases by 25%, echocardiographically demonstrable left ventricular hypertrophy by 42%, and risk of death increases by 14%[23]. Even moderate degree of anemia developing early in chronic renal disease, are associated with progressive cardiac enlargement.

PATHOGENESIS OF CARDIOVASCULAR DISEASE IN ANEMIA



1. CALCIUM, PHOSPHORUS AND PARATHORMONE IN CKD:

Progressive nephron loss is associated with phosphate retention and hypocalcemia. This triggers increased parathormone activity. Secondary hyperparathyroidism results in impaired calcitriol synthesis, increased skeletal resistance to parathormone, increased parathyroid cell hyperplasia, decreased expression of calcium receptors. These culminate in decreased cardiac contraction. Increased calcium phosphate product promotes metastatic calcification. Coronary artery calcification precipitates conduction defects, arrhythmias and myocardial fibrosis.

2. HYPOALBUMINEMIA – MALNUTRITION:

Hypoalbuminemia is emerging as a powerful risk factor for cardiovascular morbidity and mortality especially in hemodialysis patients. Malnutrition also can lead to low folate, B_{12} levels and low arginine intake leading further to hyperhomocysteinemia and impaired nitric oxide synthesis. Uremia is a state of chronic inflammation. Inflammation decreases albumin synthesis and increases albumin fractional catabolic rate.

3. ANGIOTENSIN II:

The renin angiotensin system is activated in most of the renal diseases especially in diabetics. Angiotensin II is not only a vasoactive peptide but also

a true cytokine that regulates cell growth, inflammation and fibrosis. Angiotensin II increases TNF-α production. It also upregulates other pro-inflammatory mediators like IL-6, NF-kB, etc. The various metalloproteinases induced by Angiotensin II leads to proliferation, migration and hypertrophy of vascular smooth muscles and promotes matrix expansion and fibrosis[24].

6. HYPERHOMOCYSTEINEMIA:

Homocysteine is a strong predictor of cardiovascular disease. It enhances vascular smooth muscle proliferation, increases platelet aggregation and acts on the coagulation cascade and fibrinolytic pathway directly inducing a prothrombotic environment. The proposed mechanisms of homocysteine toxicity are oxidative stress through production of oxygen species, binding to nitric oxide and production of homocysteinylated or acylated proteins.

7. LIPIDS:

Renal dyslipidemia is reflected in an abnormal apolipoprotein profile – reduced concentration of apo A containing lipoprotein in HDL and increased concentration of partially metabolized triglyceride rich apo B containing lipoprotein in VLDL, IDL and LDL. There is preferential rise in levels of IDL and small dense LDL. A significantly decreased apo A-II to apo C-II ratio is the hallmark of altered lipoprotein composition in renal disease. All of these factors promote accelerated atherosclerosis.

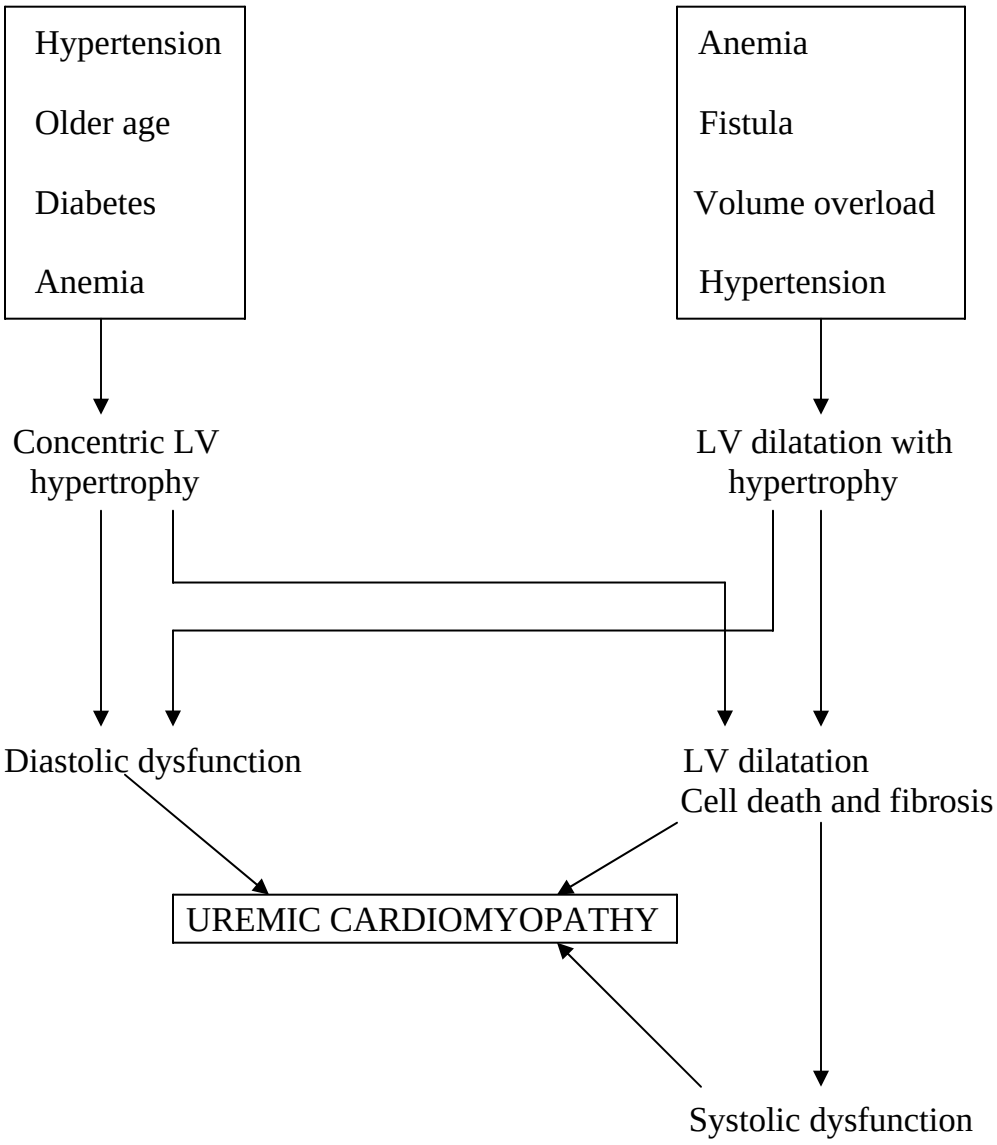
UREMIC CARDIOMYOPATHY:

ETIOLOGY:

Left ventricular hypertrophy can occur in response to both volume overload and pressure overload. Volume overload leads to proliferation of sarcomeres in series, with cardiac dilatation and augmented cardiac output, by the Frank-Starling mechanism[25]. In this situation to maintain wall tension Left ventricular hypertrophy occurs in accordance with Laplace's law (Tension= pressure x radius/2 x wall thickness). In situation of pressure overload, sarcomeres proliferate in parallel with existing sarcomeres, leading to wall thickening and increased cavity pressure[25]. This increased cavity pressure allows cardiac output to be maintained, but the trade-off is increased wall stiffness. Subjects with end stage renal disease are exposed to many factors leading to volume overload, such as anemia, arteriovenous connection and fluid overload[26]. They are also frequently exposed to factors that lead to pressure overload particularly hypertension.

The continuation of long term pressure and volume overload, with concomitant cardiac hypertrophy, is accompanied by a progressive, eventually lethal, growth abnormality that can be called as cardiomyopathy of overload[27]. Thus the adaptive hypertrophic response to both volume and pressure overload becomes maladaptive, particularly if cell death or cardiac fibrosis occurs.

ETIOLOGIC MECHANISMS OF UREMIC CARDIOMYOPATHY



In chronic uremia, not only is cardiac overload sustained, but other conditions that predispose to cell death occur. Hyperparathyroidism may cause left ventricular hypertrophy[28], but in chronic uremia it may be responsible for inadequate hypertrophy[29], cell death[30] and myocardial fibrosis. In addition

ischemia whether caused by large or small vessel disease also lead to cell death and fibrosis.

DIAGNOSIS:

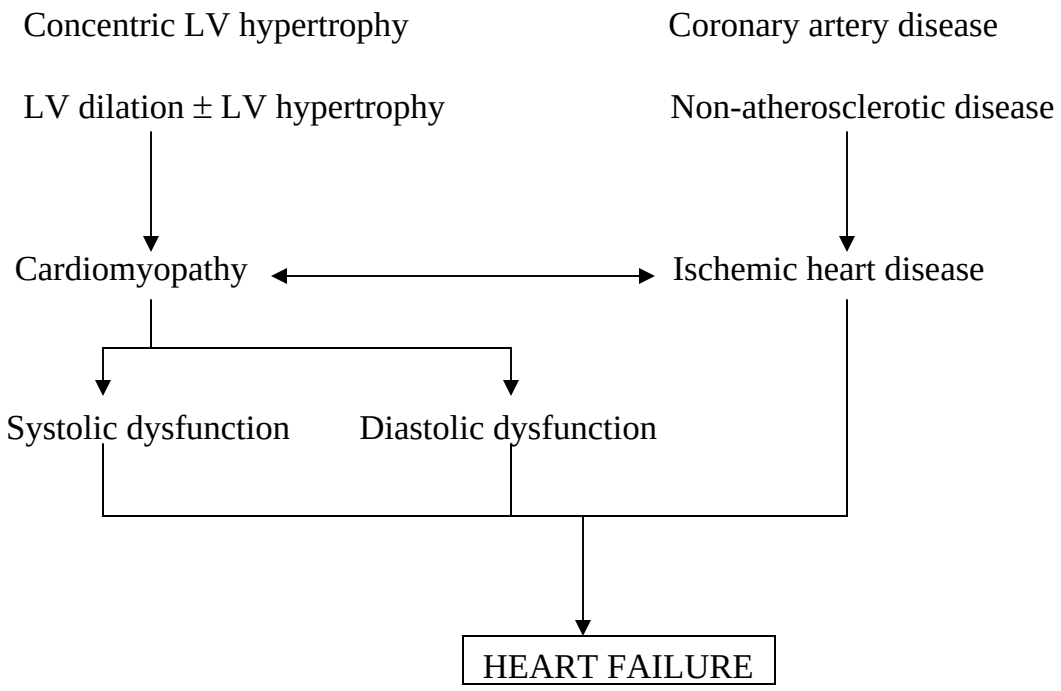
Echocardiography has been the most widely used non-invasive test in the general population because of accuracy, simplicity, lack of radiation and relatively low cost. Information on left ventricular mass, volume and contractility can be obtained, as well as assessment of regional wall abnormalities and valvular function. Aortic and mitral valve calcification has also been reported. Left ventricular mass measured by echocardiography is a strong predictor of cardiovascular morbidity.

In dialysis patients, M-mode echocardiography has been shown to have high reliability and validity[31]. Ventricular diameter, however increase with fluid reaccumulation following dialysis. This influences the LV mass index so that a high mass is calculated[32]. In practical terms, the impact of hypervolemia on the calculation of LV mass is small of the order of 9 g/m^2 for each litre of fluid accumulated.

HEART FAILURE IN CHRONIC KIDNEY DISEASE:

Heart failure may result from systolic or diastolic dysfunction, the latter occurring as a result of concentric or eccentric hypertrophy. Ischemic heart disease is an additional independent risk factor.

CARDIAC DISEASE PREDISPOSING TO HEART FAILURE IN CHRONIC UREMIA



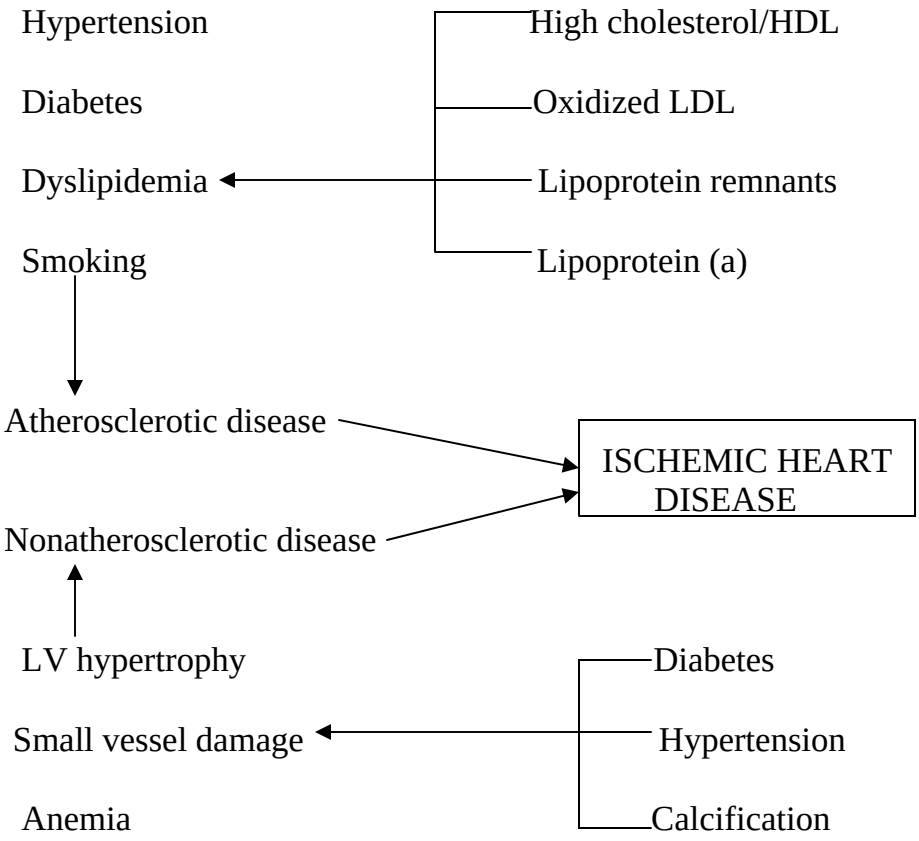
Among patients with diastolic dysfunction, congestive heart failure results from impaired ventricular relaxation which leads to an exaggerated increase in LV end diastolic pressure for a given increase in LV end diastolic volume. As ventricular volume increases, failure to have adequate hypertrophy leads to an increase in wall stress and increase in LV end diastolic pressure. This increase in LV end diastolic pressure leads to increased pulmonary capillary pressure and dyspnoea.

ISCHEMIC HEART DISEASE IN CKD:

ETIOLOGY

Symptomatic myocardial ischemia usually results from coronary artery disease, but it is nonatherosclerotic in origin in about a quarter of patients[33,34]. Disorders at several levels may contribute: large and medium size arterial disease , with luminal narrowing and inability to dilate when required; small vessel disease[35,36] and an inappropriately small density of capillaries relative to myocardial mass[37,38].

ETIOLOGIC MECHANISMS OF ISCHEMIC HEART DISEASE IN CHRONIC UREMIA



In the absence of critical coronary artery disease, ischemic symptoms may result from a reduction in coronary vasodilator reserve and altered myocardial oxygen delivery and use. The presence of left ventricular hypertrophy and anemia may predispose to nonatherosclerotic ischemia. As the demand for oxygen increases, the coronary vasculature dilates above basal, and a further increase in myocardial oxygen requirement may not be met with adequate increases in coronary flow, especially if there are pathologic changes in the large or small coronary vessels. In coronary artery stenosis, during hyperemia the relative flow progressively decreases when the degree of stenosis is above 40% and does not differ significantly from basal flow when the stenosis is 80% or greater.

Small vessel disease can occur in LV hypertrophy, diabetes and uremia. In LV hypertrophy, small vessel smooth muscle hypertrophy and endothelial abnormalities can diminish the coronary reserve. Diabetics may have abnormalities of small coronary arteries with endothelial proliferation, subendothelial fibrosis, exudative deposits of hyaline in the intima, and atheromatous thickening with cholesterol clefts.

A decrease in coronary reserve may result from small vessel calcification, the calcium x phosphorus product has been reported to be significantly elevated in symptomatic end stage renal disease without significant coronary artery disease, when compared to those with significant lesions.

The length density and surface density of capillaries in the heart of uremic rats were significantly more reduced than in rats with Goldblatt hypertension matched for LV weight and for blood pressure level[37]. Hyperparathyroidism plays a critical role in the genesis of impaired energy production, transfer and utilization by the myocardium[39].

DIAGNOSIS:

Ischemic heart disease is not a homogenous entity, especially in end stage renal failure patients. The following factors make the diagnosis of ischemic heart disease difficult.

1. Many patients have nonatherosclerotic ischemic heart disease, with typical symptoms of angina but patent coronary arteries.
2. It is also known that many end stage renal failure patients with advanced anatomic coronary artery disease are asymptomatic, without typical electrocardiographic changes.
3. The noninvasive tests used to diagnose cardiac diseases in the general population are problematic in dialysis patients.
4. Creatine phosphokinase, including its MB fraction, and lactate dehydrogenase levels are elevated in renal failure patients, which makes the diagnosis of acute myocardial infarction more difficult[40,41].

PERICARDIAL DISEASES:

Pericarditis is the consequence of an inflammation of the pericardium, the serous membrane enclosing the heart and the root of the great vessels. In azotemic patients pericarditis can be due to a number of causes including bacterial, viral or tubercular infections, diseases involving serous membranes such as systemic lupus erythematosus or some condition of azotemia itself. Pericarditis occurs in patients with both acute and chronic renal failure, with greater frequency in the latter. With the advent of dialysis therapy for the treatment of acute and chronic renal failure, the occurrence of chronic pericarditis has decreased.

In the azotemic patient, the pericarditis usually appears late in the uremic stage. It clears quickly when dialysis is started.

PATHOLOGY AND PATHOGENESIS:

Fibrinous aseptic inflammation is the hallmark of uremic pericarditis. Distribution of the inflammation can be diffuse or localized with areas of adhesion between the parietal and visceral layers of pericardium. An increase in vascularity occurs as the pericardial membranes thicken with movement between the layers, blood vessels are broken and causing

formation of a serosanguinous effusion loculated between adherent fibrous bands. The volume of effusion may grow if the time of inflammation is prolonged, the patient becomes edematous with intravascular movement of fluid into pleural, peritoneal and pericardial spaces or heparin is given for dialysis. Serious life threatening complications result from acute or chronic compression of heart, which causes a decrease in cardiac output. This can happen rapidly as a result of accumulation of fluid in a limited space (tamponade) or slowly from chronic thickening and scarring of the membrane (constriction).

Since pericarditis appears late in the course of renal failure and is reversed by dialysis, it can be assured that both the presence of dialyzate toxins and time of exposure have etiological roles. As with other signs or symptoms of uremia no single toxin has been implicated. Small molecules that clear rapidly with conventional dialysis may play a role, but larger molecules might also be involved.

SYMPTOMS AND SIGNS:

The first manifestation of pericarditis is usually chest pain. The patient will report substernal discomfort which is typically worse when lying down, alleviated when sitting up and leaning forward. This may be due to

the frequent posterior location of the pathological changes. On examination, a pericardial friction rub is usually noted. The rub is of two or three components timed with the heart cycle. The sound is scratchy or grating like rubbing two pieces of sand paper together. Low grade fever and leukocytosis may also be noted.

CLINICAL FEATURES OF UREMIC PERICARDITIS

SYMPTOMS:

- Chest pain
- Dyspnoea
- Orthostatic dizziness
- Decrease in urine output
- Rapid weight gain

SIGNS:

- Pericardial friction rub
- Fever
- Mental confusion

Edema, ascites, anasarca

Hypotension

Pulses paradoxus (tamponade)

LAB RESULTS:

Cardiomegaly on X-ray

Leukocytosis

Atrial arrhythmias

COMPLICATIONS:

Cardiac tamponade is the most serious, life threatening acute complication. Fluid accumulating in a poorly compliant compartment with thickened membranes leads to a decrease in cardiac output and hypotension. The neck veins are engorged. The heart is enlarged on percussion, cardiac sounds are muffled. A paradoxical pulse is often present.

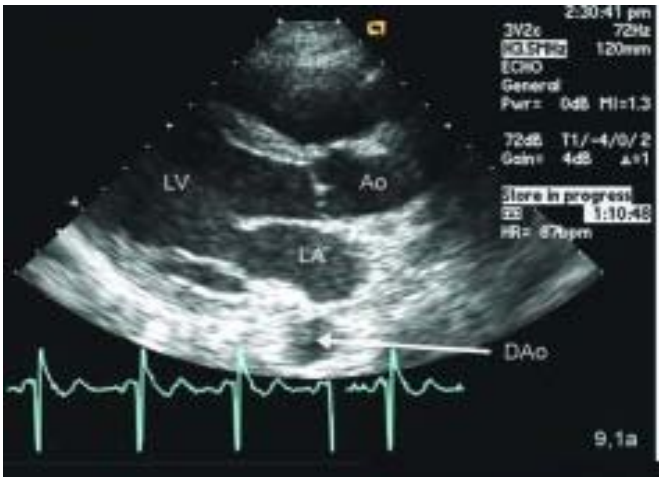
Long standing asymptomatic, subclinical pericarditis can lead to constriction of the heart as the pericardial membrane tightens. Uremia can re-activate tuberculosis, which can cause an indolent pericarditis, later manifesting with signs and symptoms of constriction.

DIAGNOSIS:

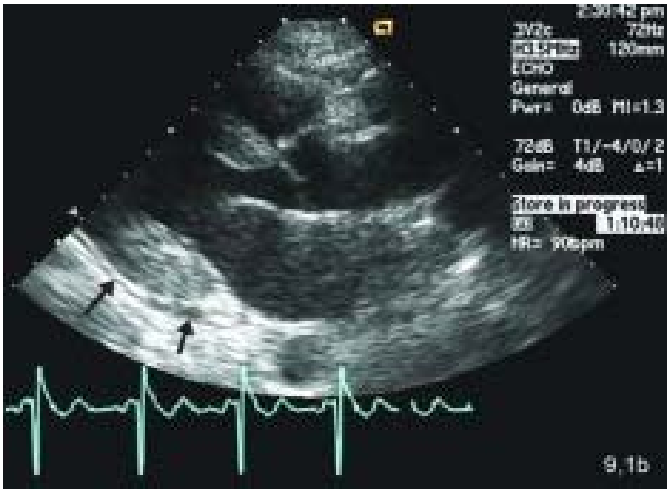
A triangular shaped, “water bottle”, heart may be noted by chest X-ray examination. Low voltage complexes in electrocardiograms are also typical of effusion. Echocardiography is the definitive diagnostic procedure for detecting fluid in pericardial space.

PARASTERNAL LONG-AXIS ECHOCARDIOGRAM SHOWING MINIMAL PERICARDIAL EFFUSION

RECORDED AT END-DIASTOLE



RECORDED AT END-SYSTOLE:

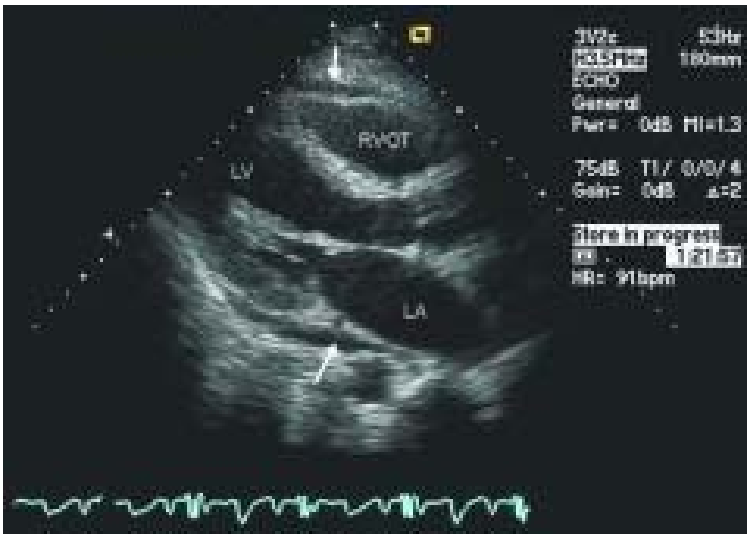


At end-systole, a mild pericardial effusion (*arrows*) is seen.

Ao-aorta; Dao-descending aorta; LA-left atrium; LV-left ventricle.

PARASTERNAL LONG-AXIS ECHOCARDIOGRAM

SHOWING MILD PERICARDIAL EFFUSION.

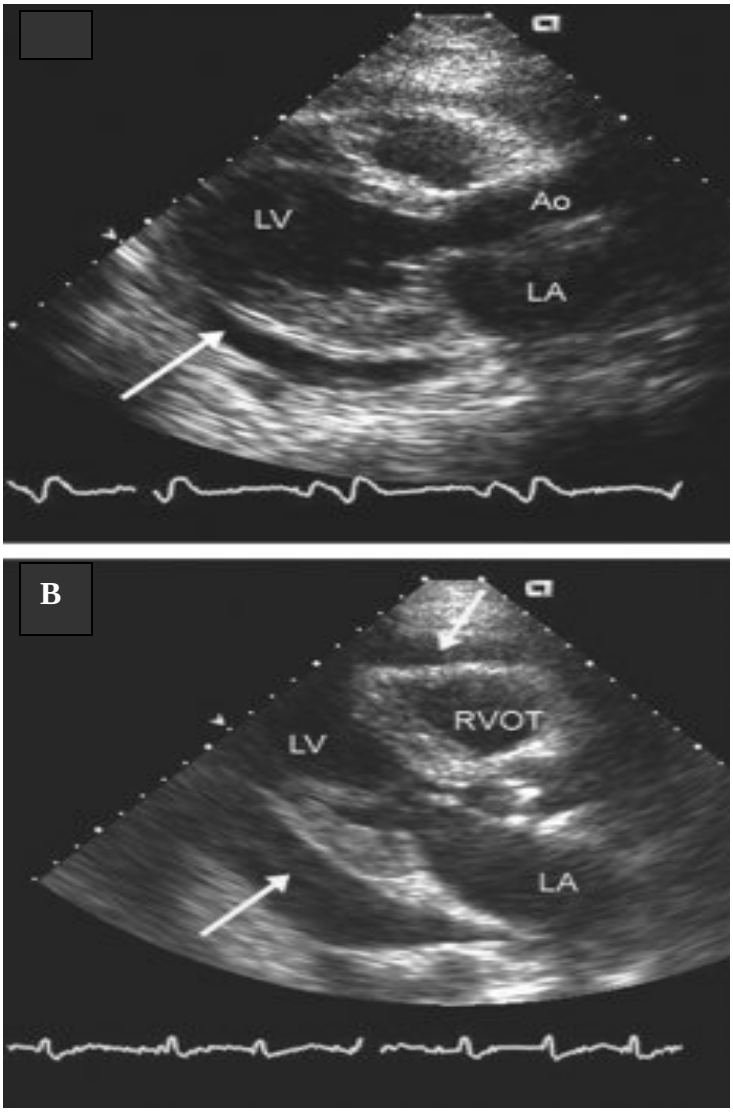


Echo-free space in the posterior interventricular groove (*arrow*).

A smaller anterior echo-free space (*downward-pointing arrow*).

LA-left atrium; LV-left ventricle; RVOT-right ventricular outflow tract.

PARASTERNAL LONG-AXIS ECHOCARDIOGRAMS SHOWING MILD (A) AND MODERATE TO LARGE (B) PERICARDIAL EFFUSION



A: Mild pericardial effusion.There is an approximately 1-cm space between the epicardium and pericardium (arrow).

B: A larger pericardial effusion is present both anteriorly and posteriorly (*arrows*).
Ao-aorta; LA-left atrium; LV-left ventricle; RVOT-right ventricular outflow tract.

HEART MURMURS AND VALVULAR ABNORMALITIES:

Heart murmurs and valvular abnormalities are common in chronic renal failure patients. Calcification of valves, infectious and non- infectious endocarditis can occur in patients with chronic renal failure. Heart murmurs may be present without obvious underlying valvular abnormalities and are probably evoked by anemia, hyper adrenergic tone and volume and pressure overload. Early diastolic murmurs of aortic or pulmonary regurgitation, generally related to pressure and volume overload, can appear during advanced stages of renal failure and often disappear following hemodialysis. Cervical venous hum can also occur in these patients.

CARDIAC ARRHYTHMIAS:

Cardiac arrhythmias because of their episodic nature makes identification and characterization difficult. Ventricular ectopic beats (couplets, non-sustained ventricular tachycardias) can occur. The frequency of ventricular ectopic beats appeared to vary directly with resting heart rate. The independent risk factors for the presence of Ventricular arrhythmias were, age over 55 years and left Ventricular dysfunction.

Factors contributing to the development of cardiac arrhythmias in patients with chronic renal failure include:

i) Underlying cardiac disease

ii) Left ventricular hypertrophy, left ventricular dysfunction.

iii) Coronary artery disease.

iv) Pericardial disease.

v) Cardiac calcification.

vi) Hemodialysis (rapid changes in serum electrolytes).

vii) Hyperadrenergic state.

viii) High calcium phosphorous product.

CARDIAC CHANGES AFTER RENAL TRANSPLANTATION:

Left ventricular systolic, diastolic volumes and ventricular mass decreases, ejection fraction increases after renal transplantation. There have been a number of reports documenting dramatic improvements in cardiac function in patients with severe dilated cardiomyopathy[42,43].

ECHOCARDIOGRAPHY

Echocardiography is one of the frequently used techniques for diagnosing cardiovascular diseases. It is so versatile, with clinical application in the entire spectrum of cardiovascular diseases. Echocardiography uses high frequency ultrasound to evaluate the structural, functional and hemodynamic states of cardiovascular diseases.

An echocardiographic examination begins with trans thoracic two dimensional (2D) scanning from four standard transducer positions: the parasternal, apical, subxiphoid and suprasternal windows. Quantitative measurements of cardiac dimensions, area and volume are derived from 2D images or 2D derived M-mode. In addition, 2D Echocardiography provides the framework for Doppler and color-flow imaging.

Doppler Echocardiography measures blood-flow velocities in the heart and great vessels and is based on the Doppler effect. The most common uses of Doppler Echocardiography are pulsed and continuous waveforms. Pulsed wave Doppler is used in determining peak-flow velocity, valvular pressure gradient, pressure half-time, dynamic left

ventricular outflow tract gradient, etc. Colour flow imaging based on Pulsed wave Doppler principles, displays intracavity blood flow in three colors (red, blue, green) or their combinations, depending on the velocity, direction and extent of turbulence. Tissue Doppler provides means for measuring and displaying cardiac wall motion velocities. Tissue Doppler is used to evaluate regional and global diastolic function and it has been noted that mitral annulus velocity measured by Tissue Doppler is an indicator of myocardial relaxation, relatively unaffected by preload or afterload.

MATERIALS AND METHODS

The study was conducted in patients with chronic kidney disease admitted in Stanley Medical College Hospital during the period August 2005 to September 2006.

INCLUSION CRITERIA:

The following criteria were used in selection of cases:

1) Patients who were known chronic kidney disease patients.
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 ultra sonogram with poor corticomedullary differentiation and type 2 or type 3 parenchymal changes. Patients with Autosomal Dominant Polycystic Kidney Disease and Obstructive Nephropathy were also included in the study though they did not have contracted kidney due to the underlying disorder.

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 above 50 years of age.
5) 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 edema, pallor were noted. Blood pressure was measured thrice and the average was taken. Cardiovascular examination was done. Complete hemogram, blood urea, serum creatinine, serum electrolytes, serum calcium, phosphorus and uric acid, serum lipid profile were measured. Patients were also subjected to abdominal ultra sonogram and chest X-ray.

Creatinine clearance had been 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 is multiplied by 0.85 for women.

Presence of cardiomegaly, pulmonary interstitial edema, pleural effusion were looked for in chest X-ray posteroanterior view. Evidence of left ventricular hypertrophy, low voltage complexes, ischemic changes were looked for in electrocardiogram.

Finally Echocardiography was done. The following parameters were looked for:

1) Chamber size:

In the 2D and M-mode echocardiography the measurements of the interventricular septum, left ventricular posterior wall thickness, left ventricular internal diameter was made in both systole and diastole. 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:

$$\text{Relative wall thickness} = \frac{\text{IVS(D) X LVPW(D)}}{\text{LVID(D)}}$$

Relative wall thickness > 0.45 cannot occur in physiologic hypertrophy and it signifies pathologic hypertrophy[44].

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 more than 3.8 cm represents dilated left atrium.

2) Systolic function:

The systolic function is assessed mainly by M-mode measurements. Ejection fraction and fractional shortening are the two parameters used. The Ejection fraction is defined as the ratio of stroke volume to end-diastolic volume.

$$\text{Ejection fraction} = \frac{\text{Enddiastolic volume - Endsystolic volume}}{\text{End diastolic volume}} \times 100$$

Normal values of Ejection fraction are 55 to 75 [45].

Grading of systolic dysfunction:

i) Mild 45 to 55 %.

ii) Moderate 35 to 45 %.

iii) Severe less than 35%.

Fractional shortening is calculated by the following equation:

$$\text{Fractional shortening} = \frac{\text{LVID(D)} - \text{LVID(S)}}{\text{LVID(D)}} \times 100$$

3) Diastolic function:

Diastolic function is 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. A (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 = irreversible restrictive pattern

4) Left ventricular wall motion abnormalities:

Left ventricular performance is assessed by many ways. Left ventricular wall is divided into a number of segments. Determining the motion of each segment provides the wall motion score.

5) 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.

6) Valvular abnormalities :

The valves were looked for stenotic lesions, regurgitant lesions, calcifications or vegetations.

OBSERVATION AND RESULTS

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

MALE	FEMALE	TOTAL
40(74%)	14(26%)	54

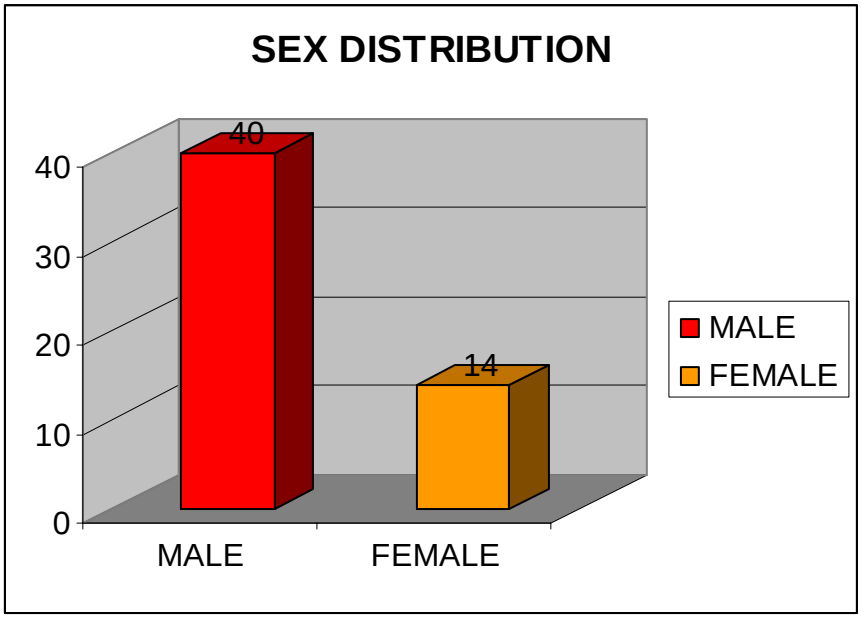
AGE DISTRIBUTION:

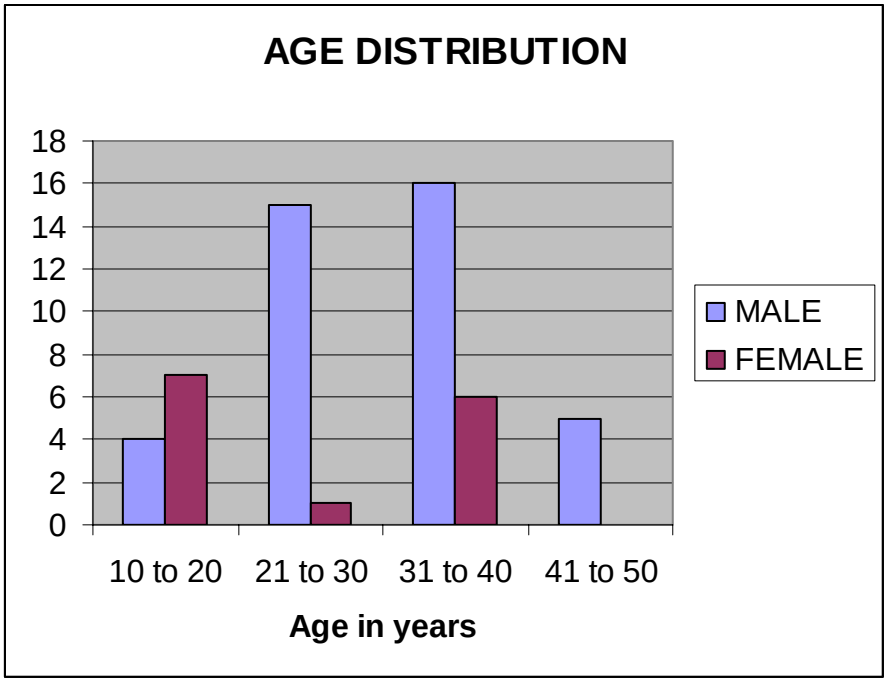
The age of the patients included in the study varied from 13 to 48 years.

Age	Male	Female	Total
10 to 20	4	7	11
21 to 30	15	1	16
31 to 40	16	6	22
41 to 50	5	0	5
	40	14	54

Mean age(males) – 31 years Mean age(females) – 26 years

Mean age(Total) – 30 years


SEX DISTRIBUTION
40
14
40
30
20
10
0
MALE
FEMALE
MALE
FEMALE


AGE DISTRIBUTION
18
16
14
12
10
8
6
4
2
0
10 to 20
21 to 30
31 to 40
41 to 50
Age in years
MALE
FEMALE

DURATION OF SYMPTOMS:

Duration of symptoms varied from 3 months to 3 years.

Duration	No. of patients
Less than 6 months	13(24.1%)
6 months to 1 year	22(40.7%)
More than 1 year	19(35.2%)

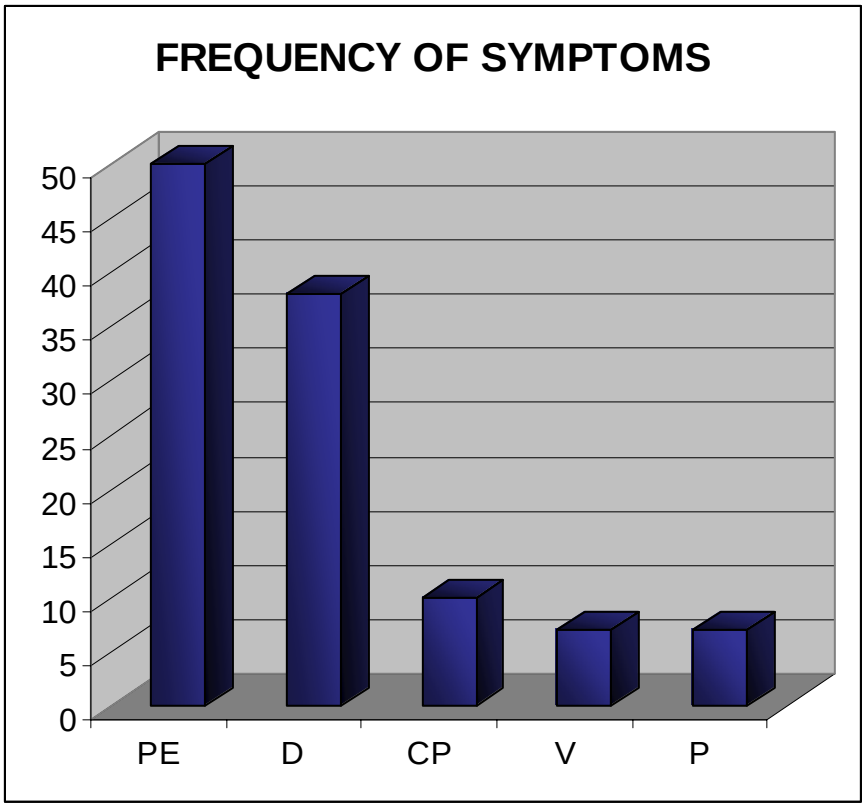
SYMPTOMS:

Easy fatiguability was present in all patients. Pedal edema and dyspnoea were the other common symptoms present.

Symptoms	No. of patients
Pedal edema	50(92.6%)
Dyspnoea	38(70.4%)
Chest pain	10(18.5%)
Palpitation	7(13%)
Vomiting	7(13%)

PALLOR:

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



PE - Pedal edema
D - Dyspnea
CP - Chest pain
V - Vomiting
P - Palpitation

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 mm of Hg and the diastolic BP from 80 to 116 mm of Hg. The mean systolic BP in both males and females was 152 mm of Hg. The mean diastolic BP was 94 mm of Hg in males and 93 mm of Hg in females.

Systolic BP	No. of patients
≤ 140	20(37%)
140 – 160	21(38.9%)
>160	13(24.1%)

Diastolic BP	No. of patients
≤ 90	32(59.2%)
90 - 110	21(38.9%)
>110	1(1.9%)

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.

HEMOGLOBIN:

Hemoglobin levels varied from 5 to 11 gm/dl, with the mean being 7.3 g/dl.

Hemoglobin(g/dl)	No. of patients
Less than 7	22(40.7%)
7 to 10	30(55.6%)
More than 10	2(3.7%)

CREATININE:

The range of Creatinine 3.5 to 16.5 mg/dl and the mean was 9.4 mg/dl.

Creatinine(mg/dl)	No. of patients
Less than 5	3(5.5%)
5 to 10	31(57.4%)
More than 10	20(37.1%)

CREATININE CLEARANCE:

Creatinine clearance varied from 7 to 27 ml/min, amd the mean value was 13 ml/min.

Creatinine clearance	No. of patients
Less than 15	37(68.5%)
15 to 30	17(31.5%)
More than 30	Nil

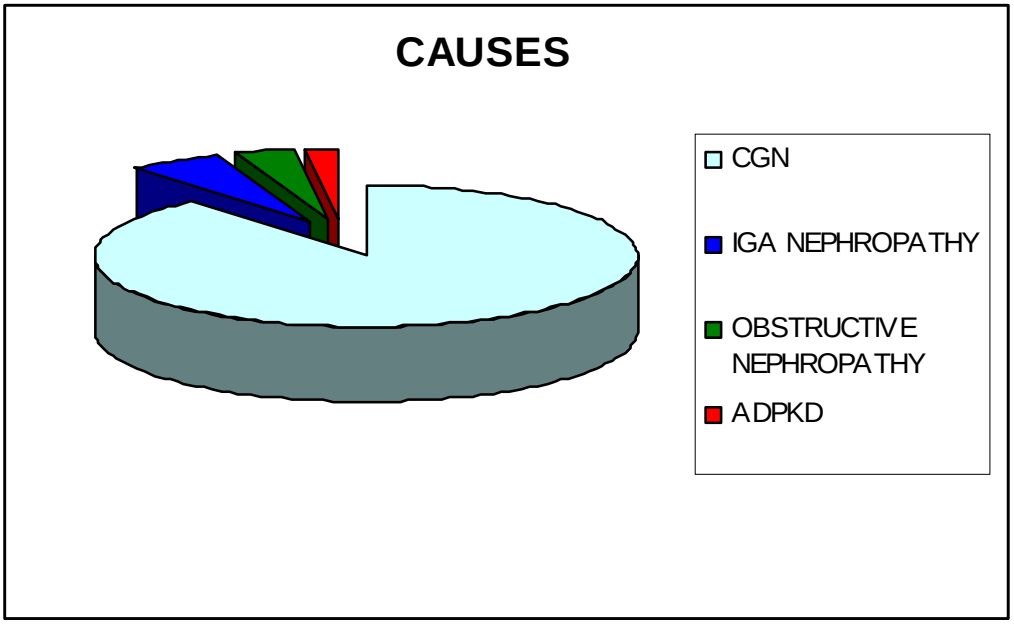
CAUSES:

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

Causes	No. of cases
CGN	48(88.9%)
IGA NEPHROPATHY	3(5.5%)
OBSTRUCTIVE NEPHROPATHY	2(3.7%)
ADPKD	1(1.9%)

CHEST X-RAY:

Normal	39(72.3%)
Cardiomegaly	12(22.2%)
Cardiomegaly with pulmonary interstitial edema	3(5.5%)


CAUSES
CGN
IGA NEPHROPATHY
OBSTRUCTIVE NEPHROPATHY
ADPKD

ELECTROCARDIOGRAPHY:

1. LVH with pressure overload pattern – 10(18.5%) cases.
2. Low voltage QRS complexes – 2(3.7%) cases.

ECHOCARDIOGRAPHIC ABNORMALITIES:

Pericardial effusion and concentric left ventricular hypertrophy were the most common abnormalities detected in echocardiography.

Pericardial effusion	25(46.3%)
Concentric LVH	24(44.4%)
Dilated LV	14(25.9%)
Dilated LA	4(7.4%)
Systolic dysfunction	11(20.4%)
Diastolic dysfunction	15(27.8%)
Normal	8(14.8%)

Systolic dysfunction - 11(20.4%)

Mild - 5

Moderate - 3

Severe - 3

Diastolic dysfunction - 15(27.8%)

Grade I - 11

Grade II - 4

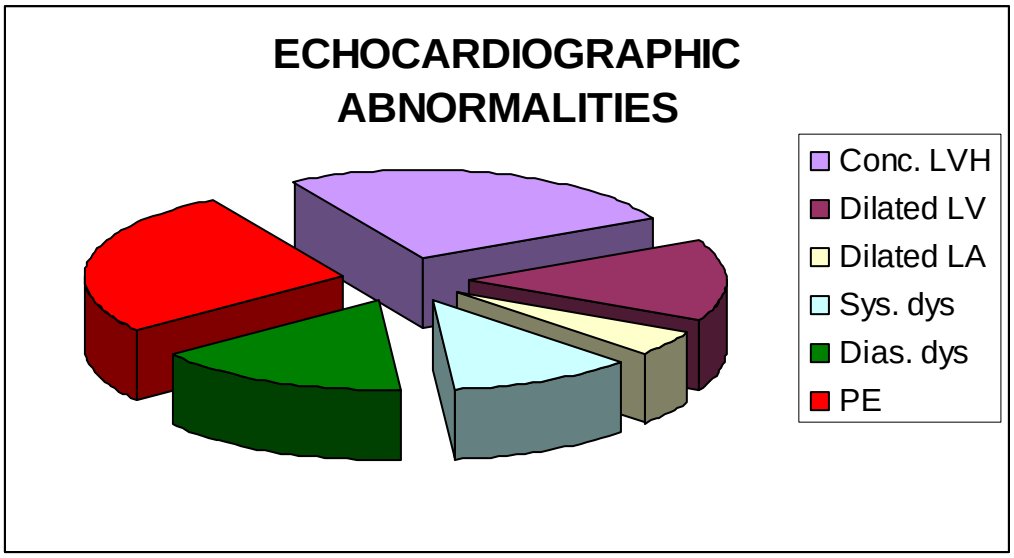
Other abnormalities:

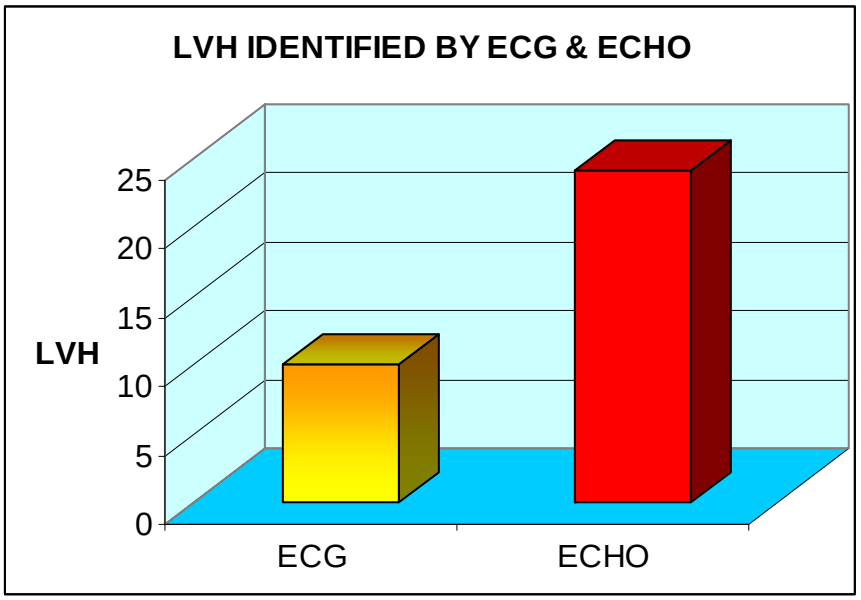
Aortic valvular calcification - 4

Moderate MR - 1

Mild MR - 7

MVPS(Incidental) - 1


ECHOCARDIOGRAPHIC ABNORMALITIES
Conc. LVH
Dilated LV
Dilated LA
Sys. dys
Dias. dys
PE


LVH IDENTIFIED BY ECG & ECHO
LVH
25
20
15
10
5
0
ECG
ECHO

DISCUSSION

The study included a total of 54 patients. Of these 54 patients, 40(74%) were males and 14 (26%) were females. The age of the patients varied from 13 to 48 years, with majority of patients falling within 31 to 40 years group. The mean age was 30 years, with mean age in males being 31years and in females being 26 years.

The duration of symptoms varied from 3 months to 3 years. 13(24.1%) patients had duration less than 6 months. 22(40.7%) patients had duration from 6 months to 1 year. Rest of the patients had duration more than 1 year.

Easy fatiguability was the most common symptom which was present in all the patients. The next common symptom was pedal edema. It was present in 50 patients. Dyspnoea on exertion was present in 38 patients. Dyspnoea may be due to anemia, 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 edema was present in 52 patients. The remaining 2 patients who did not have pedal edema presented with vomiting, dyspnoea, easy fatiguability to the general medical out patient department, and on investigations they were found to have elevated renal parameters and subsequent work up 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 mm of Hg and the mean diastolic BP was around 94 mm of Hg. About 39% of patients had moderate hypertension. One patient had severe hypertension. All the patients were receiving antihypertensives after admission during the study.

Examination of Cardiovascular System revealed the following findings.2 patients had apical impulse shifted down and out. 2 patients had pansystolic murmur in mitral area. 5 patients had ejection systolic murmur in the aortic area. Only 1 patient had pericardial rub. 2 patients had muffled heart sounds. Rest of the patients had normal cardiovascular findings on clinical examination.

The patients with shifted apical impulse had dilated left ventricle on Echocardiography. The patients with pansystolic murmur had moderate mitral regurgitation. The patients with ejection systolic murmur, was anemic and did not have any organic lesion in Echocardiography. The possible cause for this murmur

could be due to hyperdynamic circulation. 2 patients with muffled heart sounds had moderate pericardial effusion. 16 patients had bilateral fine crepitations in the base of lung fields. The remaining 38 patients had normal respiratory findings.

Almost all patients in the study had Hemoglobin less than 12 g/dl. The lowest value was 5 g/dl and the highest was 11g/dl. 22(40.7%) patients had severe anemia defined by Hemoglobin less than 7 g/dl. 30(55.6%) patients had Hemoglobin between 7 to 10 g/dl. Anemia is an independent risk factor for cardiac abnormalities. For every 1 g/dl drop in mean hemoglobin, risk of cardiac failure increases by 25%, Echocardiographically demonstrable left ventricular hypertrophy in 42% and the risk of death increases by 14%[23].

Urea and creatinine were elevated in all patients. Lowest creatinine was 3.5 mg/dl and highest was 16.5mg/dl. About 31(57.4%) patients had creatinine values ranging from 5 to 9 mg/dl and 20(37.1%) patients had creatinine value greater than 10 mg/dl. Creatinine clearance evaluated by Cockcroft Gault formula, varied from 7 to 27 ml/min. 37(68.5%) patients had Creatinine clearance less than 15 ml/min.

Analysis of the underlying primary diseases as the probable cause for chronic kidney disease revealed that chronic glomerulonephritis is the most common cause which was found in 48(88.9%) patients. 3 patients had biopsy proved IgA Nephropathy. 2 patients gave history suggestive of obstructive symptoms and found to have landed up in chronic kidney disease during follow up. One of the patients had bilateral abdominal masses, and ultrasound proved to

have Autosomal Dominant Polycystic Kidney Disease. Patients with diabetes and long standing hypertension were excluded from the study, which explains the high incidence of chronic glomerulonephritis as the cause in this study.

Chest X-Ray was normal in 39(72.3%) patients. Cardiomegaly was seen in 12(22.2%) patients. Cardiomegaly with pulmonary interstitial edema is seen in 3(5.5%) patients.

ECG showed evidence of Left ventricular hypertrophy with pressure overload pattern in 10 patients. The diagnosis of left ventricular hypertrophy in ECG was made by using Sokolow-Lyon criteria. Many patients had non-specific ST-T changes. 2 patients had low voltage complexes.

ECHOCARDIOGRAPHIC PROFILE

1. PERICARDIAL EFFUSION:

Pericardial effusion was found in 25(46.3%) cases. 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[46]. Gupta et al reported an incidence of 8.8% in patients on maintenance hemodialysis[47]. Mild pericardial effusion defined as echo free space less than 1 cm was found in 23 cases and moderate effusion defined as echo free space between 1 and 2 cm was found in 2 cases. Minimal pericardial effusion is normal and is defined when there is fluid in

the posterior atrioventricular groove and echo free space is seen only in systole[48]. 2 patients with moderate effusion had low voltage QRS complexes in ECG and cardiomegaly in chest X-Ray. About 5 patients in the study had no cardiac symptoms but proved to have pericardial effusion. 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.

2. CONCENTRIC LVH:

Concentric left ventricular hypertrophy is the second common abnormality detected next to pericardial effusion. It was found in 24(44.4%) patients. Patients with interventricular septal thickness more than 1.1 cm and the Relative wall thickness [RWT = PWD + IVSD / LVIDD], greater than 0.45 was taken as the criteria to diagnose concentric left ventricular hypertrophy. In a study done by Parfrey PS et al[5] 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[49]. Gruppen MP et al has reported LVH in 47% of male patients and 39% of female patients[50]. 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[51]. Lowering of cardiac size and increase in fractional shortening

were both associated with reduced subsequent likelihood of cardiac failure[51]. These associations were independent of baseline age, diabetes mellitus, ischemic 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 152mm of Hg (systolic) and 94 mm of Hg(diastolic). ECG showed concentric left ventricular hypertrophy with pressure overload type in 10(18.5%) patients. Echocardiography showed concentric left ventricular hypertrophy in 24(44.4%) patients. 3 of the 24 patients who had concentric left ventricular hypertrophy did not have cardiac symptoms. 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, anemia were the causes of concentric left ventricular hypertrophy in uremia[5]. Hyperparathyroidism can also cause left ventricular hypertrophy[28].

3. DILATED LEFT VENTRICLE:

Dilated left ventricle is defined as the left ventricular internal diameter in diastole more than 5.6cm. 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%[5]. Of the 14 patients with dilated left ventricle, 10 had

cardiomegaly and 2 patients had cardiomegaly and pulmonary interstitial edema on chest X-Ray. 4 out of 14 patients with dilated left ventricle had systolic dysfunction. The risk factors for dilated left ventricle, includes anemia, hypertension and hypoalbuminemia.

4. DILATED LEFT ATRIUM:

Dilated left atrium was present in 4 cases, out of which 3 had dilated left ventricle and systolic dysfunction.

5. 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%[5]. Mild systolic dysfunction was found in 5 patients. Moderate and severe systolic dysfunction accounted for each 3 patients respectively. 2 cases of Moderate dysfunction and 2 cases of severe dysfunction were found in the dilated left ventricular group. This shows that dilated left ventricle is an independent risk for systolic dysfunction. 2 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.

6. DIASTOLIC DYSFUNCTION:

Diastolic dysfunction was found in 15(27.8%) patients. Grade I diastolic dysfunction was found in 11 patients and grade II diastolic dysfunction was found in 4 patients. Of these 15 patients with diastolic dysfunction 8 patients had concentric left ventricular hypertrophy and 6 patients had dilated left ventricle.

7. OTHER ABNORMALITIES:

Aortic valve calcification was found in 4(7.5%) cases. 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. The low incidence of Aortic valve calcification in the study could be attributed to exclusion of persons above 50 years of age from the study. Raine.A.E.G, has reported an incidence of 28 to 55% of Aortic valve calcification in End-stage Renal Disease, with 3 to 13% having aortic stenosis[52].

Moderate mitral regurgitation was found in 1 patient and mild mitral regurgitation was found in 7 patients. Rest of the valvular abnormalities included trivial mitral regurgitation, trivial tricuspid regurgitation and trivial aortic regurgitation. 1 patient had mitral valve prolapse which is an incidental finding.

Results of this study done in Stanley Medical College Hospital (SMCH), Chennai and the study done by Parfrey et al., in Division of Nephrology, Salvation Army Grace General Hospital, Canada can be summarized as follows:

Parameters	Present Study	Parfrey et al.,[5]
Concentric LVH	44.4%	41%
Dilated LV	25.9%	28%
Systolic dysfunction	20.4%	16%
Normal	14.8%	16%

SUMMARY

- The study included a total of 54 patients with chronic kidney disease. There were 40 males and 14 females. Mean age was 30 years
- Pedal edema, dyspnoea and chest pain were the common symptoms. 75% had symptoms more than 6 months.
- Severe anemia 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

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.

BIBLIOGRAPHY

1. Mann JFE, et al. Cardiovascular risk in patients with mild renal insufficiency. *Kidney Int,* Vol 63 (Suppl 84) S192 – S196, 2003.
2. Foley RN, Parfrey PS, Hefferton D et al. Advance prediction of early death in patients starting maintenance hemodialysis. *Am J Kidney dis*, 23:836-845, 1994.
3. Foley RN, Parfrey PS, Harnett JD, et al. Clinical and echocardiographic disease in end stage renal disease therapy. *Kidney Int,* 47: 186-192, 1995.
4. Foley RN, Parfrey PS, Harnett JD, et al. The prognostic importance of left ventricular geometry in uremic cardiomyopathy. J *Am Soc Nephrol*, 5:2024-2031, 1995.
5. Parfrey PS, Foley RN, Harnett JD, et al: Outcome and risk factors for left ventricular disorders in chronic uremia. *Nephrol Dial Transplant,* 11: 1277-1285, 1996.
6. Parfrey PS, Foley RN, Harnett JD, et al: Outcome and risk factors for ischemic heart disease in chronic uremia. *Kidney Int,* 49: 1428-1434, 1996.
7. Harnett JD, Foley RN, Parfrey PS, et al: Congestive heart failure in dialysis patients: Prevalence, incidence, prognosis and risk factors. *Kidney Int,* 47: 884-890, 1995.

8. Levey AS, et al. National Kidney Foundation K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification and stratification. *Am J Kidney Dis*, 39(Suppl 1): S1, 2002.
9. Raine, A. E., et al. Report on management of renal failure in Europe, XXII. *Nephrol Dial Transplant*, 7(Suppl 2): 7, 1992.
10. El Reshaid K., et al. End stage renal disease and renal replacement therapy in Kuwait- epidemiological profile over the last $4^{1}/_{2}$ years. *Nephrol Dial Transplant*, 9: 532, 1994.
11. Murdochowicz G, et al. Causes of death in patients with end stage renal disease treated by dialysis in a center in Israel. *Isr J Med Sci*, 28:776, 1992.
12. Fernandez J.M, Carbonell M.E, Mazzucchi N., and Petrucelli D. Simultaneous analysis of morbidity and mortality factors in chronic hemodialysis patients. *Kidney Int*, 41: 1029, 1992.
13. Mailloux, L.U, et al. Mortality in dialysis patients: analysis of the causes of death. *Am J Kidney Dis*, 18: 326, 1991.
14. Viglino, G, et al. Ten years of continous ambulatory peritoneal dialysis. Analysis of patient and technique survival. *Perit Dial Int*, 13(Suppl 2): S175, 1993.
15. Hutting J, Kramer W, Schutterle G and Wizemann V. Analysis of left ventricular changes associated with chronic hemodialysis: A non-invasive follow up study. *Nephron* 49:284, 1998.

16. Parfrey PS, et al. The clinical course of left ventricular hypertrophy in dialysis patients. *Nephron* 55:114, 1990.
17. Morris KP, et al. Cardiac abnormalities in end stage renal failure and anemia. *Arch Dis Child*, 68: 637, 1993.
18. Greaves SC et al. Determinants of left ventricular hypertrophy and systolic dysfunction in chronic renal failure. *Am J Kidney Dis*, 24:768, 1994.
19. Churchill, DN, et al. Canadian hemodialysis morbidity study. *Am J Kidney Dis*, 19:214, 1992.
20. Levin A, et al. Left ventricular mass index increasing in early renal disease and impact of decline in hemoglobin. *Am J Kidney Dis*, 34 (I), 125-134, 1999.
21. Silverberg, et al. Impact of LVH on survival in end stage renal disease. *Kidney Int*, 36: 286-290, 1989.
22. Foley RN, et al. Impact of hypertension on cardiomyopathy, morbidity and mortality in end stage renal disease, *Kidney Int*, 49:1379-1385, 1996.
23. Metivier, et al. Pathophysiology of anemia and focus on the heart and blood vessels. *Nephrol Dial Transplant*, 15(Suppl 3) 14-18, 2000.
24. Ruiz Ortega M, et al. Angiotensin II regulates the synthesis of proinflammatory cytokine and chemokines in the kidney. *Kidney Int*, 62(Suppl): S12-S22, 2002.

25. Grossman, W, Jones, D and McLaurin, LP. Wall stress and patterns of hypertrophy in the human left ventricle. *J Clin Invest.* 56: 56, 1975.
26. London, GM, et al. Uremic cardiomyopathy: An inadequate left ventricular hypertrophy. *Kidney Int*. 31: 973, 1987.
27. Katz, AN. The Cardiomyopathy of overload: An unnatural growth response in the hypertrophied heart. *Ann Intern Med*, 121:262, 1994.
28. Stefenelli, T et al. Primary Hyperparathyroidism: Incidence of cardiac abnormalities and partial reversibility after successful parathyroidectomy. *Am J Med*, 95:197, 1993.
29. London, GM, et al. Secondary Hyperparathyroidism and cardiac hypertrophy in hemodialysis patients. *Kidney Int*. 32: 900, 1987.
30. Bogin, E. Massry, SG and Harary I. Effect of parathyroid hormone on rat heart cells. *J Clin Invest*, 67: 1215, 1981.
31. Harnett JD, et al. The reliabity and validity of echocardiographic measurement of left ventricular mass in hemodialysis patients. *Nephron*, 65: 212, 1993.
32. Levy, D et al. Echocardiographic criteria for left ventricular hypertrophy: The Framingham study. *Am J Cardiol*, 59: 956, 1987.
33. Roig, E et al. Disabling angina pectoris with normal coronary arteries in patients undergoing long term hemodialysis. *Am J Med*, 71: 431, 1981.

34. Rostand, SG, Kirk KA, and Rutsky EA. Dialysis associated ischemic heart disease: Insights from coronary angiography. *Kidney Int*, 25 :653, 1984.
35. Mosseri M, Yarom R, Gotsman MS and Hasin Y.Histologic evidence for small vessel coronary artery in patients with angina pectoris and patent large coronary arteries. *Circulation* 74: 964, 1986.
36. James TN. Morphologic characteristics and functional significance of focal fibromuscular dysplasia of small coronary arteries. *Am J Cardiol*, 65: 12G, 1990.
37. Amann K, et al. Reduced capillary density in the myocardium of uremic rats. A stereological study. *Kidney Int.* 42: 1079, 1992.
38. Rambusek M, Amann K, Mall G and Ritz E. Structural causes of cardiac dysfunction in uremia. *Ren Fail*, 15: 421, 1993.
39. Massry SG, Smogorzewski M. Mechanisms through which parathyroid hormone mediates its deleterious effects on organ function in uremia. *Semin Nephrol*, 14: 219, 1994.
40. Ma KW, et al. Serum Creatinine kinase MB isoenzyme activity in long term hemodialysis patients. *Arch Intern Med*, 141: 164, 1981.
41. Green TR, et al. Diagnostic value of creatinine kinase and creatine kinase MB isoenzyme in hemodialysis patients: A longitudinal study. *Clin Nephrol*, 25: 22, 1986.

42. Burt R, et al. Reversal of left ventricular dysfunction after renal transplantation. *Ann Intern Med,* 111:635, 1989.
43. Van Den Brook JH, Boxall JA and Thomson NM. Improved left ventricular function after renal transplantation. *Med J Aust*, 154: 279, 1991.
44. Feigenbaum. Evaluation of systolic and diastolic function of left ventricle. In Feigenbaum's Textbook of Echocardiography, 6th ed, p148, Lippincott Williams & Wilkins, Philadelphia, 2005.
45. Caroll JD, Hess OM. Assessment of normal and abnormal cardiac function. In Braunwald's Heart Disease, 7th ed, p495, Elsevier Saunders, Philadelphia, 2005.
46. Frommer JP, Young JB, Ayus JC. Asymptomatic pericardial effusion in uremic patients: Effect of long tem dialysis. *Nephron*, 39(4): 296-301, 1985.
47. Gupta Amit, Malhotra KK, Dash SC. Late pericarditis in patients on maintenance hemodialysis. *J Assoc Physicians India*, 34: 857-859. 1986.
48. Feigenbaum. Pericardial Diseases. In Feigenbaum's Textbook of Echocardiography, p250, 6th ed, Lippincott Williams & Wilkins, Philadelphia, 2005.
49. Dai Y, et al. Correlative factors of left ventricular hypertrophy in end stage renal disease. *J Tongji Med Univ*, 13(4): 252-256, 1993.

50. Gruppen MP, et al. Cardiac disease in young adult patients with end stage renal disease since childhood: A Dutch cohort Study. *Kidney Int.* 63, 1058 -1065, 2003.
51. Foley RN et al. Serial changes in echocardiographic parameters and cardiac failure in end stage renal disease. *J Am Soc Nephrol* 11: 912- 916, 2000.
52. Raine A.E.G. Acquired aortic stenosis in dialysis patients. *Nephron* 68: 159, 1994.

PROFORMA

NAME: RESIDENCE:

AGE:

SEX:

SOCIO-ECONOMIC STATUS: IP NO:

PRESENTING SYMPTOMS:

Duration of symptoms:

Dyspnoea Chest pain

Pedal edema Giddiness

Palpitation Syncope

Other symptoms

PAST HISTORY:

Hypertension Y/N Duration of hypertension:

Valvular heart disease Y/N

Coronary artery disease Y/N

NSAID use Y/N

Other drug intake:

Habit of smoking Y/N

If known CKD, duration of CKD:

EXAMINATION:

Pallor JVP

Pedal edema

CVS: RS:

Abdomen: CNS:

Fundoscopy:

PR: RR:

BP: 1. TEMP:
2.
3. BODY WEIGHT:

Mean BP:

INVESTIGATIONS:

1) Complete hemogram:

2) Urea:

3) Sr. Creatinine:

4) Creatinine clearance(Cockcroft-Gault):

5) Blood sugar:

6) Urine:

Albumin	Casts
Sugar	Culture
Deposits	24-HR protein

7) Sr. proteins:

8) Sr. cholesterol:

9) Sr. uric acid: 10) Liver function tests:

11) Sr. calcium:

12) Sr. Phosphorus: 13) Sr. Electrolytes:

14) USG abdomen:

15) Renal biopsy:

16) Chest X-Ray:

17) ECG:

18) **ECHOCARDIOGRAPHY:**

MEASUREMENTS:

IVS-S: EDV:

IVS-D: ESV:

LVID-S: SV:

LVID-D: EF:

LVPW-S: FS:

RWT:

Aorta: Left atrium:

CHAMBERS:

LA: RA:

LV: RV:

SEPTAE: CLOT:

LV WALL MOTION:

SYSTOLIC FUNCTION:

DIASTOLIC FUNCTION:

PERICARDIUM:

VALVES:

FINAL IMPRESSION OF ECHOCARDIOGRAPHY:

S,No	Name	Age	Sex	Dur of symp	Symptoms	Pallor	PE	JVP	CVS	RS	PR	BP	CAUSE	Hb	Urea	Cr.	Cr.cl	USG abd	C.X-ray	ECG
1	Manivannan	22	M	6 mon	PE	+	+	N	N	N	84	150/110	CGN	8.6	198	16.4	7	ck	N	N
2	Nagammal	35	F	2 yrs	D,PE,P	+	+	el	AI-down&out	Bas.creps	91	170/100	CGN	7.7	68	3.5	17	ck	Card, pul int ed	N
3	Kasirajan	26	M	11 mo	D,PE,	+	+	N	N	N	94	160/100	CGN	7.6	204	8.6	14	ck	N	LVH
4	Dhanalakshmi	38	F	14 mo	D,PE	+	+	N	N	N	82	160/94	CGN	8.6	168	13.8	7	ck	N	N
5	Habibullah	46	M	2yrs	D,PE,CP	+	+	el	N	Bas.creps	106	140/90	CGN	7.8	158	7.1	14	ck	N	N
6	Perumal	35	M	6 mo	PE,D	+	+	N	N	N	92	140/80	CGN	6.2	152	10.3	10	ck	N	N
7	Shankar	16	M	4 mo	D,PE,V	+	+	N	N	N	90	140/80	CGN	7	158	7.5	15	ck	N	LVH
8	Paul raj	40	M	3 Yrs	PE,P	+	+	el	ESM-AA	Bas.creps	86	170/90	ADPKD	6	166	8	15	ADPKD	N	N
9	Bhuvaneshwari	17	F	4 mo	PE	+	+	el	N	Bas.creps	84	160/90	CGN	7.6	152	6.6	14	ck	N	N
10	Munusamy	39	M	6 mo	D,PE,V	+	+	N	N	N	86	140/96	CGN	6.4	140	8	14	ck	Card	N
11	Chengamuthu	27	M	7 mo	PE	+	+	N	N	N	82	130/90	CGN	5.6	188	16.5	8	ck	N	N
12	Syed Mustafa	27	M	14 mo	CP,D,PE	+	+	N	N	Bas.creps	106	140/94	CGN	8.2	150	10.8	11	ck	Card	LVH
13	Vijay Kumar	28	M	7 mo	PE,D	+	+	N	ESM-AA	N	86	150/90	CGN	6.4	148	8.3	14	ck	N	N
14	Shafee	18	M	7 mo	PE,V	+	+	el	PSM-MA	Bas.creps	100	160/80	IgA Neph	8	187	12.7	9	ck,GR2 PC	Card ,pul int ed	N
15	Shanthi	37	F	1 Yr	PE,P,CP	+	+	el	N	Bas.creps	90	170/100	CGN	5	152	8.8	12	ck	Card	LVH
16	Abdul Salam	31	M	2 Yrs	D,PE	+	+	N	N	N	76	142/86	CGN	9.6	138	6	17	ck	N	N
17	Kumeresan	26	M	16 mo	PE	+	+	N	N	N	78	160/100	CGN	6	162	7.1	18	ck	N	N
18	Vallava Das	31	M	6 mo	PE,D,V	+	+	el	N	Bas.creps	112	160/90	CGN	7.7	188	9.4	11	ck	N	N
19	Raj Mohan	32	M	6 mo	PE,CP	+	+	N	N	N	80	160/90	CGN	7.8	178	8.2	16	ck	Card	LVH
20	Ramesh Kumar	19	M	5 mo	D,PE	+	+	N	N	N	82	130/90	CGN	7	180	9.2	12	ck	N	N
21	Kalai Selvi	33	F	9 mo	D,PE,V,CP	+	+	el	AI-down&out	Bas.creps	96	170/100	CGN	6.4	168	10.7	9	ck	Card	N
22	Dhayalan	37	M	4 mo	D,PE,P	+	+	el	PSM-MA	Bas.creps	80	190/100	CGN	7.6	147	6.2	20	ck	N	N
23	Sreenivasan	32	M	14 mo	D,PE	+	+	N	ESM-AA	N	102	150/96	Obs.Neph	5	148	6.5	19	ck,Ct	N	N
24	Ramesh	27	M	4 mo	D,CP	+	+	N	N	N	96	130/90	CGN	8	128	5.2	22	ck	N	LVH
25	Shiva kumar	26	M	1 Yr	PE,P	+	+	N	N	N	88	140/90	CGN	7.2	148	7.8	14	ck	N	N
26	Malini Devi	16	F	4 mo	PE,D	+	+	N	N	N	86	140/86	CGN	5.9	120	12.6	8	ck	N	N
27	Abdullah	36	M	13 mo	D,PE	+	+	N	N	N	70	170/116	CGN	9.8	178	15.1	7	ck	N	LVH
28	Narendran	24	M	6 mo	PE,CP	+	+	N	N	N	91	146/80	CGN	7.2	140	9.8	13	ck	N	N
29	Sundaram	30	M	8 mo	PE	+	+	el	N	Bas.creps	86	140/100	CGN	7.2	176	10.7	12	ck	Card	N
30	Karpagasumathy	19	F	5 mo	PE	+	+	N	N	N	84	140/90	CGN	8	130	11.3	8	ck	N	N
31	Lakshmipathy	25	M	2Yrs	PE,D	+	+	N	PR+	N	80	150/90	IgA Neph	6.6	150	8	16	ck,Gr 3 PC	N	N
32	Mahendran	20	M	7 mo	PE,D	+	+	el	HS muf	N	81	170/100	CGN	6	149	6.9	19	ck	Card	Low Vol
33	Loganathan	45	M	5 mo	PE	–	+	N	N	N	86	130/90	Obs.Neph	11	104	4.9	24	B.HUN,ct	N	N

S,No	Name	Age	Sex	Dur of symp	Symptoms	Pallor	PE	JVP	CVS	RS	PR	BP	CAUSE	Hb	Urea	Cr.	Cr.cl	USG abd	C.X-ray	ECG
34	Syed Mansoor	35	M	1 Yr	PE,D	+	+	el	N	Bas.creps	76	174/110	CGN	8	170	11	11	Ck	Card	N
35	Chella Muthu	36	M	2 Yrs	PE,D	+	+	N	N	N	84	170/100	CGN	6.4	188	13.5	9	Ck	N	N
36	Venkatesh	25	M	4 mo	D	+	+	N	N	N	70	140/90	CGN	8	160	9	14	Ck	N	N
37	Anbazhagan	41	M	6 mo	D,PE,CP	+	+	el	N	N	74	170/90	CGN	9.2	172	14.4	9	Ck	Card	N
38	Vijaya	40	F	6 mo	PE,D,P	+	+	N	N	N	74	140/86	CGN	7.4	156	8.1	11	Ck	N	LVH
39	Subramani	31	M	7 mo	PE,D	+	+	N	ESM-AA	N	84	160/110	CGN	6	102	4.8	27	Ck	N	N
40	Ganga	28	F	8 mo	PE,D	+	+	el	N	N	102	160/90	CGN	6	168	9.3	11	ck	N	N
41	Hassan Mohammed	26	M	18 mo	PE	+	+	N	N	N	86	160/110	CGN	8.8	160	8.2	15	ck	N	N
42	Ramalingam	48	M	1 Yr	PE,D	+	+	N	N	N	84	150/100	CGN	6	144	12.2	7	ck	N	N
43	Amjath Basha	22	M	1 Yr	PE,D	+	+	el	ESM-AA	Bas.creps	98	150/90	CGN	6	132	12.8	9	ck	Card,pul int ed	N
44	Arumugham	28	M	5 mo	PE,D	+	+	N	N	N	84	170/90	CGN	7.2	148	5.8	21	ck	N	N
45	Selvaraj	36	M	6 mo	D,PE,CP	+	+	N	N	N	102	140/90	CGN	6.5	186	15	8	ck	N	LVH
46	Mahizhan	31	M	3 mo	V	+	–	N	N	N	86	170/90	CGN	8.2	146	15.4	7	ck	N	N
47	Sangeetha	18	F	10 mo	D,PE	+	+	N	N	N	76	150/100	CGN	6.6	120	8.6	10	ck	Card	N
48	Ramachandran	40	M	4 mo	D,PE	+	+	N	N	N	86	140/90	CGN	6.8	180	12	10	ck	N	N
49	Hemavathy	16	F	3 mo	D,PE	+	+	N	N	N	82	130/90	IgA Neph	9	128	5.8	15	ck	N	N
50	Suresh	43	M	11 mo	PE,P	+	+	El	N	N	87	160/90	CGN	6.4	166	7.5	14	ck	N	N
51	Usha	13	F	6 mo	PE,D	+	+	El	HS muf	Bas.creps	72	140/90	CGN	7.8	168	10.9	8	ck	Card	Low Vol
52	Vijayalakshmi	36	F	9 mo	PE,D	+	+	El	N	Bas.creps	96	170/110	CGN	6.6	140	8.6	12	ck	Card	N
53	Jeyapriya	16	F	3 mo	V,D	–	–	N	N	N	84	130/84	CGN	10.8	128	8	10	ck	N	N
54	Gowri Shankar	34	M	1 Yr	PE,D,CP	+	+	El	N	Bas.creps	100	160/108	CGN	8.6	140	6.2	19	ck	N	LVH

PE - pedal edema
D – dyspnoea
CP – chest pain
P – palpitation
V – vomiting
CGN – chronic glomerulonephritis
Obs. Neph – obstructive nephropathy
IgA Neph – IgA nephropathy
Gr 2 PC – grade 2 parenchymal changes
Ck – contracted kidneys
Ct – cortical thinning
B.HUN – bilateral hydroureteronephrosis.
card – cardiomegaly
pul int ed – pulmonary interstitial edema
el – elevated
HS muf – heart sounds muffled
LVH – left ventricular hypertrophy
Low vol – low voltage complexes