A DISSERTATION ON

"PREDICTORS OF LEFT VENTRICULAR MASS IN CHRONIC KIDNEY DISEASE - eGFR AND PROTEINURIA"

A Dissertation Submitted to

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

CHENNAI

In partial fulfilment of the regulations

For the award of the Degree of

M.D. (GENERAL MEDICINE) - BRANCH – I

GOVERNMENT KILPAUK MEDICAL COLLEGE

CHENNAI

APRIL- 2014

BONAFIDE CERTIFICATE

This is to certify that the dissertation entitled **"eGFR AND PROTEINURIA – PREDICTORS OF LEFT VENTRICULAR MASS IN CHRONIC KIDNEY DISEASE"** is a bonafide work done by **Dr. M. JENIFER SINEKALATHA**, Post Graduate student, Department of General Medicine, Kilpauk Medical College, Chennai-10, under our able guidance and supervision in partial fulfilment of the Rules and Regulations of **The Tamilnadu Dr.M.G.R.Medical University** for the award of **M.D. Degree Branch I, (General Medicine)** during the Academic period from May 2011to April 2014.

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DECLARATION

I solemnly declare that the dissertation entitled "**eGFR AND PROTEINURIA – PREDICTORS OF LEFT VENTRICULAR MASS IN CHRONIC KIDNEY DISEASE"** is done by me at Kilpauk Medical College, Chennai – 10 during May 2011 to April 2014 under the able guidance and supervision of **Prof. Dr. K.T. JAYAKUMAR M.D.,** to be submitted to **The Tamilnadu Dr.M.G.R.Medical University** towards the partial fulfilment of requirements for the award of **M.D. DEGREE IN GENERAL MEDICINE BRANCH - I**

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ACKNOWLEDGEMENT

I sincerely thank **Prof. Dr. Ramakrishnan, M.D., DLO.** Dean, Kilpauk Medical College, Chennai for permitting me to utilize the facilities needed for this dissertation work.

I am extremely grateful to **Prof. Dr. N. Gunasekaran M.D., D.T.C.D.,** Director of Institute of Non Communicable Diseases, Superintendent of Government Royapettah Hospital, Professor and Head of the Department of Internal Medicine, Kilpauk Medical College for permitting me to carry out this study and for his constant encouragement and guidance.

I also express my sincere gratitude to **Prof. Dr. K.T.Jayakumar, M.D.,** my Unit Chief and Professor of Medicine for his guidance and constant support during the entire period of my study.

I am immensely thankful to Prof**. Dr. R. Sabarathinavel, M.D., Prof. Dr. S. Mayilvahanan, M.D., for** their help and guidance rendered during the entire period of my work.

I whole heartedly express my sincere thanks to **Prof. Dr. Venkataraman M.D., D.M.,** Professor and Head, Department of Nephrology, Government Royapettah Hospital, **Prof. Dr. M. Nandakumar, M.D., D.M.,** Professor and Head, Department of Cardiology, Government Royapettah Hospital, Chennai for their valuable guidance and support throughout my dissertation work.

I wish to thank **Dr. Manickam**, **M.D.,** Medical Registrar**, Dr. Shaik Sulaiman Meeran, M.D., Dr.Swarnalatha, M.D., Dr. Ramesh Kumar., M.D., Dr. Govindarajulu, M.D.,** Assistant Professors, Department of Medicine, Government Royapettah Hospital for their valuable suggestions and help rendered throughout this work.

I also extend my thanks to the Statistician and all the laboratory technicians for their valuable support throughout my dissertation work.

I also thank my parents, colleagues, friends and staff of our hospital for their support of this work.

Last but not the least, with sincere gratitude; I thank all the patients who contributed so much to this study without whom this study would not been possible.

CONTENTS

ABSTRACT

BACKGROUND

Chronic kidney disease is the growing epidemic of the 21st century. With the rising burden of diabetes and hypertension, chronic kidney disease is becoming rampant in our country. About 40 – 50% of the death in chronic kidney disease patients is attributed to cardiovascular causes. Individuals with the most severe form of chronic kidney disease have a risk for cardiac death 15 times higher than patients with preserved glomerular filtration rate. The two classical features of cardiac disease in end stage renal disease (ESRD) are atherosclerotic vascular disease and left ventricular hypertrophy. The prevalence of left ventricular hypertrophy is around 80% in a dialysis population. Multiple afterload and preload related factors act in the pathogenesis of this uremic cardiomyopathy, which once initiated, lead on to myocyte ischemia and myocardial fibrosis and eventually death. Hence if the risk factors which contributed to left ventricular hypertrophy in chronic kidney disease patients could be lined out, it would be possible to prevent and regress the left ventricular wall thickness. In our study, two variables glomerular filtration rate and the amount of proteinuria are used to predict the left ventricular mass index in chronic kidney disease.

AIMS AND OBJECTIVES:

1. To calculate the left ventricular mass index in CKD patients who are maintained on conservative medical management
2. To calculate the glomerular filtration rate of CKD patients using 24 hour creatinine clearance and Cockcroft Gault formula and the amount of proteinuria using urine spot PCR and 24 hour quantification.
3. To study whether there is a significant correlation between the amount of proteinuria and glomerular filtration rate to the left ventricular mass index.
4. To also correlate the association between other variables in chronic kidney disease and left ventricular mass index.

MATERIALS AND METHODS:

A total of 75 patients attending the Nephrology OP and admitted in the Nephrology ward satisfying the inclusion and exclusion criteria were included in the study over a period of 6 months. Blood samples and urine samples were drawn at the time of admission and in the Outpatient department for urine spot protein creatinine ratio calculation and renal function test. 24 hour urine collection was scrutinized and analysed for proteinuria quantification and creatinine clearance. Left ventricular mass was measured using 2D

Echocardiography. Devereux formula was used for the calculation of left ventricular mass index.

OBSERVATION AND RESULTS:

Among the variables studied **age and sex of the patient, prevalence of diabetes and hypertension in the study population, systolic blood pressure, diastolic blood pressure, serum albumin and hemoglobin, serum alkaline phosphatase, total cholesterol and serum triglycerides, blood urea of the patients in the study group** did not have a significant p value, suggesting that all these variables did not influence or predict the development of left ventricular hypertrophy in chronic kidney disease patients in our study.

The variables **duration of chronic kidney disease, serum creatinine, creatinine clearance (24 hour urine estimation, Cockcroft Gault equation, and MDRD equation), and urine spot PCR and 24 hour proteinuria** all had a significant p value demonstrating their predictive potential for left ventricular hypertrophy in chronic kidney disease.

Among the significant parameters, a statistically highly significant negative correlation was observed between declining GFR (Stage 4/5) and increased left ventricular mass index (p value < 0.001). Highly significant positive correlation was also observed with serum creatinine values and increased left ventricular mass (p value < 0.001). Regarding proteinuria, a

highly significant positive correlation was obtained between urine spot protein creatinine ratio, 24 hour urine protein and the left ventricular wall thickness (p value < 0.001). These parameters were found to be significant in both univariate and multivariate regression analysis.

CONCLUSION:

1. Glomerular filtration rate and the amount of proteinuria significantly influence the left ventricular wall thickness in chronic kidney disease patients.
2. Declining GFR had a strong negative correlation with left ventricular mass, where the amount of protein excreted positively predicted the significant risk of left ventricular hypertrophy in these patients.
3. These predictors of LV mass could be easily measured and are highly sensitive and specific for the same.
4. Hence routine measurement of these variables, and its correlation to left ventricular thickness could be easily ascertained compared to the costly investigations like cardiac MRI and Echocardiography.
5. On arriving at a suspicion of possible LV hypertrophy, rigorous measures to reduce protein excretion and frequent hemodialysis session could improve patients survival from the deadly cardiovascular diseases.

KEYWORDS:

Chronic kidney disease, left ventricular hypertrophy, left ventricular mass index, glomerular filtration rate, proteinuria, cardiovascular disease, Devereux formula

INTRODUCTION

INTRODUCTION

Chronic Kidney Disease is the burgeoning epidemic of the 21st century. This disease is a potential threat to our country, both economy wise and as well as proportion wise. More than 50 million people in the world are afflicted by kidney disease. There are more than 2 million people all over the world who needs either dialysis or renal transplant for sustaining their life. But this fraction represents a meagre 10% of the deserving [1]. The percentage of people in the early stages of disease, when the patient is a potential candidate for conservative management is around 11% of the adult population [2]. The population that meets the spiteful end of untreated renal failure because of unaffordability is around 1 million per year [1].

Looking into the risk factors, diabetes and hypertension top the rank list worldwide. With the rising burden of diabetes and hypertension, no wonder chronic kidney disease is becoming rampant in our country. The recent update of World Health Statistics in 2013 has proclaimed that one in three adults has hypertension and one in ten adults have diabetes worldwide [3]. Apart from the major risk factors mentioned, poverty and social deprivation are also of additional risk for developing chronic kidney disease in both developed and developing countries.

Talking about costs, the global economic impact of chronic Kidney Disease is tremendous. At one end, the Government spends in billions for improving the survival rate and at the other end; there is loss of productivity because of the life consuming disease. The Medicare expenditure of the CKD population has doubled over the past 10 years. In the developed countries, 3% of the health care budget every year is allocated for the management of chronic kidney disease and its complications [1]. Where as in the developing and the underdeveloped countries, it is a dream yet to come true, not afforded by the dying population.

The adverse outcome of chronic kidney disease includes kidney failure, complications due to decreased kidney function and cardiovascular diseases. About 40 – 50% of the death of CKD patients is attributed to cardiovascular causes [4]. In particular, increased left ventricular wall thickness is found to underlie this predisposition for cardio-renal syndrome. Individuals with the most severe form of chronic kidney disease have a risk for cardiac death 15 times higher than patients with preserved glomerular filtration rate [4][5].

Various studies done in kidney diseases suggest that early detection and treatment of CKD patients could prevent or at least delay these adverse outcomes [6].But the gruesome fact is CKD is often underdiagnosed and

undertreated, because of the lack of clear definitions and classification, unpredictable course of the disease progression.

But the increasing rate of morbidity and mortality of coronary artery disease in kidney disease make it necessary to develop further research in these populations. If the risk factors which contributed to left ventricular hypertrophy in chronic kidney disease patients could be lined out, it would be a lot easier to treat them[7][8].

Therefore it's high time now to check for the risk factors of left ventricular hypertrophy in end stage renal disease [9]. This study is designed using the variables, proteinuria and glomerular filtration rate to predict the left ventricular hypertrophy in chronic kidney disease patients. So that, the early prevention of massive proteinuria and progressive deterioration in glomerular filtration rate with drugs and dialysis could improve the cardiovascular health of chronic kidney disease patients and sustain their struggle to live [10].

AIMS AND OBJECTIVES

AIM OF THE STUDY

1. To calculate the left ventricular wall thickness in CKD patients who are maintained on conservative medical management.
2. To calculate the glomerular filtration rate of CKD patients using 24 hour creatinine clearance and Cockcroft Gault formula.
3. To calculate the left ventricular wall thickness in CKD patients who are maintained on conservative medical management.
4. To study whether there is a significant correlation between the amount of proteinuria and glomerular filtration rate to the left ventricular wall thickness in chronic kidney disease
5. And also to correlate the association between other variables and left ventricular hypertrophy in chronic kidney disease patients.

REVIEW OF LITERATURE

HISTORICAL PERSPECTIVE

The concept of chronic kidney disease and its treatment began in the history as early as the 100 AD. The Romans were the first nephrologists who made dialysis machines from their bath tub. The idea was to "sweat out" the building up urea and creatinine by soaking in the bath tubs [11]. Dr. Willem Kolff known today as "The Father of Dialysis" who created the first crude kidney machine in 1943 would have surely laughed at it [11]. From the first living-related kidney transplant done by Dr. Joseph E. Murray in 1954 to the world's first "triple swap" kidney transplantation done by surgeons at The Johns Hopkins Comprehensive Transplant Centre in February 2004, the field of nephrology has been ever growing [12].

INCIDENCE AND SIGNIFICANCE OF CKD

The incidence of chronic kidney disease and its most adverse outcome, end-stage renal disease (ESRD) are increasing now in multiples. This is due to the fact that the most common causes of CKD, hypertension and diabetes are also increasing by the minute [12]. So, the early identification and reduction of CKD population has become a matter of utmost importance.

THE RISE OF DIABETICS WORLDWIDE

The population plagued by diabetes exceeds 240 million all over the world. This fraction is expected to shoot up to 380 million largely by 2025[13]. The predisposing culprits include our unhealthy food practises and obesity, sedentary life and comforts of urbanization, growing and aging population. India followed by China, the United States, and Russia and Japan top the rank in diabetes worldwide. The bitter fact about this sweet disease is that more than half of the diseased people is unaware of their diagnosis and hence not treated. No wonder, around 40% of people with diabetes are assumed to develop CKD in the near future with the increased risk of cardiovascular diseases and other deadly complications of diabetes [13].

THE GROWING HYPERTENSIVE POPULATION

A major cause of CKD, a global health worry which is supposed to worsen all the more in the immediate future is hypertension. As the people in the world are getting older, so is the prevalence of hypertension and kidney disease. One million population all over the world suffer from high blood pressure and are projected to increase to 1.56 million by year 2025[13]. In developing regions like India, the prevalence of hypertension is 80% which is a threefold rise from that of the developed countries (24%)[13].

THE MAGNITUDE OF CHRONIC KIDNEY DISEASE PROBLEM

The CKD prevalence in India has been reported between 0.16% and 0.79% [14]. The studies were designed to detect stage 3 – 5 CKD and thus the real prevalence of CKD is higher than this. The ESRD incidence has been reported to be 160–232 per million populations (pmp) and the projected ESRD prevalence was 785–870 per million populations [14]. "Screening and Early Evaluation of Kidney Disease" (SEEK), a community-based voluntary health screening program was started in India in 2006 and tests serum creatinine and urine analysis. SEEK reported a17.4% of CKD in Indian population (using an abbreviated modified diet in renal disease (MDRD) formula, a glomerular filtration (GFR) estimation formula [14].

The chronic kidney diseases accounts for 60% of all deaths worldwide. Eighty percentages of these deaths worldwide occur in low- and middle-income countries. Globally, CKD is the 12th cause of death and the 17th cause of disability, respectively. In India, the projected number of deaths due to chronic disease was around 5.21 million in 2008. This death toll is presumed to increase by 2020 to 7.63 million which accounts for 66.7% of all deaths [14].

DEFINITION OF CHRONIC KIDNEY DISEASE

Chronic kidney disease is defined as either kidney damage or decreased kidney function (decreased GFR) for 3 or more months. According to KDOQI guidelines, definition of chronic kidney disease includes

1. "Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either pathological abnormalities; or markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR < 60 mL/min/1.73 m2 for ≥ 3 months, with or without kidney damage".

TABLE 1: CLASSIFICATION OF CKD BASED ON K/DOQI GUIDELINES:

STAGE	DESCRIPTION	GFR (mL/min/1.73 m^2)
1	Kidney damage with normal or ↑ GFR	≥ 90
2	Kidney damage with mild ↓ GFR	60 - 89
3	Moderate ↓ GFR	30 - 59
4	Severe ↓ GFR	15 - 29
5	Kidney failure	< 15 (or dialysis)

Table 1 shows the classification of chronic kidney disease into 5 stages based on glomerular filtration rate (K/DOQI Guidelines)

POTENTIAL RISK FACTORS IN THE PATHOGENESIS OF CKD [18]

These factors can be further classified based on their role in pathogenesis

FIGURE 1

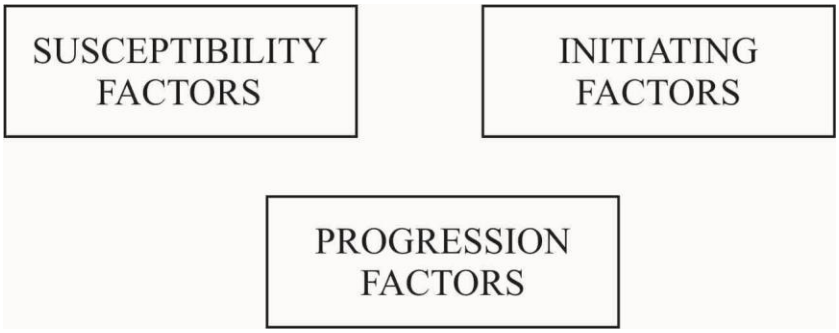


Figure 1 shows the three potential risk factors for developing chronic kidney disease. These factors play an important role in the pathogenic mechanism of chronic kidney damage.

SUSCEPTIBILITY FACTORS

These factors increase the susceptibility to kidney damage

1. Older age
2. Family history

INITIATION FACTORS

TABLE 2

Diabetes
Hypertension
Systemic infections
Urinary tract infections

Urinary stones
Recovery from acute renal injury
Reduction in renal mass
Autoimmune diseases
Neoplasia
Family history of chronic kidney disease
Exposure to certain drugs
Low birth weight

Table 2 lists the initiation factors which play a vital role in initiating kidney damage in chronic kidney disease.

Any of the above factors can initiate an injury/ damage to the kidney which acts as “the first hit” to the kidney.

PROGRESSION FACTORS

These factors cause worsening kidney damage and faster decline in kidney function after initiation of kidney damage

- Higher level of proteinuria
- Higher blood pressure level
- Poor glycaemic control in diabetes
- Smoking

PATHOPHYSIOLOGY

In chronic kidney disease, the pathologic process includes a double hit/ insult to the kidney:

(1) INITIATING MECHANISMS[15]

The aetiology of the initiating mechanism of injury to the kidney can be

- A genetically determined abnormality in kidney structure, development or function
- Inflammatory processes and deposition of immune complexes
- Exposure to toxins
- Diseases of the renal interstitium and tubules
-

(2) PROGRESSIVE MECHANISMS[15]

The common consequences that follow an insult/ injury to the kidney are as follows:

- Hyper filtration of remaining nephrons
- Hypertrophy of the viable nephrons

Increased activity of the renin-angiotensin axis in the kidney, due to the stimulation of transforming growth factor (TGF) causes the initial short term adaptations. The other factors responsible for this effect are vasoactive hormones, growth factors and cytokines.

FIGURE 2

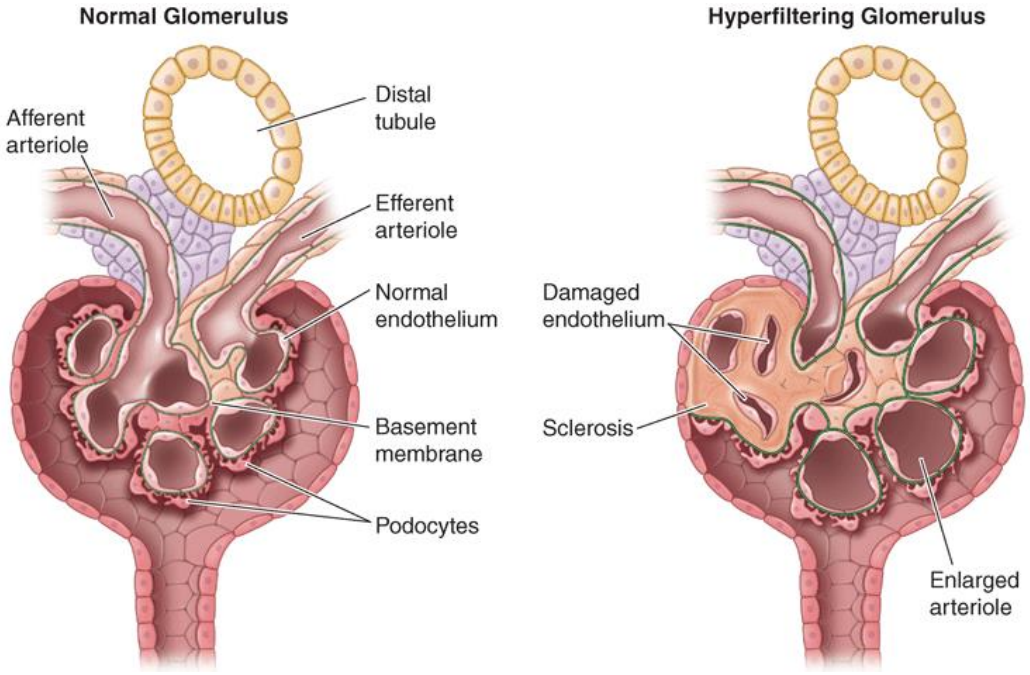


Figure 2 shows the secondary glomerular changes that occur following an insult to the kidney and reduction in nephron number. Focal adhesions and enlargement of capillary lumens are consequent to the hyper filtration and hypertrophy of the viable nephrons.

However, these short-term adaptations become ineffective as the increased pressure and flow causes destruction of glomerular architecture. There is sclerosis of the glomerular membrane and the remaining nephrons dropout [15]. This process explains the progressive decline in renal function following an isolated injury to the kidney.

CARDIOVASCULAR MORBIDITY IN CHRONIC KIDNEY DISEASE:

Cardiovascular disease is an important cause of morbidity and mortality in patients at every stage of CKD. The incremental risk of cardiovascular disease in those with CKD ranges from 10- to 200-fold based on the stage of CKD. As a result, most patients with CKD succumb to cardiovascular disease before ever reaching stage 5 CKD [16]. Thus, the focus of patient care in earlier CKD stages should be directed to prevention of cardiovascular complications

FIGURE 3

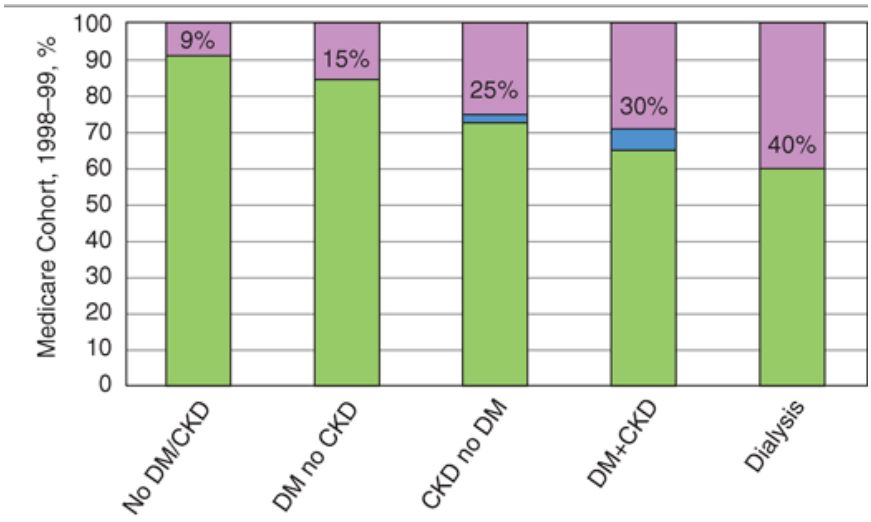


Figure 3 shows the increasing mortality rate as the stage of chronic kidney disease progresses. The patient has increased likelihood of dying rather than starting dialysis or reaching stage 5 chronic kidney disease.

RISK FACTORS OF CARDIOVASCULAR DISEASES IN CKD [4] [17]

The risk factors for cardiovascular disease in chronic kidney disease has been divided as clinical and socio demographic factors.

TABLE3

CLINICAL FACTORS
Diabetes
Hypertension
Autoimmune diseases
Neoplasia
Systemic infections
Reduction in renal mass

SOCIODEMOGRAPHIC FACTORS
Older age
Ethnicity
Exposure to chemical and environmental conditions
Low income and education

Table 3 lists the clinical and socio demographic risk factors for cardiovascular disease in chronic kidney disease.

These above factors act in concert, predispose and progress to early atherosclerosis and vascular damage thereby causing cardiovascular disease in the chronic kidney disease population as depicted in the chart below.

FIGURE 4

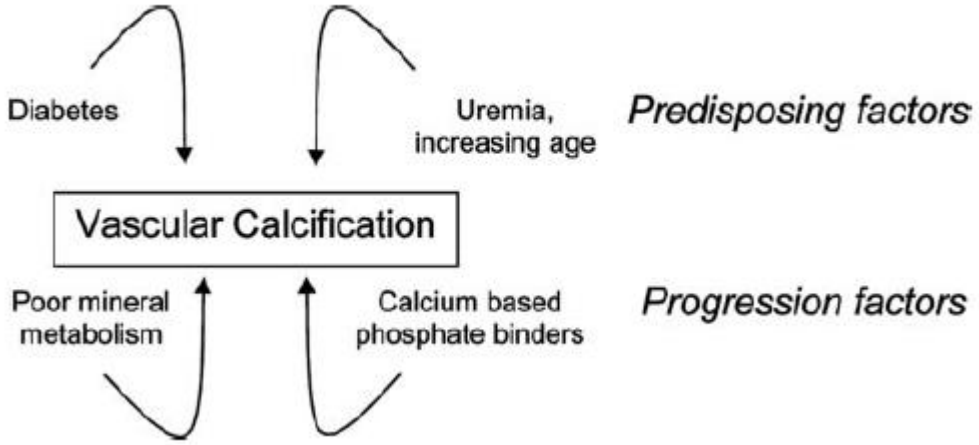


Figure 4 shows the predisposing and progression factors which leads to vascular calcification and hence cardiovascular disease in chronic kidney disease.

TRADITIONAL AND NON-TRADITIONAL RISK FACTORS:

The risk factors for coronary vascular disease in chronic kidney disease can be classified as traditional cardiovascular risk factors and non-traditional risk factors which are specific for the underlying predisposition [19].

The following table lists the traditional Vs. Chronic Kidney Disease-related factors potentially related to increased risk for Cardiovascular Disease

TABLE 4:

Traditional CVD Risk Factors
Older age
Male gender
White race
Hypertension
Elevated LDL cholesterol
Decreased HDL cholesterol
Diabetes mellitus
Tobacco use
Physical inactivity
Menopause
Psychosocial stress
Family history of CVD

TABLE 5:

CKD-Related (Non-traditional) CVD Risk Factors
Type (diagnosis) of CKD
Decreased GFR
Proteinuria
Renin-angiotensin system activity
Extra-cellular fluid volume overload
Abnormal calcium and phosphorus metabolism
Dyslipidaemia
Anaemia
Malnutrition
Inflammation
Infection
Thrombogenic factors
Oxidative stress
Elevated homocysteine
Uremic toxins

Table 4 lists the traditional risk factors for cardiovascular disease

Table 5 lists the non-traditional (CKD related) risk factors for the development of cardiovascular disease in chronic kidney disease

MECHANISM OF CARDIOVASCULAR DISEASE IN CKD

Cardiac disease in CKD patients is a growing pandemic of the century [20]. Many individuals with chronic kidney disease die early of cardiovascular morbidity even before they realise the impact of the disease [21] [22]. Coronary disease is diagnosed in 75% of adults who are started on dialysis [23].

FIGURE 5

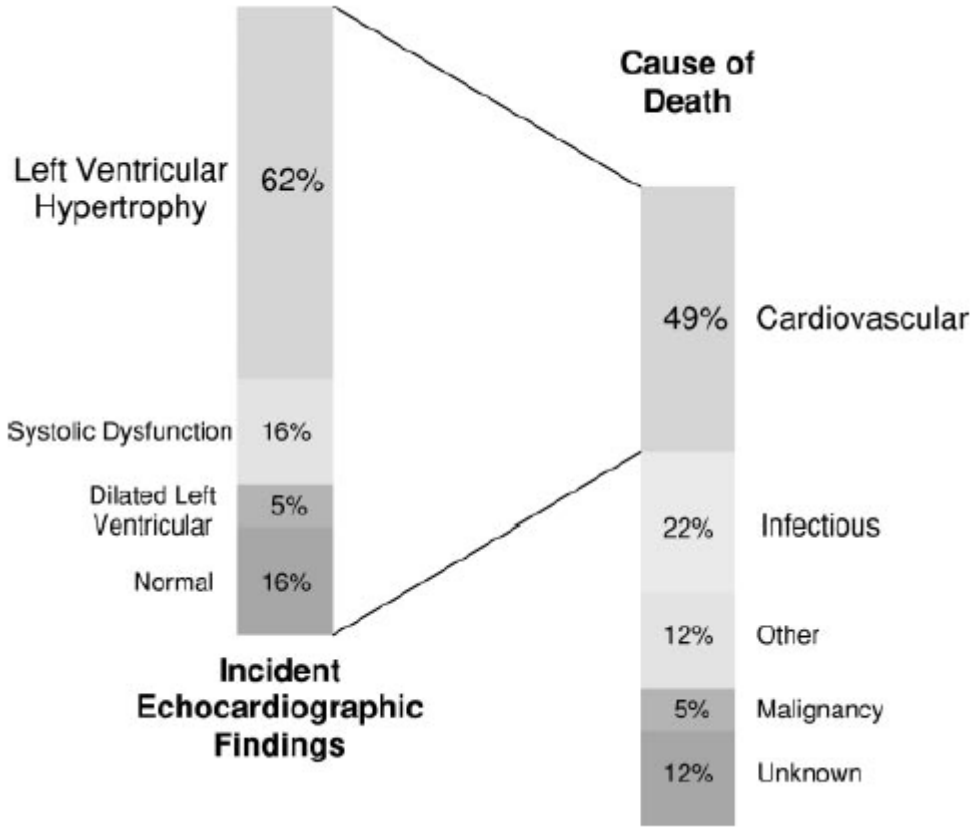


Figure 5 lists the causes of death in chronic kidney disease and the various cardiovascular mechanisms that culminate in the death of CKD patients.

The above chart shows the proportion of mortality due to cardiovascular causes in chronic kidney disease. Various abnormalities like left ventricular hypertrophy, systolic dysfunction, dilated ventricles are common [24]. But, the two classical features of cardiac disease in ESRD are atherosclerotic vascular disease and left ventricular hypertrophy [25].

Accelerated atherosclerosis in CKD patients progressed as GFR kept decreasing. The major increase for cardiac disease and death occurred when the GFR dropped below 60ml/min [26].

A second presentation of cardiac problem in CKD population is LVH (left ventricular hypertrophy) [27]. The prevalence of increased left ventricular thickness is approximately 80% in a dialysis population [28]. There is myocyte to arteriolar capillary mismatch in patients having left ventricular hypertrophy [29].

There are two types of left ventricular hypertrophy

- Eccentric
- Concentric

Volume overloading of the ventricles causes dropout of cardiac myocytes which causes eccentric hypertrophy. Hypertension and other causes of increased systemic vascular resistance cause concentric hypertrophy of the ventricles [30].

Diastolic dysfunction is the dominant LV physiology accompanying LVH [31]. This results in a sharp increase in LV diastolic pressure with modest

increments in LV volume. This physiology explains the lower threshold for pulmonary edema under these circumstances. Patients with LVH also often have a reduction in systolic function and this exposes the patient to the risk of sudden cardiovascular death [32].

At the extreme edge of the cardiac diseases, cardiac arrthymias and sudden cardiac death [33] are more common in the elderly people.

TABLE 6

MECHANSIMS OF SUDDEN CARDIAC DEATH IN CHRONIC KIDNEY DISEASE
Changes in the coronary microcirculation
Impaired coronary reserve
Reduced cardiac compliance
Increased activity of sympathetic nervous system
Increased concentration of Angiotensin II
Dense myocardial fibrosis
Changes in the concentration of electrolytes during dialysis

Table 6 mentions the various mechanisms responsible for sudden cardiac death in chronic kidney disease.

LEFT VENTRICULAR HYPERTROPHY [34]

Increased LV wall thickness known as LVH is a significant cause of heart disease in ESRD populations. LVH alters the mechanics of the myocardium, thereby altering the contractile mechanism and resulting in hypoxia of the heart itself, at the end predisposing to cardiac arrhythmia, diastolic dysfunction and progressing to overt heart failure.

UREMIC CARDIOMYOPATHY [34]

The influence of impaired renal failure on cardiac function is better known by the term Uremic cardiomyopathy. Cardiac hypertrophy is the signature manifestation of this uremic cardiomyopathy. Although this may be due to excess serum levels of urea, impaired GFR levels of even as little as 50% increased the cardiovascular mortality to 5 fold [25]. The exact pathogenesis of increased ventricular wall thickness remains uncertain.

PATHOPHYSIOLOGY OF LVH [35]:

The pathogenesis and causes of LVH/ CAD in ESRD is complicated due to the fact that there are independent risk factors complicating both cardiac disease and chronic kidney disease like diabetes, hypertension and high oxidant stress [36].

The pathophysiology of LVH in CKD is dealt under three headings

1. Afterload related[37] [38]
    - Systemic arterial resistance[39]
    - Increased systolic blood pressure[40]
    - Increased diastolic blood pressure[40]
    - Large vessel compliance (aortic calcification)[41] [42]
2. Preload related[43]
    - Expansion of LV volume (salt/ fluid loading)[44]
    - Anaemia [45]
    - Large flow arteriovenous fistula[46]
3. Neither afterload nor preload related

AFTERLOAD RELATED FACTORS

One hypothesis suggested pressure overload as a cause of cardiac hypertrophy due to the prevalence of increased blood pressure in patients with chronic kidney disease [47]. However experimental correction of high blood pressure in lab rats with renal injury did not stop the progression of left ventricular hypertrophy. In human studies, cardiac hypertrophy occurred in kidney disease patients even after the control of blood pressure [48] [49]. The following are the proposed hypothesis:

1. High calcium phosphorus product present in CKD reduces the aortic compliance. This increases the stress on the left ventricle causing increased afterload [51] [52].
2. Vasoactive peptides (Endothelin/ Angiotensin II) are elevated in the serum acting as potent vasoconstrictors. These peptides also exacerbate coronary vessels vasoconstriction.
3. Fetuin A is the recently proposed factor to play a major role in the calcification scheme. It is supposed to increase the mineralization of vascular smooth muscle [53].
4. In diabetic nephropathy, a blood pressure-independent increase in LV mass index occurs. In those receiving conventional dialysis, both medication and dialytic therapy successfully reduce ventricular mass and these treatments are effective even in normotensive patients [54] [55].
5. The important signal transduction molecules responsible for left ventricular hypertrophy are
    a. endothelin 1 (ET 1)
    b. parathormone (PTH)[56]
    c. tumour necrosis factor-alpha (TNF α)
    d. leptin
    e. interleukin 1 alpha (IL 1α)
    f. interleukin 6 (IL 6)[57]

The above said conditions basically cause activation of intracardiac renin-angiotensinogen system which causes myocardial cell thickening and concentric left ventricular remodelling. There is also increased oxidative stress and xanthine oxidase activation predisposing to LVH [58] [59].

PRELOAD RELATED FACTORS:

Another potential cause of uremic cardiomyopathy is volume overload which triggers LVH by increasing its left ventricular end diastolic pressure [60].These conditions predispose to lengthening of the myocardial cell and eccentric hypertrophy. Thus, both the above factors act synergistically to produce cardiovascular morbidity in ESRD [61].

FIGURE 6

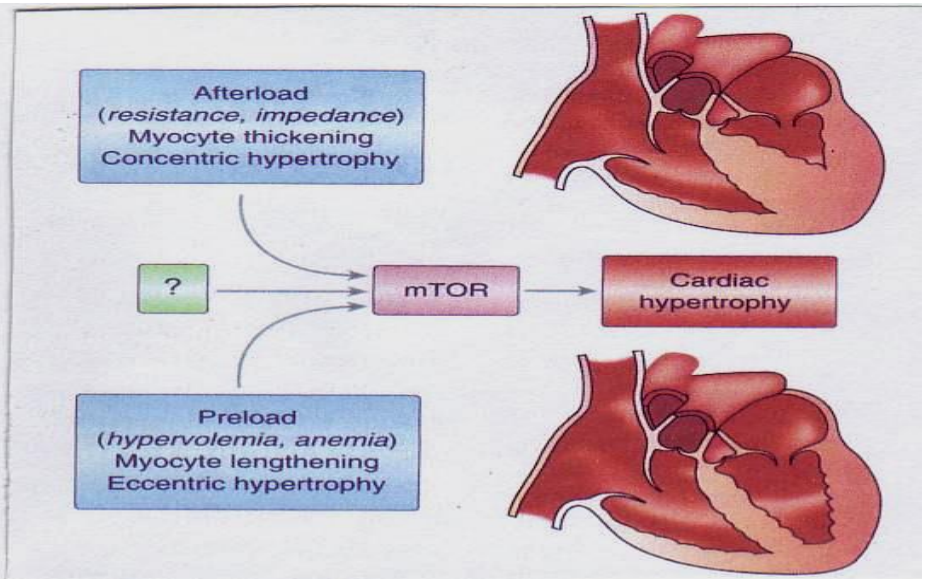


Figure 6 shows the preload and afterload factors which contribute to the process of cardiac hypertrophy.

OTHER MISCELLANEOUS FACTORS

1. Hyperhomocystinaemia [62]

Increased serum homocyteine levels are associated with left ventricular thickness in chronic kidney disease.

2. Vitamin D deficiency

Due to the lack of active Vitamin D in chronic kidney disease, renin angiotensin system is activated which causes secondary hyperparathyroidism. This further leads to the development of hypertrophy of the ventricles and accelerated systemic hypertension.Studies done in the past show significant regression of left ventricular mass following treatment with active vitamin D supplements in end stage renal disease patients.

3. Activation of mTOR[23]

This is described in detail in the molecular mechanism of left ventricular hypertrophy.

4. Renin Angiotensinogen system[63]

Increased levels of angiotensin II causes hypertrophy of the cardiac myocytes probably through myocardial stretch irrespective of the blood pressure level.

5. Phosphate levels

Higher phosphate loads are associated with vascular calcification and increased aortic impedance which contribute to the left ventricular hypertrophy in chronic kidney disease.

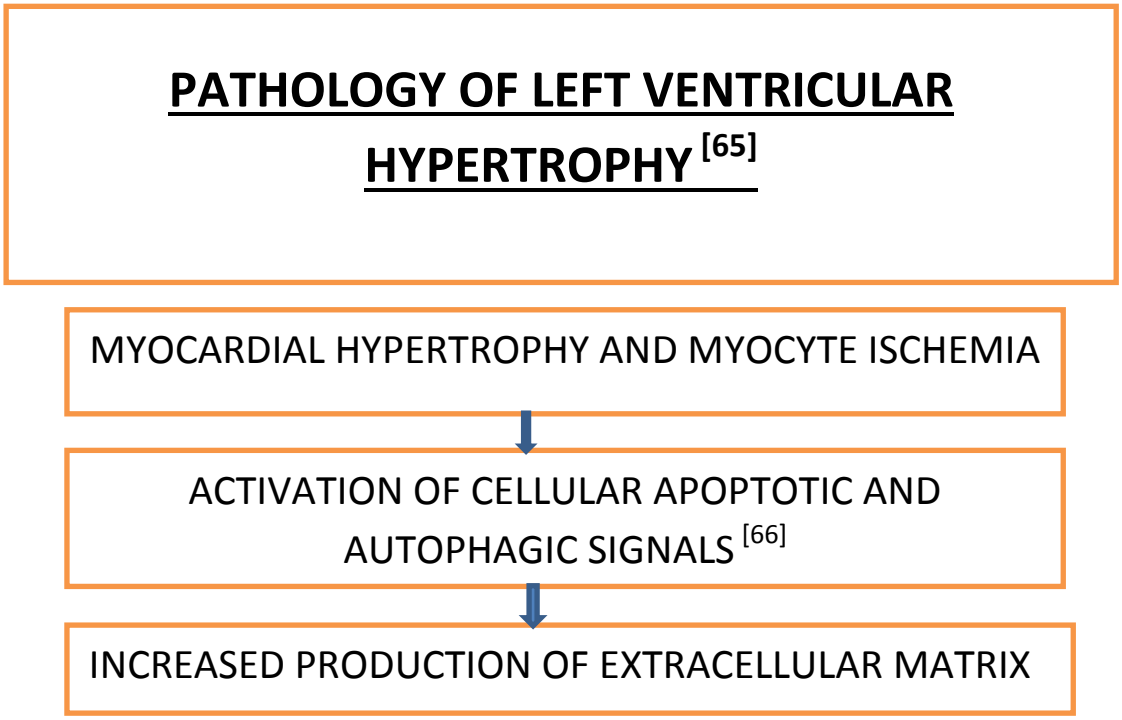
6. **Markedly elevated Parathormone levels[64]**

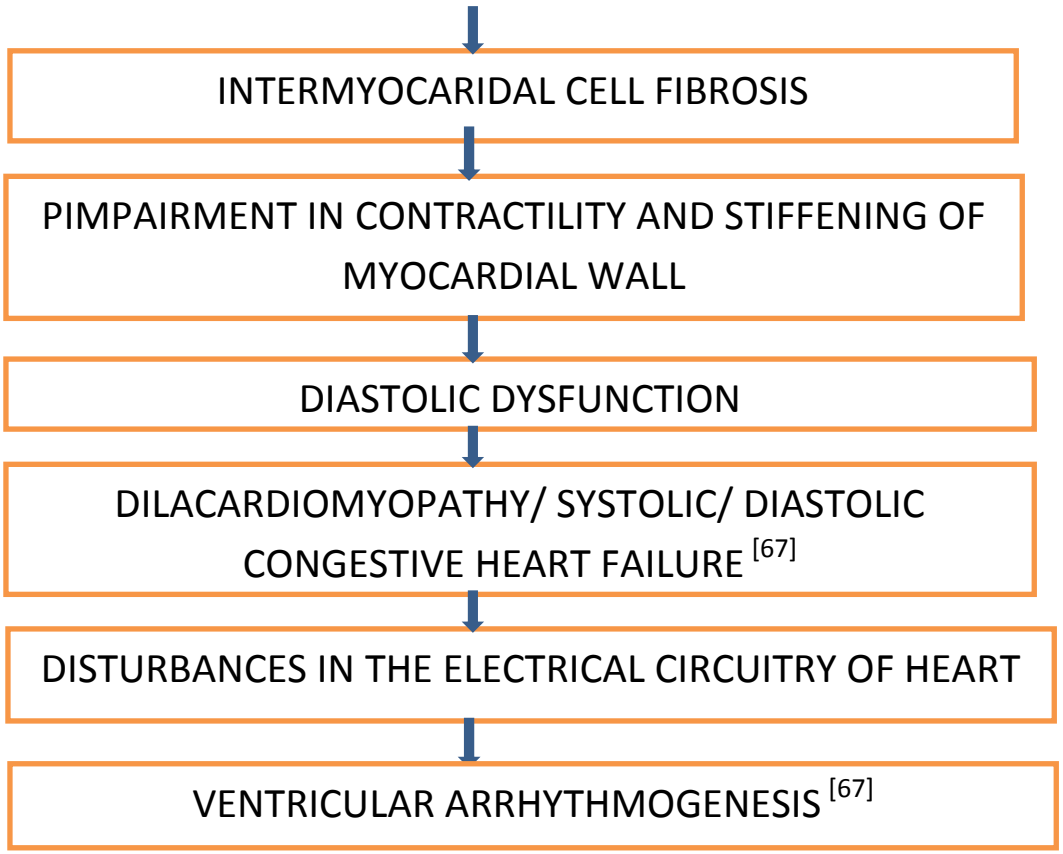
Left ventricular hypertrophy occurs in both primary and secondary hyperparathyroidism and is directly proportional to its levels in CKD.

7. **Carnitine deficiency.**
8. **Sympathetic Nervous System Activation**
9. **Cytokine/Hormone/Catechol production- (aldosterone, endothelin-1, TNFα, Leptin. Il-1$^{\alpha}$, Il-6, TGFβ, nor-epinephrine)**
10. **Gender**

Regardless of the underlying cause, be it afterload or preload or miscellaneous, the following steps are the dictum in ESRD.

FLOWCHART 1





Flowchart 1 shows the various end stage processes that occur following left ventricular hypertrophy that results in cardiovascular mortality.

MOLECULAR MECHANISMS [23]

Cardio tonic steroids (CTS) are the recently studied molecules. They are of low molecular weight of 500 daltons, which can be filtered by a semipermeable membrane. These cardio tonic steroid particles are dialyzable which explain how hemodialytic process alone reversed cardiac hypertrophy without altering intravascular volume or reducing blood pressure.

Ouabain and marinobufagenin are such endogenous CTS which interact with the alpha subunit of Na+ K+ ATPase Trans membrane protein. These both compounds play a major role in the blood pressure regulation, cardiac contractility and cardiac hypertrophy.

Intracellular signalling proteins and extracellular signal regulated kinases (ERK) are activated in response to increased concentrations of marinobufagenin which causes the development of uremic cardiomyopathy.

Experimental evidence suggested that the mTOR (mammalian target of Rapamycin) was involved in the development of pressure overload-stimulated cardiac hypertrophy [23]. Rapamycin, a direct inhibitor of mTOR blocked the development of left ventricular hypertrophy in patients with increased afterload.

LV MASS MEASUREMENT

1. Physical examination may reveal the shift of the point of maximum impulse. Postero-anterior view of chest radiograph may reveal increased cardiothoracic index. This is a simple, easy, inexpensive and insensitive form of evaluating left ventricular mass.

2. The first non-invasive test was the electrocardiogram. This method was insensitive but specific method

3. Serum Troponin-T levels correlate to the left ventricular mass in any patient.[68].

4. Serum Atrial and Brain Natriuretic Peptides are significant markers of hypertrophy as the serum levels of these peptides are augmented following a stretch response of the myocytes [68].

5. Echocardiography 2D echo/ M mode are used for left ventricular mass calculation. 2D echo is more accurate than M mode. M mode overestimates the presence of increased LV Mass (due to volume changes and geometry in ESRD)[69] [70]

6. 3D echo gives precise measurement of left ventricular wall thickness, left ventricular volume and ejection fraction [71] [72].

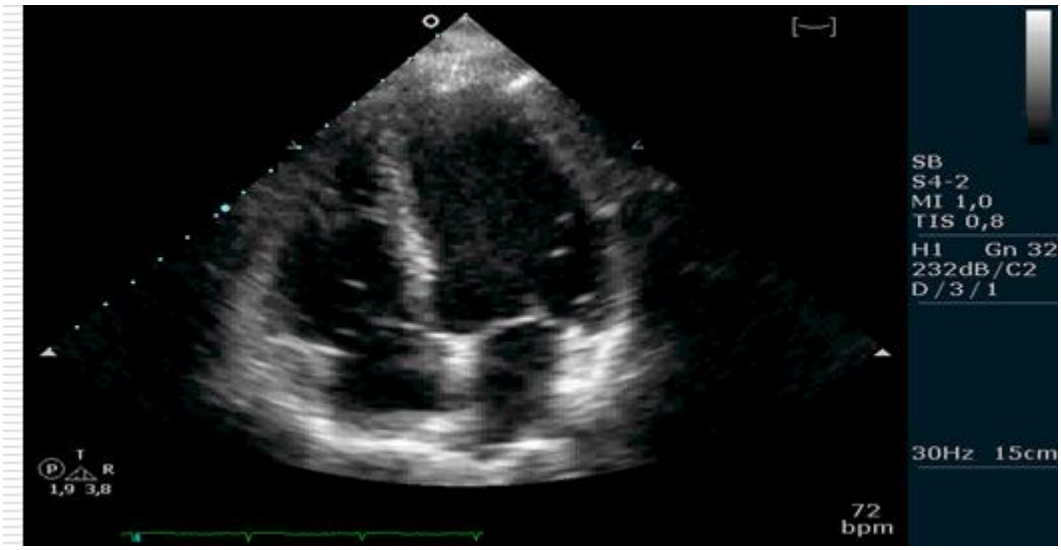
7. Cine computed CT measures LV mass accurately. The disadvantage is radiation exposure and limited availability.

8. The gold standard for assessment of LV dimension is cardiac magnetic resonance imaging (CMRI). Left ventricular mass, volume and pattern of LVH independent of geometric assumption and myocardial fibrosis can be found out [69].

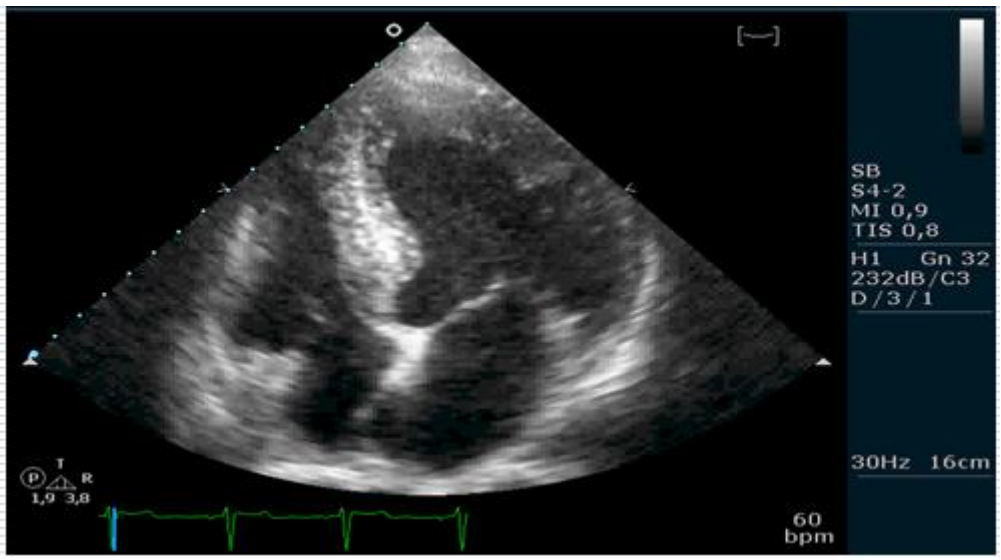
COMPARISON OF ECHOCARDIOGRAPHY VS CARDIAC MRI IN THE STUDY OF LEFT VENTRICULAR HYPERTROPHY

M-Mode (1 D), 2 D and 3 D Echocardiography is the commonly used methods of quantifying left ventricular mass in patients. But in patients who are on dialysis, calculation of LVmass by these methods can be erroneous due to influence of volume changes associated with hemodialysis. On the contrary, 3DEchocardiograms tend to overestimate the left ventricular mass due to asymmetric remodeling of ventricles in some patients [73][74].

FIGURE 7

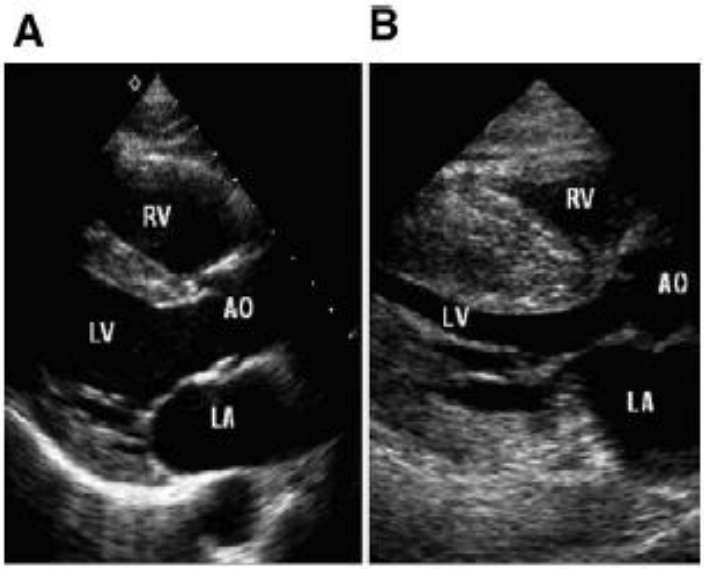


The above picture shows a normal ventricle on Echocardiography



Increased left ventricular mass is seen in the above echocardiography

FIGURE 8

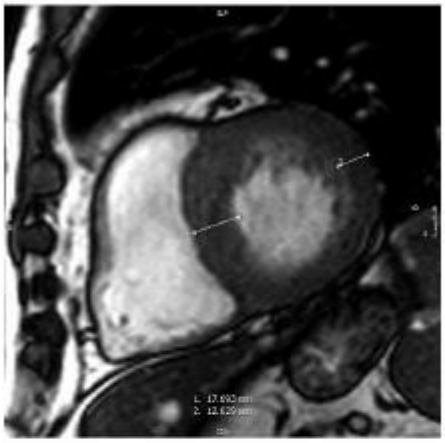


Normal Ventricles Hypertrophied ventricles

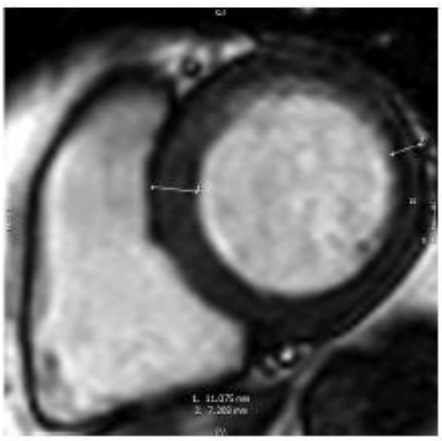
Figure 7 & 8 show pictures comparing a normal ventricle with a thickened and hypertrophied ventricle measured using echocardiography.

Cardiac MRI with contrast is the gold standard investigation in the evaluation of left ventricular hypertrophy. But the disadvantage of this investigation is that, it cannot be performed with contrast (gadolinium) in patients in end stage renal disease.

FIGURE 9



MRI image showing thickened & hypertrophied ventricular wall



MRI image of a normal ventricle

Figure 9 shows a MRI image of a hypertrophied ventricle with increased ventricular wall thickness and a normal ventricle.

PREVENTION AND TREATMENT

The basic goals in the treatment of chronic kidney disease are:

1. To reduce the progress of the kidney disease itself
2. To prevent the extra renal complications such as cardiovascular disease and stroke

MANAGEMENT OF CHRONIC KIDNEY DISEASE

Since diabetes mellitus and hypertension are the two most frequent causes of advanced CKD, no wonder cardiovascular disease predominate in chronic kidney disease. There are various measures suggested to treat both the traditional and non-traditional cardiovascular risk factors in CKD patients [4]. These include hypertension, elevated serum level of homocysteine, which promote dyslipidaemia. The role of "inflammation" causing endothelial damage and accelerated atherosclerosis is more important in patients with kidney disease. However, effective control of the risk factors is the only weapon possible in the treatment for these patients until the nature of disease progression and mechanism of complications in CKD and its treatment are better understood.

TREATMENT OF HYPERTENSION INDUCED RENAL DISEASE [15]

Reducing intraglomerular hypertension and proteinuria

Following an initial insult to the kidney, short term adaptive responses like increased glomerular filtration and glomerular hypertrophy occurs. But since the underling inciting cause is not resolved, the responses become maladaptive progressing to chronic kidney damage [15]. Therefore control of systemic and glomerular hypertension is an important milestone in the treatment of CKD. Persistent elevation of blood pressure causes proteinuria through increased excretion, thus worsening of kidney damage. Hence, antihypertensive therapy slows the progression of kidney damage by decreasing the intraglomerular blood pressure as well as through decrease of proteinuria excretion [75]. In fact, the efficacy of the antihypertensive treatment is established by its ability to decrease protein excretion in the urine and subsequent progression of GFR decline.

Blood pressure of 125/75 mmHg is the target in CKD patients with proteinuria. The preferred antihypertensives are the renin-angiotensin system inhibitors (ACE inhibitors/ ARBs) [76] [77]]. These drugs reduce both the intraglomerular hypertension and as well as protein excretion [78]. These drugs are effective in slowing the progression for both diabetic and non-diabetic CKD. The second groups of drugs preferred are the calcium channel blockers

(Diltiazem Verapamil) when proteinuria is insignificant and the intraglomerular pressure is less prominent.

DECREASING THE RACE OF DIABETIC RENAL DISEASE [15]

Control of Blood Glucose

Maintaining euglycemic status decreases the decline in renal function and the progression of the disease. The recommended value is a pre-prandial glucose of 90 – 130 mg/dl and HBA1C value of less than 7%.

Control of Blood pressure and proteinuria

Hypertension is an important risk factor in the progression of diabetic nephropathy. Micro albuminuria is an important predictor of cardiovascular mortality and kidney disease. Hence antihypertensive drugs are used to reduce albuminuria and diminish the progression of normotensive diabetic patients. In particular, use of renin angiotensin blockers has a superior rule in renoprotection in diabetes [79]. These effects are mediated by reducing intraglomerular pressure and blockade of RAS pathways through inhibition of TGF-β mediated pathways.

MANAGEMENT OF CARDIOVASCULAR DISEASE IN CKD

The following measures are suggested in the control and treatment of cardiovascular risk factors [18]:

1. Regular daily physical activity and dietary modification including salt restriction, protein enriched diet are important measures in the early stage of the disease [80].

2. Meticulous control of volume status is the measure of utmost importance. Control of the extracellular volume requires sodium restriction and diuretics. The preferred drugs are loop diuretics [81] [82].

3. Another measure suggested for maintaining volume status is long duration of dialysis periods or extra sessions of dialysis should be planned [83].

4. The preferred hemoglobin range is between 10 – 12 g/dl and that of the haematocrit should be of minimum 30[84]. The above parameters should be achieved using small and divided doses of erythropoietin and parenteral iron [85] [86] [87]].

5. Maintaining euglycemic status is important in diabetic patients. High blood pressure and proteinuria complicating diabetes should be treated with a hypertensive inhibiting the renin angiotensin system, either an angiotensin converting enzyme inhibitor or an angiotensin receptor [88] [89].

6. Angiotensin converting enzyme inhibitors or angiotensin receptor blockers is the preferred antihypertensive due to their action on the both intraglomerular hypertension and reduction of proteinuria. The target systolic blood pressure is 130 – 140 mmHg [90].

7. The LDL cholesterol should be lowered to <100 mg/dl in dialysis patients and <70 mg/dl in patients with known coronary disease. For control of hyperlipidaemia, if dietary measures are not sufficient, lipid-lowering medications, such as statins, should be used.

8. Maintaining the calcium phosphorus product is necessary to prevent vascular calcification and aortic impedance. This could be achieved through calcium supplementation and removal of the excess phosphate through phosphate binders [56].

9. The desired serum phosphorus level to maintain the calcium phosphorus product is 4 – 6 mg/dl [56]. Serum levels of phosphorus can be reduced using phosphate binders, so as to maintain the calcium phosphorus product.

10. Due to the falling calcium level and hyperphosphatemia, secondary hyperparathyroidism is a common manifestation causing renal osteodystrophy. The preferred serum PTH value is 500 pg/ml. Severe hyperparathyroidism should be treated with intravenous calcitonin [64].

11. Chronic kidney disease causes vitamin D deficiency due to the lack of the formation of active vitamin D there by causing bone resorption and osteomalacia. This could be avoided by active Vitamin D

supplementation. (serum levels of 30 ng/ml of ergocalciferol is preferred)[91].

12. Patients suffering from both coronary disease and kidney disease should be treated with a combination of low-dose aspirin and β blockers. Other potential nephrotoxic NSAIDs should be avoided.

13. In patients considered to be at high risk of developing adverse events like obstructive sleep apnoea, prolonged QT interval, and severe left ventricular hypertrophy, prophylactic use of cardio-selective blockers (e.g. Carvedilol) should be added.

14. Patients at risk of sudden cardiac death due to ventricular fibrillation should have an implantable cardiac defibrillator (ICD).

15. Frequent and longer dialysis period including nocturnal haemodialysis, daily in-centre haemodialysis is strongly encouraged [93]. Studies have shown that regular hemodialysis could cause regression of left ventricular hypertrophy.

16. The course of left ventricular hypertrophy in haemodialysis patients should be monitored every 12 -18 months, every 2 years in conservatively managed CKD patients [94].

MATERIALS AND METHODS

MATERIALS AND METHODS

SETTING **:** Government Royapettah Hospital, Chennai

COLLABORATIVE

DEPARTMENT **:** Department of Nephrology, GRH

Department of Cardiology, GRH

STUDY DESIGN **:** Observational Study

PERIOD OF STUDY **:** April 2013 to October 2013

SAMPLE SIZE **:** 75 cases

INCLUSION CRITERIA:

All Chronic kidney disease irrespective of the aetiology

EXCLUSION CRITERIA:

1. Age less than 18 years
2. History of cigarette smoking
3. History of alcohol consumption
4. Obesity
5. Patients receiving maintenance hemodialysis treatment
6. Patients with arterio-venous fistulae

7. Post renal transplant status
8. Aortic stenosis/ aortic insufficiency
9. Hypertrophic obstructive cardiomyopathy
10. Athletic training

Cases and Controls were selected after considering the above inclusion and exclusion criteria

ETHICAL CLEARANCE: Obtained

INFORMED CONSENT

All the cases in the Study Groups were informed about the nature of the study. Members who were willing to participate in this study were included after getting their written informed consent.

METHODOLOGY

Patients admitted in the Nephrology ward and those patients attending the Nephrology Outpatient department of Government Royapettah Hospital were chosen as cases. A total of 75 cases that satisfied the inclusion and exclusion criteria above were included in the study over a period of 6 months.

A Data collection form was prepared to note the Name, Age, Sex, Occupation, Address, Complaints, Past Medical History, Smoking, Alcoholism, Drug Intake and other relevant history. General Examination

with examination of the Vital Signs, Cardiac, Respiratory, Abdomen and Central Nervous System were done. Each Patient's clinical profile was noted.

LABORATORY INVESTIGATIONS

Blood samples and urine samples were drawn at the time of admission and in the Outpatient department for urine spot protein creatinine ratio calculation and renal function test. 24 hour urine collection was scrutinized and analysed for proteinuria quantification and creatinine clearance.

Left ventricular mass was measured using 2D Echocardiography.

Devereux formula was used for the calculation of left ventricular mass index.

STATISTICAL ANALYSIS

Data was entered in Microsoft Excel Spreadsheet and analysed.

Data analysis was done with the use of standard SPSS software. Descriptive

Statistics were used to calculate the frequency, mean and standard deviation. Students'' values was applied for significance. Significance was considered if the 'p' value was below 0.05.

CONFLICT OF INTEREST

There was no conflict of interest

FINANCIAL SUPPORT: Nil

DEFINITIONS USED IN

THE STUDY

DEFINITIONS USED IN THE STUDY

SERUM CREATININE VALUE:

0.7 to 1.3 mg/dL for men

0.6 to 1.1 mg/dL for women

URINE CREATININE VALUE:

Urine creatinine (24-hour sample) values can range from 500 to 2000 mg/day. Results depend greatly on age and amount of lean body mass

CREATININE CLEARANCE FORMULA:

$$\frac{[\text{Urine creatinine (mg/dL)}] \times [\text{24-Hour Urine Volume (mL/day)}/1440\ \text{(min/day)}]}{[\text{Serum Creatinine (mg/dL)}]}$$

COCKCROFT GAULT FORMULA:

$$\frac{(140 - \text{Age}) \times \text{Mass (in kilograms)} \times [0.85 \text{ if female}]}{72 \times \text{Serum Creatinine (in mg/dL)}}$$

DEFINITION OF PROTEINURIA

TABLE 7

URINE COLLECTION METHOD	NORMAL	PROTEINURIA
24-Hour Excretion	<300 mg/day	>300 mg/day
Spot Urine Protein-to-Creatinine Ratio	<200 mg/g	>200 mg/g

Table 7 shows the normal and pathologic range of proteinuria measured by 24 hour protein excretion and urine spot protein creatinine ratio.

MODIFIED DEVEREUX FORMULA

Left ventricular mass was calculated using the American society of echocardiography formula modified by Devereux

LVmass: 0.8 (1.04 ([LVIDD + PWTD + IVSTD]^3- [LVIDD]^3))+ 0.6

- LVIDD = Left Ventricular Internal Diameter in Diastole
- PWTD = Posterior Wall Thickness in Diastole
- IVSTD = Interventricular Septum Thickness in Diastole

BODY SURFACE AREA

The DuBois and DuBois formula:

$$BSA\ (m^2) = 0.20247 \times Height\ (m)^{0.725} \times Weight\ (kg)^{0.425}$$

LEFT VENTRICULAR MASS INDEX

$$\frac{\text{Left ventricular mass (g)}}{\text{Body surface area } (m^2)}$$

Left ventricular hypertrophy was defined in absolute terms as LVMI >134 g/m2 in men and >110 g/m2 in women

OBSERVATION AND

RESULTS

OBSERVATION AND ANALYSIS

STUDY POPULATION CHARACTERISTICS

A total of 75 patients of chronic kidney disease were included in this study of which 35 were females and 40 were males. Both male and females between ages 18 to 60 years were included in the study.

TABLE 8: NO.OF MALE AND FEMALE PATIENTS IN THE STUDY

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	**F**	35	46.67	46.67	46.67
	M	40	53.33	53.33	100
	Total	75	100	100	

Table 8 shows the frequency and percentage distribution of male and female in the study population.

This frequency table says that almost equal numbers of male and female patients participated in this study. The male population represented 53.33% of the study while the female population represented 46.67% of the study group.

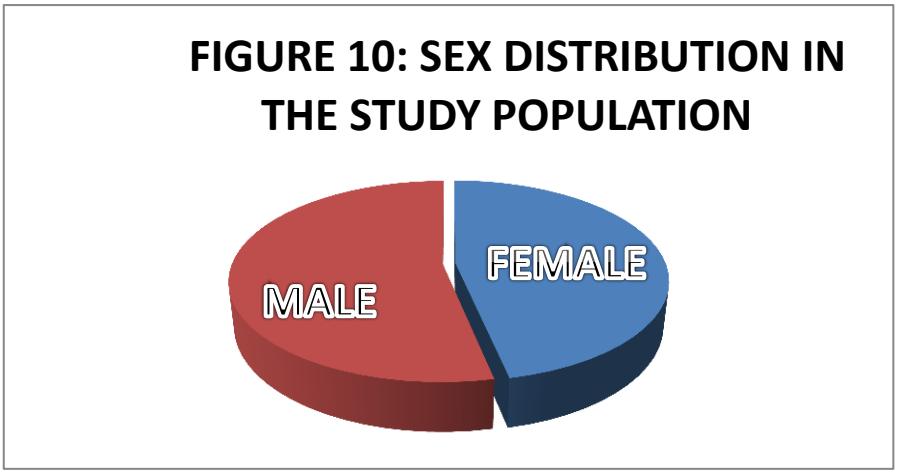


Figure 10 shows a pie chart demonstrating equal distribution of male and female in the study population.

TABLE 9: AGE WISE DISTRIBUTION OF PATIENTS

AGEGROUP	**18-29**	**30-39**	**40-49**	**50-59**
TOTAL	14	18	25	18

Table 9 shows the distribution of the patients in each age group beginning from 18 to 59.This frequency table shows that patient in all age group are evenly distributed in the study population. 14 patients are present in the age group 18-29. The number of patients in the age group 40 to 49 is 25. 18 people are there in both 30-39 age groups and 50-59 age groups.

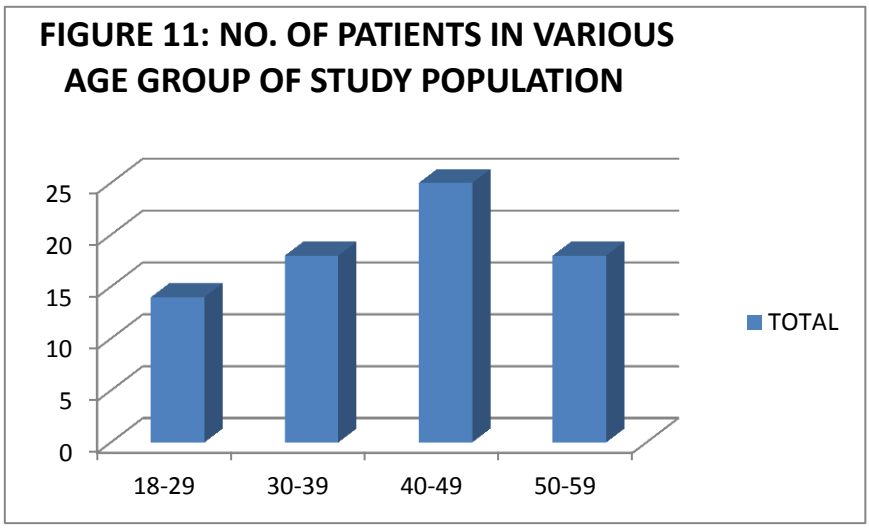


TABLE 10: SEX DISTRIBUTION IN VARIOUS AGE GROUPS

	AGEGROUP	18-29	30-39	40-49	50-59
MALE		7	10	16	7
FEMALE		7	8	9	11
TOTAL		14	18	25	18

Table 10 shows the frequency distribution of male and female in the different age group. Regarding the sex distribution in the divided age groups, both the male and female patients are equally distributed in all age groups in this study population.

FIGURE 12: SEX DISTRIBUTION IN THE DIFFERENT AGE GROUP OF THE STUDY POPULATION

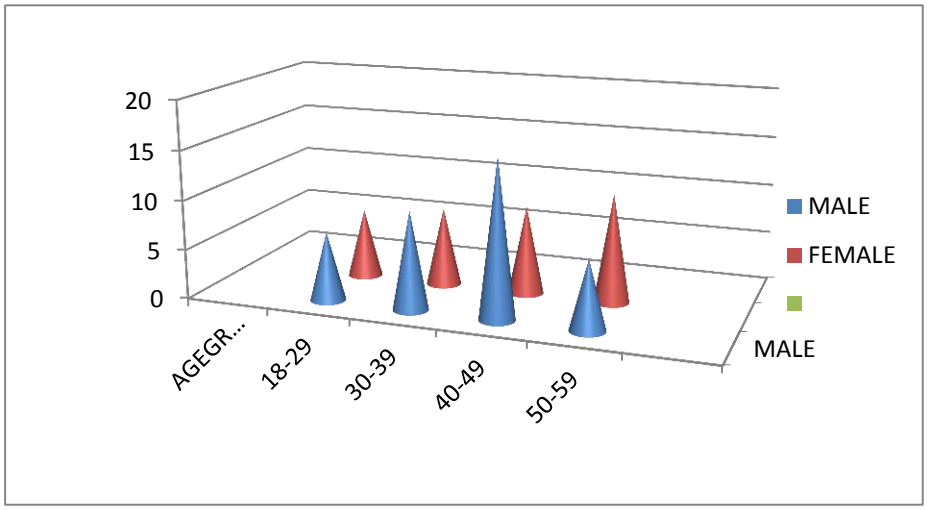


Figure 12 is a column chart showing the distribution of male and female in the different age group of the study population.

DURATION OF CKD IN THE STUDY POPULATION

A frequency table correlating the duration of chronic kidney disease and the number of patients in each group is formulated.

TABLE 11: NO. OF PATIENTS Vs DURATION OF CKD

Duration of CKD(years)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
No. of Patients	**5**	**14**	**17**	**17**	**16**	**5**	**1**	**1**

Table 11 shows the frequency distribution of patients based on the duration of chronic kidney disease. More number of patients is having chronic kidney

disease of the duration 2 – 5 years. A chart showing this distribution is as follows:

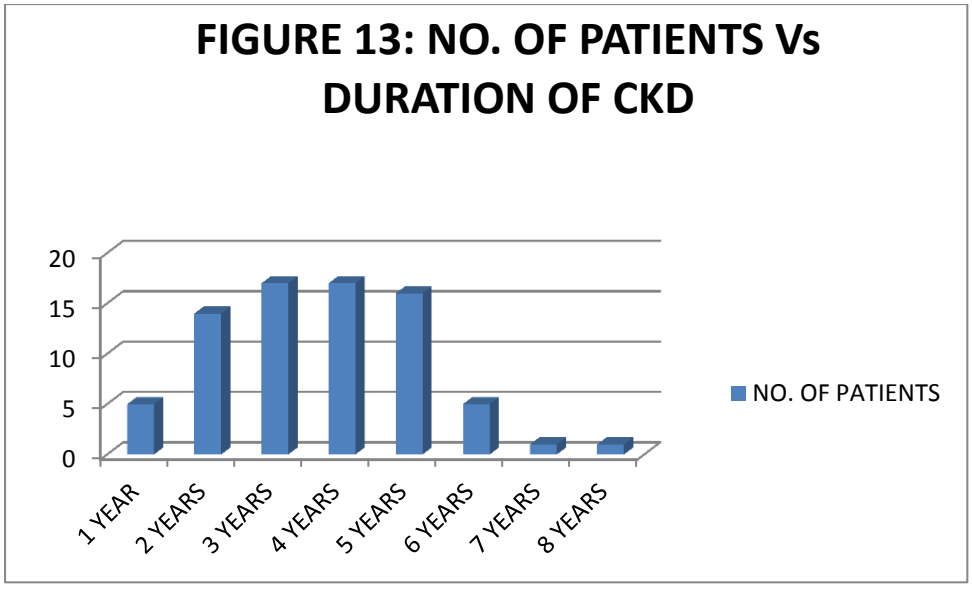


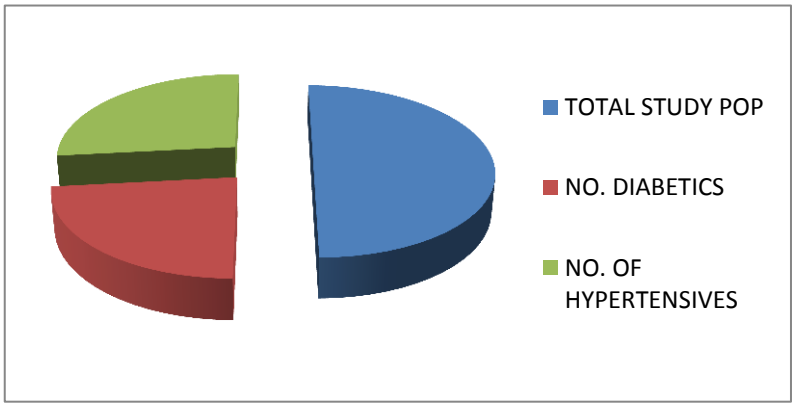
Figure 13: is a column chart showing the distribution of patients based on their duration of disease.

TABLE 12: PREVALENCE OF DIABETES AND HYPERTENSION IN THE STUDY POPULATION

TOTAL STUDY POPULATION	75
NO. DIABETICS	35
NO. OF HYPERTENSIVES	40
NO. OF BOTH DIABETIC AND HYPERTENSIVE	21

Table 12 shows the prevalence of diabetes and hypertension in the study population. The number of diabetics in the study population of 75 is 35.

Hypertensive comprises around 40 of the total study group. Patients with the both risk factors are evenly distributed in the group. Number of patients harbouring both the risk factors of diabetes and hypertension are 21.



Equal number of hypertensive and diabetics has participated in this study. There is no significant difference between these two risk factors in the study.

TABLE 13: STAGE WISE DISTRIBUTION OF CKD PATIENTS IN THE STUDY GROUP

	MALE	**FEMALE**	**TOTAL**
STAGE OF CKD			
1	1	1	2
2	6	8	14
3	11	10	21
4	9	10	19
5	13	6	19

Table 13 shows the frequency distribution of male and female in the different stages of chronic kidney disease.

In the above frequency table, patients are classified into groups based on the stage of chronic kidney disease. The staging is based on the glomerular filtration rate obtained from the creatinine clearance formula.

FIGURE 15: SEX DISTRIBUTION IN THE VARIOUS STAGES

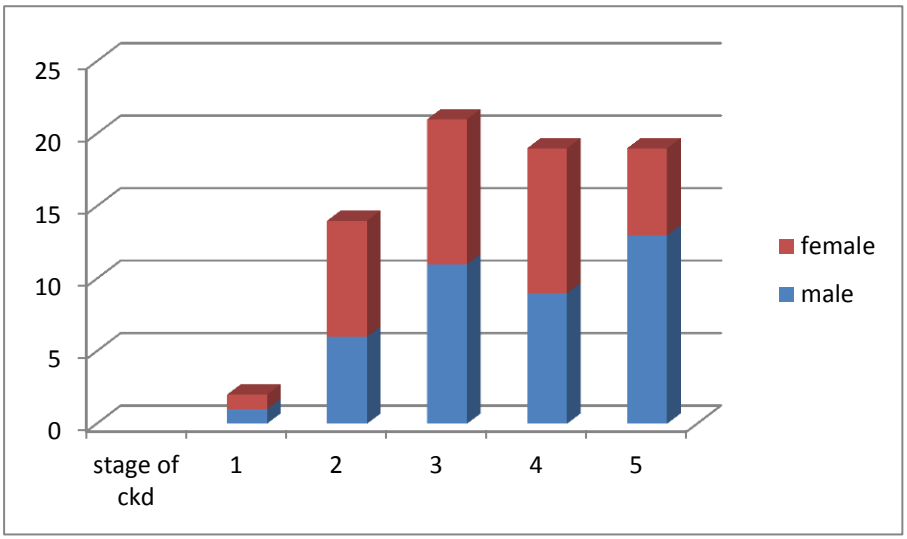


Figure 15 column chart shows the sex distribution of patients in each stage of the disease.

The majority of the study group is distributed between the stage 2 and above up to the stage of end stage renal disease.

TABLE 14: DESCRIPTIVE ANALYSIS

	N	Range	Minimum	Maximum	Mean	Std.deviation
AGE	**75**	**37**	**19**	**56**	**41**	**10**
DURATION OF CKD	**75**	**7**	**1**	**8**	**4**	**1**
STAGE OF CKD	**75**	**4**	**1**	**5**	**4**	**1**
SYSTOLIC BLOOD PRESSURE	**75**	**42**	**98**	**140**	**124**	**13**
DIASTOLIC BLOOD PRESSURE	**75**	**20**	**70**	**90**	**81**	**5.2**
SERUM ALBUMIN	**75**	**1.4**	**2.1**	**3.5**	**2.84**	**0.36**
HEMOGLOBIN	**75**	**4.3**	**5.7**	**10**	**8.4**	**1**
SERUM ALKALINE PHOSPHATASE	**75**	**240**	**180**	**420**	**289**	**69**
SERUM CHOLESTEROL	**75**	**280**	**98**	**378**	**201**	**64.9**
SERUM TRIGLYCERIDES	**75**	**217**	**80**	**297**	**167**	**53.3**
BLOOD UREA	**75**	**182**	**28**	**210**	**87.2**	**41.7**
SERUM CREATININE	**75**	**12.2**	**0.8**	**13**	**4.7**	**3.1**
24 HR CREATININE CLEARANCE	**75**	**95**	**3**	**98**	**36**	**27**
CREATININE CLEARANCE(CCG)	**75**	**89**	**4**	**93**	**34**	**24**
CREATININE CLEARANCE(MDRD)	**75**	**83**	**4**	**87**	**33**	**24**
URINE SPOT PCR	**75**	**20.43**	**0.57**	**21**	**7.33**	**6.42**

24 HR PROTEINURIA	**75**	**13249**	**571**	**14000**	**5992**	**4300**
BODY SURFACE AREA	**75**	**0.73396**	**1.3225**	**2.05646**	**1.59829**	**0.17693**

Table 14 lists the descriptive variables which are to be compared in the normal and abnormal ventricular mass group.

Descriptive variables in the study were age, sex, duration of chronic kidney disease, prevalence of diabetes and hypertension, systolic blood pressure, diastolic blood pressure, serum albumin, hemoglobin, serum alkaline phosphatase, total cholesterol, serum triglycerides, blood urea, serum creatinine, 24 hour creatinine clearance, estimated creatinine clearance by Cockgraft-gault formula and MDRD equation, stage of CKD, urine spot creatinine ratio, 24 hour proteinuria quantification and waist circumference.

Patients in this study were divided into two group based on their left ventricular mass index. Female with LV mass index more than 110 g/m^2 and male with LV mass index more than 134 g/m^2 were categorized as abnormal/ increased left ventricular mass group and those patients with values below than this were categorized as the group with normal left ventricular mass. The above said descriptive variable of each patient is compared in either group and significance of “p” value of the descriptive variable is noted.

TABLE 15: PREVALENCE OF INCREASED LEFT VENTRICULAR MASS INDEX IN THE STUDY POPULATION

Stage of CKD	Normal	Abnormal
1	2	0
2	14	0
3	13	8
4	0	19
5	0	19

Table 15 shows the distribution of patients with normal and increased ventricular mass based on the stage of chronic kidney disease.

In the study population, 29 patients had normal ventricular mass and 46 patients had increased left ventricular mass. The stage wise distribution of patients with normal and increased left ventricular mass is above. The prevalence of increased/ abnormal left ventricular mass is stage 1 and 2 CKD is nil. In stage 3, the prevalence of increased left ventricular mass is 17.4% among the study population. The prevalence of increased left ventricular mass in stage 4 of CKD is 41.3% and in stage 5 of CKD, 41.3%

FIGURE 16: PREVALENCE OF VENTRICULAR MASS Vs STAGES OF CHRONIC KIDNEY DISEASE

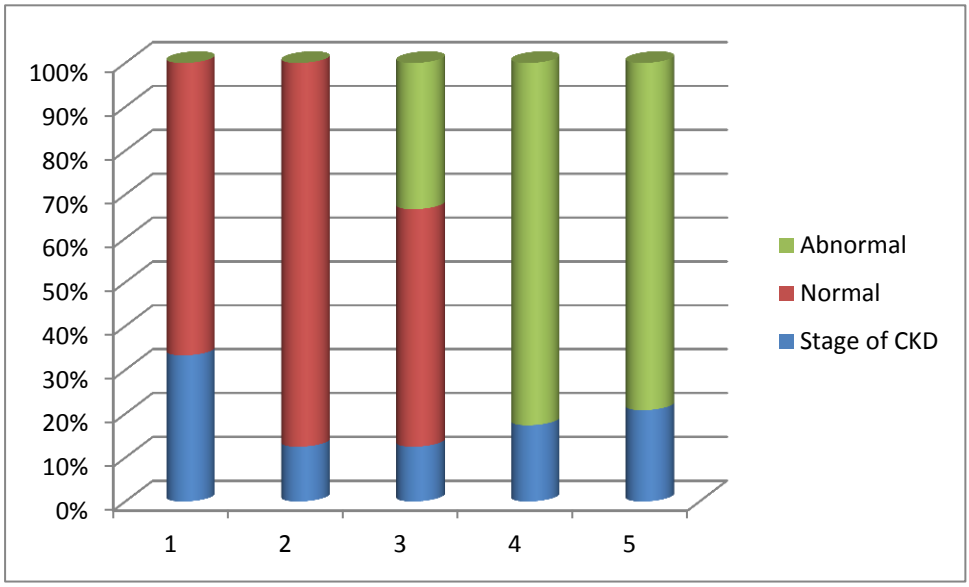


Figure 16 shows the distribution of patients in each stage with normal and increased left ventricular mass. In this chart, the progressive increase in the prevalence of increased left ventricular mass is evident as the stage of chronic kidney disease progresses.

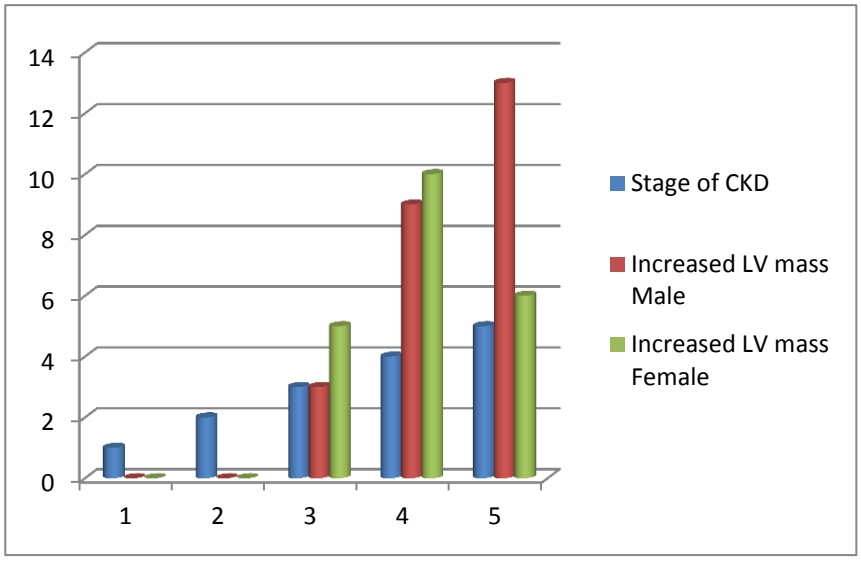
TABLE 16: PREVALENCE OF INCREASED LVMI IN THE MALE AND FEMALE STUDY POPULATION

Stage of CKD	**Increased LV mass**	
	Male	**Female**
1	0	0
2	0	0
3	3	5

4	9	10
5	13	6

.In the above table, sex wise distribution in the left ventricular thickness is documented. The numbers of female patients with increased LV mass are 5 in stage 3, 10 in stage 4 and 6 patients in stage 5 of CKD. The numbers of male patients in the increased LVmass group are 3 in stage 3, 9 in stage 4 and 13 in stage 5 of CKD.

FIGURE 17: PREVALENCE OF INCREASED LV MASS IN THE MALE AND FEMALE STUDY POPULATION



The above chart displays the progressive in left ventricular mass as the stage of CKD increases, with equal incidence in both male and female patients.

TABLE 17: SEX * LVMI

			LVMI		Total	
			Normal	Abnormal		p value
Sex	**Male**	Count	15	25	40	0.824
		% within Sex	37.5%	62.5%	100.0%	
		% within LVMI	51.7%	54.3%	53.3%	
	Female	Count	14	21	35	
		% within Sex	40.0%	60.0%	100.0%	
		% within LVMI	48.3%	45.7%	46.7%	
Total		Count	29	46	75	
		% within Sex	38.7%	61.3%	100.0%	
		% within LVMI	100.0%	100.0%	100.0%	

Table 17 shows the frequency distribution of male and female in the study group with regard to normal and abnormal ventricular mass.

FIGURE 18: SEX Vs LVMI

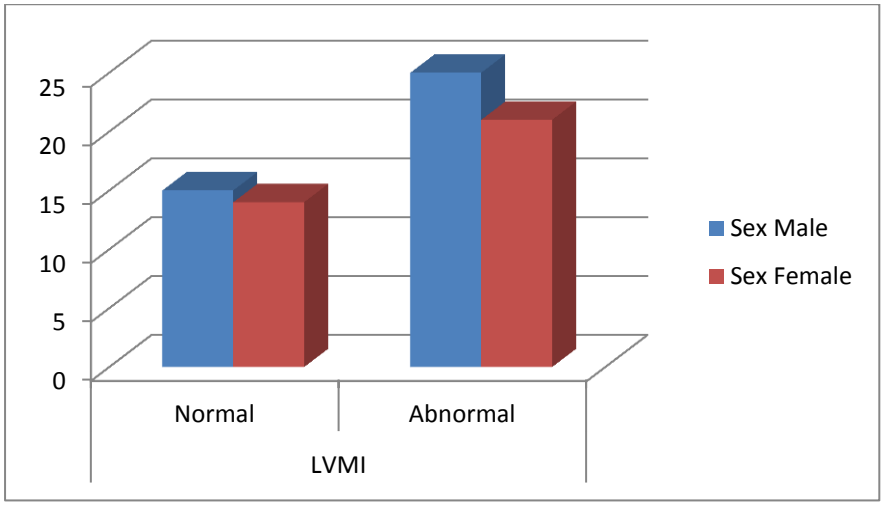


Figure 18 compares the sex distribution between the normal and increased left ventricular mass group.

The “p” value between the two groups male and female with regard to the variable left ventricular mass index is 0.824. Hence the sex difference regarding the left ventricular wall thickness was not significant.

TABLE 18: AGE * LVMI

	LVMI	**N**	**Mean**	**Std. deviation**	**p value**
Age in years	**Normal**	29	41.21	9.507	0.912
	Abnormal	46	40.89	10.963	

Table 18 shows the frequency distribution of age in both the normal and increased left ventricular mass group.The difference in the age distribution between the two groups with normal and abnormal ventricular mass was not statistically significant. The p value for age in either of the study group is 0.912 which is not at all significant value.

TABLE 19: DURATION OF CHRONIC KIDNEY DISEASE * LVMI

	LVMI	**N**	**Mean**	**Std. Deviation**	**p value**
Duration of CKD	**Normal**	29	3.52	1.184	0.028
	Abnormal	46	3.7	1.685	

Table 19 shows the frequency distribution of patients in the two groups based on the duration of chronic kidney disease and p value for the same.

There was a significant correlation between the two groups in the duration of chronic kidney disease. This implies that the left ventricular mass increases progressively as the number of years of disease increases. The p value for duration of chronic kidney disease in either group is 0.28 which is statistically significant.

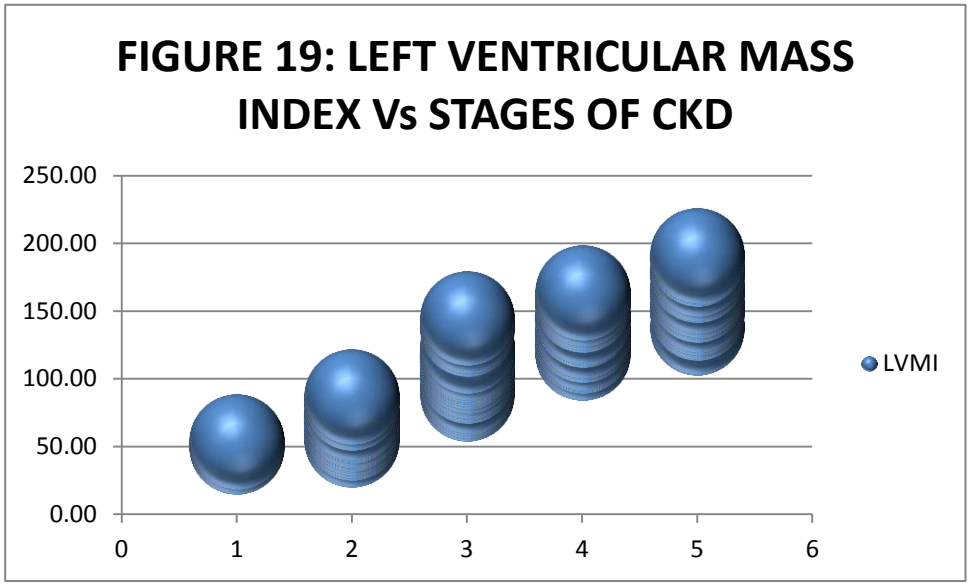


Figure 19 shows the increasing prevalence of left ventricular hypertrophy in the study population as the stage of the chronic kidney disease increases

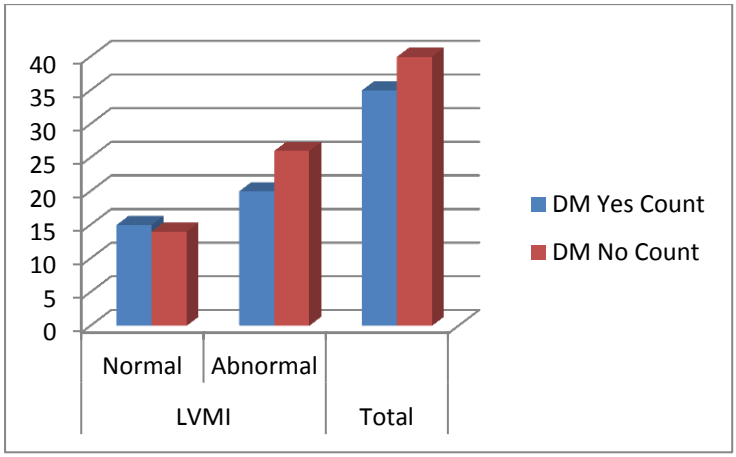
TABLE 20: DIABETES MELLITUS * LVMI

			LVMI		**Total**	
			Normal	**Abnormal**		p value
DM	**Yes**	Count	15	20	35	0.486
		% within DM	42.9%	57.1%	100.0%	
		% within LVMI	51.7%	43.5%	46.7%	
	No	Count	14	26	40	
		% within DM	35.0%	65.0%	100.0%	

		% within LVMI	48.3%	56.5%	53.3 %	
Total		Count	29	46	75	
		% within DM	38.7%	61.3%	100. 0%	
		% within LVMI	100.0 %	100.0%	100. 0%	

Table 20 shows the distribution of diabetic population in the both the normal and increased left ventricular mass group and the p value for the same.

FIGURE 20: DIABETES Vs LVMI



Regarding the distribution of diabetes in both the normal and abnormal left ventricular mass group, there was no significant relation. The p value for the number of diabetes in either group is 0.486 which is not at all statistically significant.

TABLE 21: SYSTEMIC HYPERTENSION * LVMI

			LVMI		Total	
			Normal	**Abnormal**		p value
SHT	**Yes**	Count	15	25	40	0.824
		% within SHT	37.5%	62.5%	100.0%	
		% within LVMI	51.7%	54.3%	53.3%	
	No	Count	14	21	35	
		% within SHT	40.0%	60.0%	100.0%	
		% within LVMI	48.3%	45.7%	46.7%	
Total		Count	29	46	75	
		% within SHT	38.7%	61.3%	100.0%	
		% within LVMI	100.0%	100.0%	100.0%	

FIGURE 21: SYSTEMIC HYPERTENSION Vs LVMI

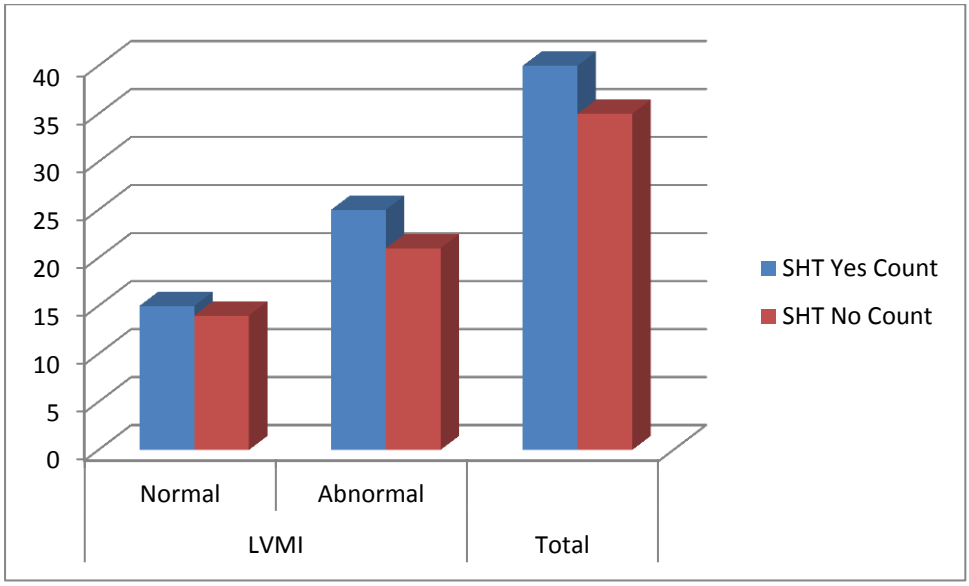


Figure 21 compares the frequency distribution of hypertensive patients in the both groups of normal and increased left ventricular mass.

Regarding the distribution of hypertension in both the normal and abnormal left ventricular mass group, there was no significant relation. The p value for the number of diabetes in either group is 0.824 which is not at all statistically significant.

TABLE 22: SYSTOLIC BLOOD PRESSURE VS LVMI

Systolic BP	**LVMI**	**N**	**Mean**	**Std. deviation**	**p value**
	Normal	29	124.55	12.07	0.65
	Abnormal	46	122.87	13.055	

Table 22 compares the variable systolic blood pressure in the normal and abnormal LV mass group and the p value for the same.

The mean systolic blood pressure in the normal left ventricular mass group is 124.55 and in the increased left ventricular mass group are 122.87. There was no significant difference in systolic blood pressure in both group, and the p value is0.65 which is not statistically significant.

TABLE 23: DIASTOLIC BLOOD PRESSURE VS LVMI

Diastolic BP	**LVMI**	**N**	**Mean**	**Std. deviation**	**p value**
	Normal	29	81.93	5.669	0.131
	Abnormal	46	79.87	4.87	

Table 23 compares the variable diastolic blood pressure in the normal and abnormal LV mass group and the p value for the same

The mean diastolic blood pressure in the normal left ventricular mass group is 81 and in the abnormal left ventricular mass group is 79. There was no statistically significant difference in either of the group when compared with the variable diastolic blood pressure. The p value is 0.131

TABLE 24: SERUM ALBUMIN VS LVMI

Serum Albumin	LVMI	N	Mean	Std. deviation	p value
	Normal	29	2.934	0.3866	0.12
	Abnormal	46	2.781	0.3308	

Table 24 compares the variable serum albumin in the normal and abnormal Left Ventricular mass group and the p value for the same

When compared to the variable serum albumin in either of the group of normal and increased left ventricular mass group, there was no significant difference in the groups. The mean serum albumin in the normal LVmass group is 2.934 and in the increased left ventricular mass group, the serum albumin is 2.781. The p value is 0.12 which is not statistically significant.\

TABLE 25: HEMOGLOBIN VS LVMI

Hemoglobin	LVMI	N	Mean	Std. deviation	p value
	Normal	29	8.33	1.052	0.406
	Abnormal	46	8.44	1.042	

Table 25 compares the distribution of the variable hemoglobin in both the normal and increased left ventricular thickness group.

The variable, hemoglobin is generally reduced in chronic kidney disease group. The mean hemoglobin in the normal ventricular mass group is 8.33

and in the increased ventricular mass group are 8.44. The p value for this variable in both the group is 0.406 which is not statistically significant.

TABLE 26: SERUM ALKALINE PHOSPHATASE VS LVMI

Serum Alkaline Phosphatase	LVMI	N	Mean	Std. deviation	p value
	Normal	29	285.86	77.969	0.451
	Abnormal	46	290.65	64.339	

Table 26 compares the distribution of patients in the two groups of normal and increased left ventricular mass based on the variable, serum alkaline phosphatase.

There was no statistically significant difference in either group when compared with serum alkaline phosphatase. The mean serum alkaline phosphatase is 285 in the normal LV mass group and in the abnormal group are 290. The p value is 0.451 which is not at all statistically significant.

TABLE 27: SERUM CHOLESTEROL AND LVMI

Serum Cholesterol	LVMI	N	Mean	Std. deviation	p value
	Normal	29	206.07	67.928	0.667
	Abnormal	46	198.52	64.181	

Table 27 compares the serum cholesterol levels in both the group of normal and increased left ventricular mass and the p value for the same.

The mean serum cholesterol in the normal ventricular mass group is 206 and in the increased ventricular mass group are 198. There was no significant difference in either group and the p value for this variable is 0.667 which is not statistically significant.

TABLE 28: SERUM TRIGLYCERIDES VS LVMI

Serum Triglycerides	**LVMI**	**N**	**Mean**	**Std. deviation**	**p value**
	Normal	29	166.24	51.465	0.895
	Abnormal	46	167.07	55.569	

Table 28 compares the serum triglyceride levels in both the group of normal and increased left ventricular mass and the p value for the same.

The mean serum triglyceride in the normal group is 166 and in the abnormal group are 167. There is no significant difference in either group and the p value is 0.895

TABLE 29: BLOOD UREA VS LVMI

Blood Urea	LVMI	N	Mean	Std. deviation	p value
	Normal	29	76.97	48.252	0.41
	Abnormal	46	93.67	36.531	

Table 29 compares the serum urea levels in both the group of normal and increased left ventricular mass and the p value for the same.

The serum urea in the normal ventricular mass group is 76 and in the abnormal group are 93. There is no statistically significant difference in either group when compared with blood urea concentration the p value is 0.41.

TABLE 30: SERUM CREATININE VS LVMI

Serum Creatinine	LVMI	N	Mean	Std. deviation	p value
	Normal	29	1.872	0.7745	<0.001
	Abnormal	46	6.515	2.6802	

Table 30 compares the serum creatinine levels in both the group of normal and increased left ventricular mass and the p value for the same.

The mean serum creatinine in the normal ventricular mass group is 1.872 and in the increased left ventricular mass group is 6.515. The p value comparing

serum creatinine in either of the group is less than 0.001 which is statistically highly significant

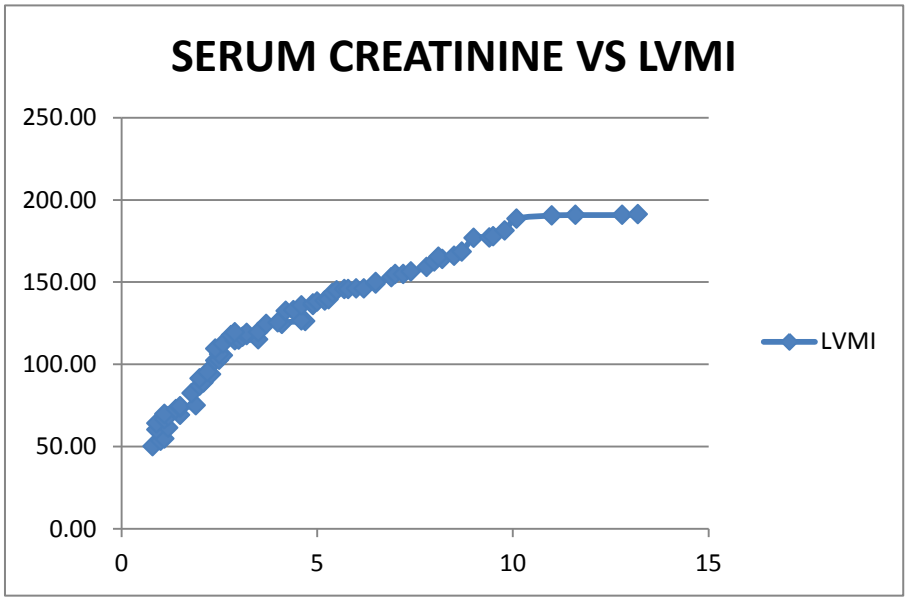


Figure 22 shows a line diagram comparing the variables, left ventricular mass index and serum creatinine.

In the above chart, the serum creatinine is compared with left ventricular mass index. There was a positive correlation between the two variables, as suggested by the progression of the line upwards and to the left. As the serum creatinine increased, the left ventricular mass increased.

TABLE 31: 24 HOUR CREATININE CLEARANCE VS LVMI

24 hrcreatinine clearance	LVMI	N	Mean	Std. deviation	p value
	Normal	29	64.28	20.898	<0.001
	Abnormal	46	17.96	9.328	

Table 31 compares the 24 hour creatinine clearance levels in both the group of normal and increased left ventricular mass and the p value for the same.The normal group has a mean 24 hour creatinine clearance of 64 and in the increased left ventricular mass group; the mean value of 24 hour creatinine clearance is 17 which has a statistically significant p value of less than 0.001.

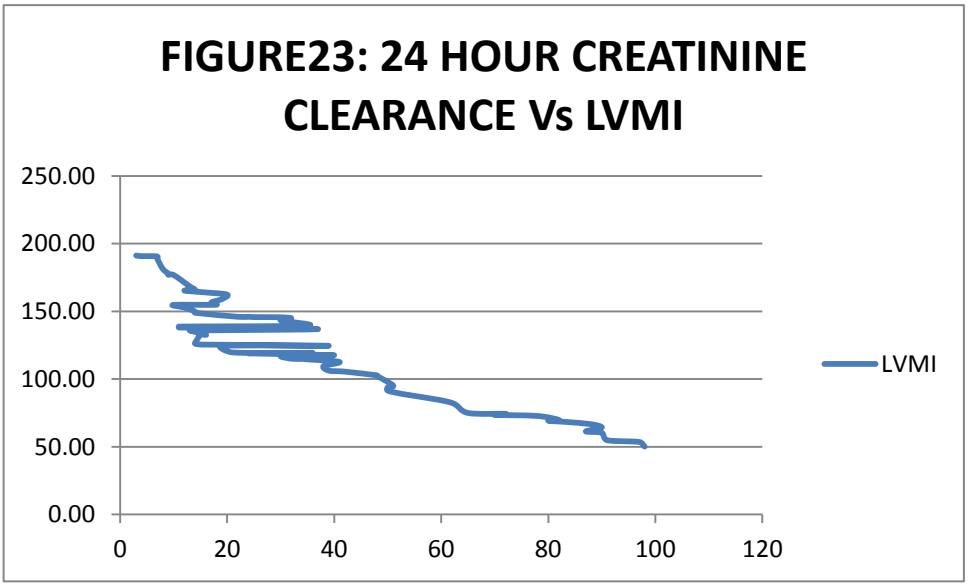


Figure 23 shows a line diagram comparing the variables, left ventricular mass index and 24 hour creatinine clearance.

The above chart confirms the hypothesis that a declining glomerular filtration rate has a significant correlation with the left ventricular mass index. The correlation is a negative correlation, showing the decrease in creatinine clearance, is associated with increasing ventricular mass.

TABLE 32: CREATININE CLEARANCE BY CCG VS LVMI

creatinine clearance (CCG)	LVMI	N	Mean	Std. deviation	p value
	Normal	29	61.17	15.531	<0.001
	Abnormal	46	17.39	9.332	

Table 32 compares the creatinine clearance levels (by Cockcroft Gault formula) in both the group of normal and increased left ventricular mass and the p value for the same. The creatinine clearance measured by Cockcroft Gault formula also had a significant difference in either of the group with a p value of less than 0.001 which is statistically highly significant. The mean value in the normal group is 61 and in the abnormal group are 17.

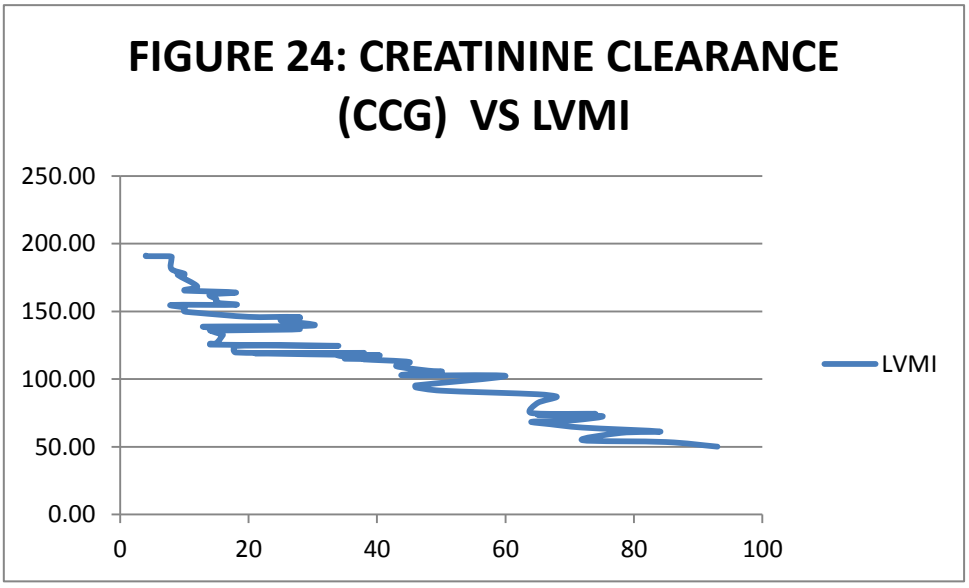


Figure 24 shows a line diagram comparing two variables, creatinine clearance and left ventricular mass index.

The creatinine clearance has a negative correlation with left ventricular mass index group. As the creatinine clearance declined, the ventricular mass index progressed which is suggested by the above chart.

TABLE 33: CREATININE CLEARANCE BY MDRD VS LVMI

creatinine clearance (MDRD)	LVMI	N	Mean	Std. deviation	p value
	Normal	29	58.69	14.912	<0.001
	Abnormal	46	17.09	9.904	

Table 33 compares the creatinine clearance levels (calculated by MDRD equation) in both the group of normal and increased left ventricular mass and the p value for the same.

When the creatinine clearance measured by MDRD equation is compared in either of the group, the mean clearance value is 58 in the normal group and in the increased LV mass group, the mean clearance value is 17 which has a statistically highly significant p value of less than 0.001.

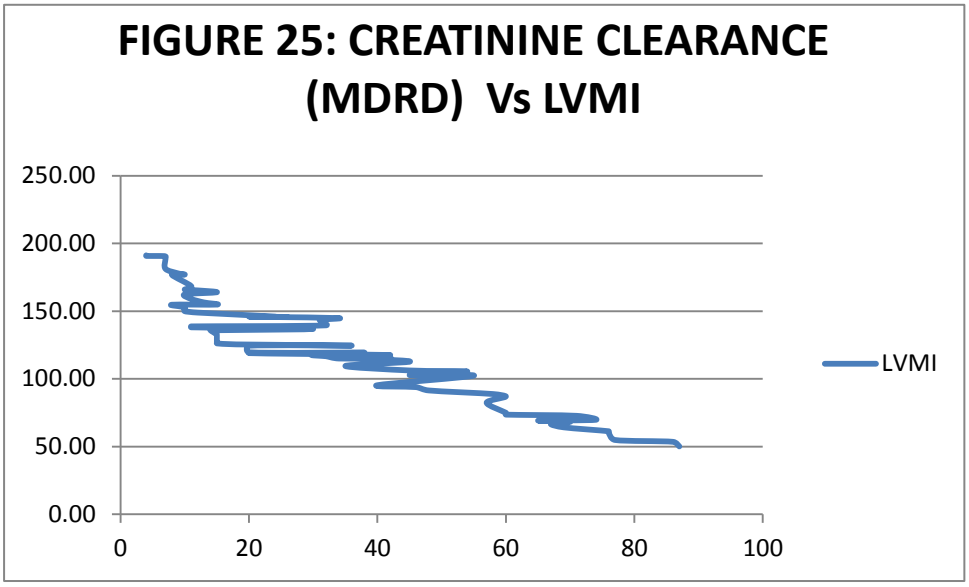


Figure 25 shows a line diagram comparing the variables, creatinine clearance and left ventricular mass index.

In this chart, there is progressive increase in left ventricular mass index group as the creatinine clearance kept decreasing showing a significant negative correlation between the two groups.

TABLE 34: URINE SPOT PCR VS LVMI

Urine spot PCR	**LVMI**	**N**	**Mean**	**Std. deviation**	**p value**
	Normal	29	1.8224	0.96362	<0.001
	Abnormal	46	10.8097	6.01479	

Table 34 compares the urine spot PCR ratio levels in both the group of normal and increased left ventricular mass and the p value for the same.

In the above table, a statistically significant p value of less than 0.001 was obtained between the two groups with regard to urine spot PCR. The mean value of spot PCR in the normal group was 1.8 and in the increased left ventricular mass group was, 10.8 thus identifying it as an independent predictor of increased left ventricular mass.

FIGURE 26: COMPARISON BETWEEN URINE SPOT PCR AND LVMI

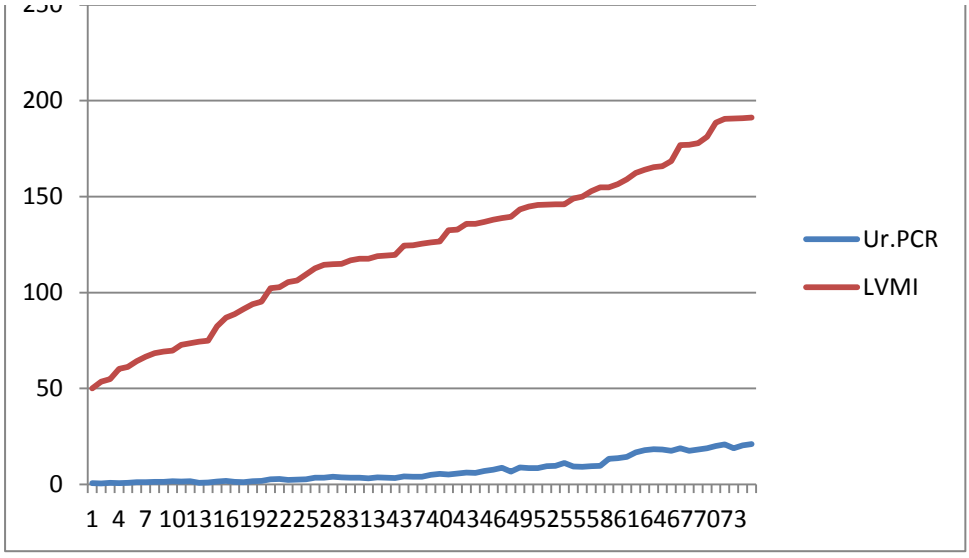


Figure 26 shows a line diagram comparing the variable, urine spot PCR ratio and left ventricular mass index.

The table shows the positive relation between the two variables, urine spot PCR and Left ventricular mass. As the amount of urine PCR increases, the left ventricular thickness increases.

TABLE 35: 24 HOUR PROTEINURIA VS LVMI

24 hour proteinuria	LVMI	N	Mean	Std. deviation	p value
	Normal	29	1821.62	969.84	<0.001
	Abnormal	46	8621.74	3457.595	

Table 35 compares the 24 hour proteinuria levels in both the group of normal and increased left ventricular mass and the p value for the same.

In the above table, there was a statistically significant difference in the variable proteinuria, when compared in the two groups of normal and abnormal/ increased left ventricular mass. The mean proteinuria in the group with normal LV mass was 1821 and in the left ventricular hypertrophy group was 8621 giving a highly significant p value of less than 0.001.

FIGURE 27: COMPARISON BETWEEN 24 HOUR PROTEINURIA AND LVMI

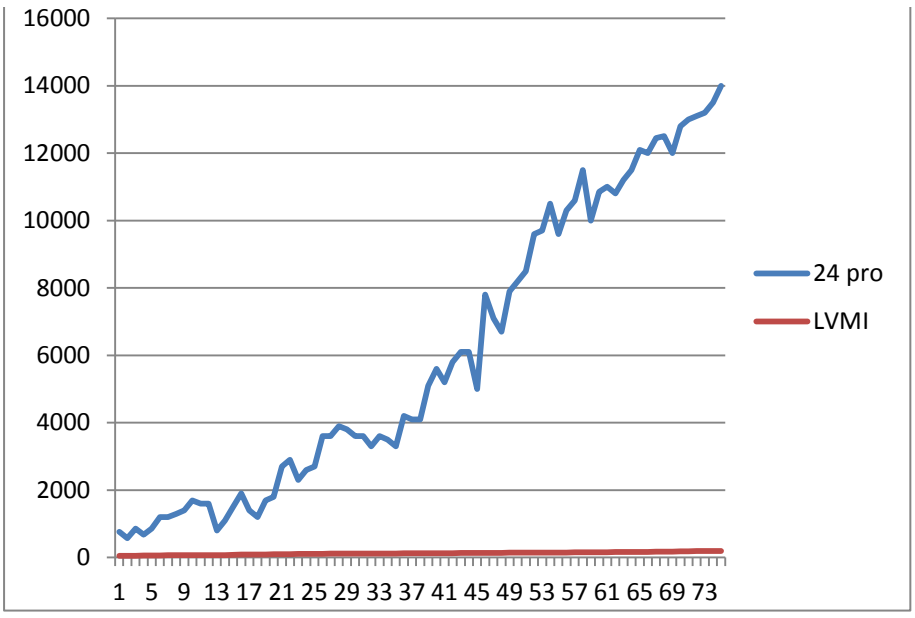


Figure 27 shows a line diagram comparing the variables, 24 hour proteinuria and left ventricular mass index.

The above chart shows the positive correlation between the amount of proteinuria and left ventricular mass, thus signifying its importance as an independent risk factor and predictor of left ventricular hypertrophy.

TABLE 36: BODY SURFACE AREA VS LVMI

Body surface area	**LVMI**	**N**	**Mean**	**Std. deviation**	**p value**
	Normal	29	1.5962	0.16146	0.713
	Abnormal	46	1.5996	0.18959	

Table 36 compares the variable, body surface area in both the group of normal and increased left ventricular mass and the p value for the same.

There was no significant difference between the two groups of normal and increased ventricular mass, when compared to the variable body surface area. The p value was not significant (0.713) indicating that the body surface area did not vary significantly between the two groups and it is not an predictor of left ventricular hypertrophy.

TABLE 37: CORRELATION BETWEEN SERUM CREATININE AND CREATININE CLEARANCE

		24 CrCl	**ECrCl**	**MDRD CrCl**
Serum creatinine	Sig. (2-tailed)	<0.001	<0.001	<0.001
	N	75	75	75

Table 37 shows the correlation between the variables, serum creatinine and creatinine clearance measured by various methods (24 hour creatinine clearance, Cockcroft Gault equation and MDRD equation)

TABLE 38: COMPARISON OF THE CREATININE CLEARANCE OBTAINED BY VARIOUS METHODS

		24 CrCl	**ECrCl**	**MDRD CrCl**
24 CrCl	Sig.(2 tailed)	-	<0.001	<0.001
	N	75	75	75
ECrCl	Sig.(2 tailed)	<0.001	-	<0.001
	N	75	75	75
MDRD CrCl	Sig.(2 tailed)	<0.001	<0.001	-
	N	75	75	75

Table 38 shows the comparison between the creatinine clearance of the study population obtained by various methods (24 hour creatinine clearance, Cockcroft Gault equation and MDRD equation)

The serum creatinine value showed a negative correlation with the creatinine clearance values measured by various methods. 24 hour creatinine clearance, Cockcroft Gault, MDRD equation clearance value decreased as serum creatinine values steered up. The correlation showed a highly significant p value less than 0.001.

TABLE 39: CORRELATION BETWEEN URINE SPOT PCR AND 24 HOUR URINE PROTEIN QUANTIFICATION

		24 hour proteinuria
Urine spot PCR	Sig. (2-tailed)	<0.001
	N	75

Table 39 shows the comparison between the variables, urine spot PCR and 24 hour proteinuria**.**

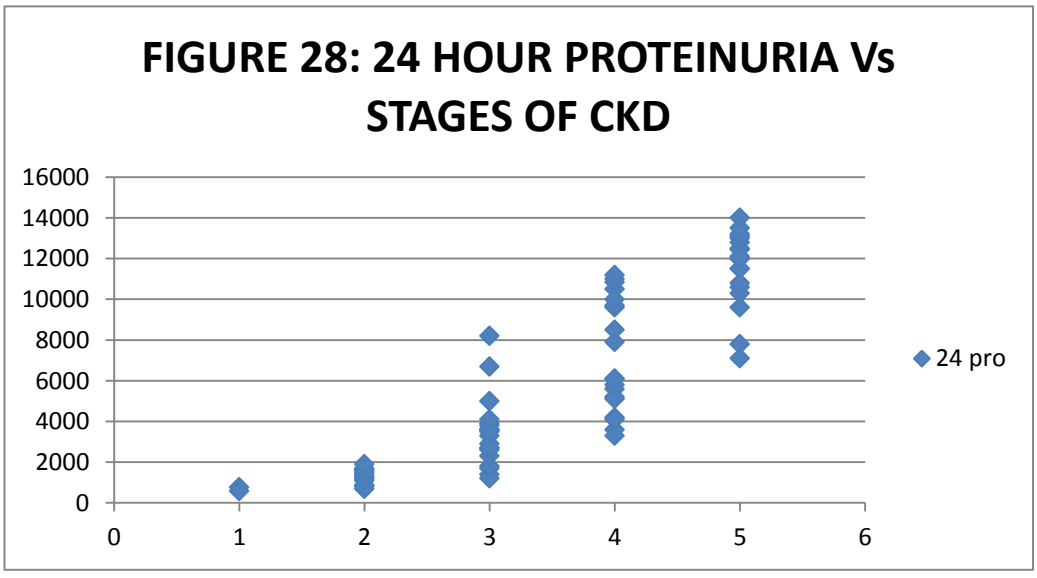


Figure 28 is a scatter diagram showing the distribution of the variable 24 hour proteinuria based on the stages of chronic kidney disease.

The correlation between the variables urine spot protein creatinine ratio and 24 hour proteinuria shows a highly significant p value of less than 0.001. This proves the reliability of using urine spot PCR value as a surrogate marker of 24 hours proteinuria.

TABLE 40: CORRELATION BETWEEN SERUM CREATININE AND PROTEINURIA

		Urine spot PCR	**24 hour proteinuria**
Serum Creatinine	Sig. (2-tailed)	<0.001	<0.001
	N	75	75

Table 40 shows the comparison of the variables urine spot PCR and 24 hour proteinuria with regard to serum creatinine.

In this table, serum creatinine values are compared with proteinuria (urine spot PCR and 24 hour proteinuria). There is a highly significant p value of less than 0.001 between the two variables, indicating the positive correlation that amount of proteinuria increases as serum creatinine increases.

TABLE 41: CORRELATION BETWEEN CREATININE CLEARANCE AND PROTEINURIA

		Urine spot PCR	**24 hour proteinuria**
24 Creatinine Clearance	Sig.(2 tailed)	<0.001	<0.001
	N	75	75
Creatinine Clearance (CCG)	Sig.(2 tailed)	<0.001	<0.001
	N	75	75
Creatinine Clearance (MDRD)	Sig.(2 tailed)	<0.001	<0.001
	N	75	75

Table 41 shows the comparison between the variables, urine spot PCR, 24 hour proteinuria and creatinine clearance obtained by various methods (24 hour creatinine clearance, Cockcroft Gault equation and MDRD equation)

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

In the above table, correlation between creatinine clearances measured by various methods is compared with proteinuria. The proteinuria quantification includes both urine spot protein creatinine ratio and the 24 hours urine proteinuria. The methods used for calculating creatinine clearance are 24

hour creatinine clearance, Cockcroft Gault equation and MDRD (Modified Diet in Renal Disease) equation. When the creatinine clearances measured are compared with the amount of protein excreted, there was a negative correlation. As the Glomerular filtration rate declined, the amount of proteinuria increased indicating end stage renal disease. The negative correlation was statistically significant with a p value of less than 0.001 which is highly significant.

DISCUSSION

DISCUSSION

Cardiovascular disease is the killer under the hood in chronic kidney disease. The incidence of adverse events and mortality due to cardiovascular causes in chronic kidney disease is fifteen times higher when compared to the normal population. When the underlying cause to this increased predisposition is analysed, left ventricular hypertrophy ideally known as uremic cardiomyopathy plays the major role. Hence, if the risk factors which increased the ventricular mass in a CKD patient could be identified; it could pave a way for preventing and delaying left ventricular hypertrophy and thereby cardiovascular mortality in these patients.

In our study, we included 75 cases of known chronic kidney disease on conservative management. The percentage of females in the study group was 46% and males were 53%. Patients with uncontrolled hypertension, on maintenance hemodialysis, on arteriovenous fistula and other factors which influenced the left ventricular mass independently were excluded from the study.

Investigation like serum albumin, alkaline phosphatase, total cholesterol and triglycerides, hemoglobin, serum urea and creatinine, creatinine clearance, urine spot PCR and proteinuria were measured in the study population.

The patients in the study had proteinuria ranging from physiological limits to nephrotic range and massive protein excretion. The glomerular filtration rate in the study population ranged from near normal to end stage renal disease. These variables were used to predict the risk for left ventricular hypertrophy in chronic kidney disease patients, which predicts future cardiovascular events.

Left ventricular hypertrophy was measured using 2D echocardiography by Devereux formula in the study population. Around 61% of the patients in this study had increased left ventricular mass on echocardiography.

The limit for left ventricular hypertrophy for females was > 110 g/m2and 60% of the female cases in the study had increased left ventricular mass. The mean GFR was 25 ml/min and mean proteinuria was > 3.5 g in females that was associated with left ventricular hypertrophy.

The cut-off for left ventricular hypertrophy in males was >134 g/m2 and 62.5% of the male cases had increased left ventricular mass according to Devereux Formula. The mean GFR was 20 ml/min and the mean proteinuria was more than 7 g.

AGE AND LVMI

In our study, there was no significant association between different age groups and increased left ventricular mass. Chronic kidney disease had an equal distribution among all the age groups in our study population. 14 patients are present in the age group 18-29. The number of patients in the age group 40-49 is 25. 18 people are there in both 30-39 age groups and 50-59 age groups, the aetiology being inherited and congenital in the younger age group, with diabetes and hypertension dominating the picture in the older age groups. The p value between the groups for the variable age was not statistically significant ($p = 0.912$).

But, in a study by **John D. Hamett et al** [95], the study showed that age was associated with the development of LVH after the initiation of dialysis. They found that cases that developed left ventricular hypertrophy were significantly older than controls at baseline; the reason cited was that the aging ventricle is more sensitive to the hypertrophic stimulus of an elevated systolic blood pressure.

In a similar study by **Lawrence P. McMahon et al** [99], age factor was found to contribute to the initial presence of LV hypertrophy. The effects of age contributed to disease progression through both an increase in large vessel stiffness and age relation reduction in glomerular filtration rate.

SEX AND LVMI

In our study, no gender variation was found between the two groups of normal and increased left ventricular mass. Almost equal number of male (53.33%) and female (46.67%) patients participated in the study. The left ventricular mass index calculated by Devereux formula, was based on body surface area which considerably reduced the gender bias due to body mass index. The mean left ventricular mass was taken as 110 g/m2 and above in females whereas in males, increased left ventricular mass was taken to be more than 138 g/m2 and above.Hence accounted for the gender bias, we did not find any significant association between the gender distributions of left ventricular hypertrophy in our patients. The p value was not statistically significant between the two groups (p = 0.824).

In a study by **Robert N. Foley et al** [98], male gender was found to have increased left ventricular mass compared to the female study population. The possible explanation was that the higher body mass index led to increased left ventricular mass in the male gender.

DURATIONOF THE DISEASE AND LVMI

In our study, left ventricular hypertrophy was found frequently in patients with longer duration of chronic kidney disease. The p value for the duration

of CKD in the two groups of normal and increased left ventricular mass was statistically significant (p = 0.028).

In a study by **Yilmaz BA et al** [102], left ventricular hypertrophy was found frequently among patients with longer duration of chronic kidney disease. The prevalence of left ventricular hypertrophy progressively increased as the duration of the disease increased

STAGE OF THE DISEASE AND LVMI

In our study, 61% of the study population had increased left ventricular mass in the predialysis period.In an article by **Kimura et al**, a Japanese journal, left ventricular hypertrophy which is a strong predictor of mortality in chronic kidney disease patients is present in over 70% of patients commencing dialysis.

In our study, the prevalence of left ventricular hypertrophy was 17.4% in stage 3 CKD, 41.3% in stage 4 and 41.3% in stage 5 CKD.The prevalence of LVH in the **Kimura et al study**was 22.7% in stage 3,43.6% in stage 4, and 48.3% in stage 5 (creatinine clearance > 10 mL/min) (p = 0.15)which tends to increase with progression of renal decline. Thus, from the above variables, a significant association was found between the stages of chronic kidney disease and left ventricular hypertrophy indicating a progressive decline in glomerular filtration rate as the disease progresses through the various stages.

DIABETES AND LVMI

In our study of 75 patients, 35 were diabetics. The number of diabetics with normal ventricular mass was 15 and those with increased LV mass were 20. No statistically significant correlation was found between the two groups with regard to the risk factor, diabetes (p = 0.486). Thus, presence of diabetes in the study did not influence the ventricular mass of the study population.

Similar finding was seen in the study by **Lawrence P. McMahon et al** [99], where presence of diabetes in the study population did not seem to influence left ventricular mass in any group.

SYSTEMIC HYPERTENSION AND LVMI

In our study population of 70, 40 patients were having hypertension (57%) and were on treatment for it. Of the 40 patients, 15 patients had normal ventricular mass and 25 patients had increased left ventricular mass. This correlation between the two group was not statistically significant (p = 0.824).

But, in the study by **Daniel E Jesuorobo et al** [96], most patients in the study population had hypertension (70.7%) and demonstrated a statistically significant difference in systolic blood pressure between those with and without left ventricular hypertrophy.

SYSTOLIC BLOOD PRESSURE AND LVMI

In our study, hypertensive patients who were under control with medications were taken as the study population; to eliminate the bias of uncontrolled hypertension inducing left ventricular hypertrophy. Elevated systolic blood pressure is a well-known independent factor for left ventricular mass index. But in our study, the risk factor was eliminated from the study population, so that the influence of the other risk factors for LVH could be studied well.

Thus, the mean systolic blood pressure in the normal group was 124.44 and in the abnormal group were 122.87. No statistically significant difference was found between the two groups ($p = 0.65$).

In a study by **Lawrence P. McMahon et al** [99], elevated systolic blood pressure was found to contribute to left ventricular hypertrophy. Both volume and pressure overload caused the twin processes of an increase in left ventricular cavity and wall thickness.

In the study by **Kosaku Nitta et al** [100], systolic blood pressure was independent risk factors for left ventricular hypertrophy.

In the study by **Yilmaz BA et al**[102], one of the independent predictor of the final left ventricular mass index was baseline day-time systolic blood pressure ($p = 0.01$)

DIASTOLIC BLOOD PRESSURE AND LVMI

In our study, the mean diastolic blood pressure in the normal group was 81.93 and in the abnormal/ increased left ventricular mass group was 79.87 which was not statistically significant (p = 0.131).Thus, the diastolic blood pressure in chronic kidney disease is not an independent risk factor for left ventricular hypertrophy as suggested in our study.

Similar results were seen in the study by **XueSen Cao et al** [97], where systolic blood pressure but not diastolic blood pressure was accepted as a risk factor for left ventricular hypertrophy in the hemodialysis population.

SERUM ALBUMIN AND LVMI

In our study population, the mean serum albumin value in the normal group was 2.934 and in the increased LV mass group was 2.781, thus there was no statistically significant difference between the either groups with regard to serum albumin level. Thus, the serum albumin did not independently predict the risk for left ventricular hypertrophy in chronic kidney disease patients in this study (p = 0.12).

In the study by **Kimura et al** [103], univariate analyses revealed that serum albumin was significantly different between the groups with and without left ventricular hypertrophy. Stepwise logistic regression analysis showed that

serum albumin was an independent risk factor for left ventricular hypertrophy.

SERUM CHOLESTEROL AND LVMI

In our study, the mean serum cholesterol in the normal LV mass group was 206.07 and in the abnormal left ventricular mass group was 198.52 which was not statistically significant for the two groups (p = 0.667). Thus, serum cholesterol level did not independently predict the risk for left ventricular hypertrophy in CKDIn the study by **Daniel E Jesuorobo et al** [96], variable like total cholesterol, HDL-cholesterol and LDL-cholesterol had significantly higher mean values in patients compared with controls but none had any correlation with left ventricular mass index similar to our study results.

SERUM TRIGLYCERIDES AND LVMI

In our study population, the mean triglycerides level in the normal left ventricular mass group was 166.24 and in the abnormal group was 167.07 which did not have a statistically significant correlation between the either groups (p = 0.895).

In the study by **Daniel E Jesuorobo et al**[96], variable like serum triglycerides had significantly higher mean values in patients compared with controls but none had any correlation with left ventricular mass index similar to our study.

SERUM ALKALINE PHOSPHATASE AND LVMI

In our study population, the mean level of serum alkaline phosphatase in the normal group was 285.86 and in the abnormal left ventricular mass group was 290.65 which was not statistically significant. The p value for this correlation was 0.451 and thus serum ALP did not independently predict the risk for left ventricular hypertrophy.

But in the study by **Harnett J.D. et al**[101], the most important factor which independently related to left ventricular hypertrophy in all the patients studied, using multiple logistic regression was serum alkaline phosphatase which probably reflects hyperparathyroidism ($p = 0.03$). In a subset of patients with severe left ventricular hypertrophy (left ventricular wall thickness > 1.4 cm), a high serum alkaline phosphatase level was the best predictor of LVH ($p < 0.001$).

HEMOGLOBIN AND LVMI

In our study, the mean hemoglobin value in the normal group was 8.33 and in the abnormal group was 8.44 which did not have a statistically significant relation in either groups ($p = 0.406$). Thus in this study, the severity of anaemia did not predict the left ventricular dimension and thickness

In the study by**Daniel E Jesuorobo et al** [96], the hemoglobin levels of the study population had a negative correlation with left ventricular mass index and it was statistically significant.

BLOOD UREA AND LVMI

No significant correlation was found between the amount of blood urea and the left ventricular wall thickness in chronic kidney disease. The mean serum urea concentration in the normal group was 76.97 and in the abnormal increased LV mass group was 36.531 which did not hold a statistically significant relation ($p = 0.41$).

SERUM CREATININE AND LVMI

Our study population had significant difference in serum creatinine between the two groups. The mean serum creatinine in the normal LV group was 1.873 and in the increased left ventricular mass group were 6.515. These two groups had a statistically highly significant difference with regard to serum creatinine ($p = <0.001$). Thus serum creatinine value is an independent predictor for the risk of left ventricular hypertrophy in chronic kidney disease patients.

Similar findings were obtained in a study by **Harnett J.D.et al** [101], where one of the most important factor associated with LVH in chronic kidney disease was high serum creatinine.

GLOMERULAR FILTRATION RATE AND LVMI

In our study, we found a statistically high significant correlation between declining GFR (Stage 4/5) with increased left ventricular thickness in chronic kidney disease patients. The mean glomerular filtration rate in the normal group was 58 – 64 ml/min and in the increased left ventricular mass group, the mean GFR value was 17 ml/min, giving a high significant statistical correlation between the two groups ($p = <0.001$). Thus, there was a strong negative correlation between glomerular filtration rate and left ventricular hypertrophy, the declining GFR being an important and independent predictor of increased left ventricular mass index.

In a study by **Daniel E Jesuorobo et al** [96], estimated glomerular filtration rate correlated negatively with left ventricular mass index and also emerged the strongest predictor of LVMI in patients with CKD accounting for 24.1% of the variation in LVMI.

In the study by **XueSen Cao et al** [97], even in the predialysis population, the prevalence of LVH increases with progressive decline in renal function.

In the study by **Lawrence P. McMahon et al** [99], low glomerular filtration rate contributed to the initial presence of left ventricular hypertrophy.

In the study by **Yilmaz BA et al** [102], the independent predictor of the left ventricular mass index was decrease in the glomerular filtration rate (p =

0.002). Left ventricular hypertrophy is quite frequent among patients with stage 3 or 4 chronic kidney disease, and its prevalence increases while glomerular filtration rate decreases during the follow-up.

PROTEINURIA AND LVMI

In our study, the mean urine spot PCR value in the normal group was 1.8 and in the increased left ventricular mass group was 10.8 which had a highly significant statistical correlation with a p value less than 0.001. Similarly in the study by **Emily P. McQuarrie et al** [104], proteinuria was significantly and independently associated with left ventricular mass index patients with chronic kidney disease. This relationship was independent of the baseline systolic blood pressure. Urine spot PCR values had a significant correlation with the left ventricular hypertrophy in Emily McQuarrie study.

Regarding 24 hour proteinuria excretion, in our study, the mean proteinuria in the normal group was 1821 mg and in the abnormal group was 8621 mg which had a highly significant p value of less than 0.001. This positive correlation had a statistically significant relation**. Emily P. McQuarrie et al** study also found a significant correlation of 24 hour proteinuria with left ventricular hypertrophy in chronic kidney disease.

BODY SURFACE AREA AND LVMI:

No significant correlation was found between the left ventricular thickness and body surface area. The mean BSA in the normal group was1.5962 and in the abnormal group was 1.5996, showing no significant correlation between the two groups ($p = 0.713$).

SERUM CREATININE AND PROTEINURIA

According to our study, there was a highly significant statistical correlation between the serum creatinine value and the amount of proteinuria (urine spot PCR & 24 hour proteinuria) in chronic kidney disease. As the stage of the CKD worsened, both the serum creatinine and the quantity of protein excretion exponentially increase. The p value for the two groups is statistically highly significant ($p = <0.001$).

CREATININE CLEARANCE AND PROTEINURIA

According to our study, there was a negative correlation between the glomerular filtration rate and the amount of protein excreted. As the glomerular filtration rate decreases, the quantity of protein excreted increases progressively. There was a highly significant correlation between the glomerular filtration rate and urine spot PCR ($p = <0.001$). Also, the 24 hour proteinuria showed a significant correlation with that of the glomerular filtration rate, p value being less than 0.001.

LIMITATIONS OF THE STUDY

LIMITATION OF THE STUDY

1. This study is done in a small number of patients. Study in a large sample of population is further needed.

2. Chronic kidney disease patients who were managed on conservative management were the subjects of this study. Thus, the effect of hemodialysis and its effect on left ventricular thickness could not be obtained from this study.

3. Early diagnosis of diseases like diabetes, hypertension and chronic kidney disease is not possible in all the patients. Hence the duration of the underlying risk factors, control of the blood pressure and glycaemic prior to the treatment could not be commented.

4. The left ventricular wall thickness is best measured by the cardiac MRI study. LVMI measured by 2D echocardiography has a lower sensitivity when compared to the gold standard investigation.

5. The left ventricular thickness measured by 2D echocardiography is prone for inter observer variations.

6. A follow up study measuring and monitoring the left ventricular mass regularly in chronic kidney disease was not done, which could have provided valuable information in the treatment and management of uremic cardiomyopathy of chronic kidney disease patients.

CONCLUSION

CONCLUSION

- Glomerular filtration rate and the amount of proteinuria significantly influence the left ventricular wall thickness in chronic kidney disease patients.
- Declining GFR had a strong negative correlation with left ventricular mass, where the amount of protein excreted positively predicted the significant risk of left ventricular hypertrophy in these patients.
- These predictors of LV mass could be easily measured and are highly sensitive and specific for the same.
- Hence routine measurement of these variables, and its correlation to left ventricular thickness could be easily ascertained compared to the costly investigations like cardiac MRI and Echocardiography.
- On arriving at a suspicion of possible LV hypertrophy, rigorous measures to reduce protein excretion and frequent hemodialysis session could improve the patients' survival from the deadly cardiovascular diseases.

DISCLOSURE

The investigator has not received any form of grants or support from any institution or pharmaceutical company.

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ANNEXURES

DATA COLLECTION

FORM

HISTORY

1. NAME :

2. AGE :

3. SEX :

4. OCCUPATION :

5. LOCATION :

6. CHRONIC KIDNEY DISEASE: Conservative management

Haemodialysis (arteriovenous fistula)

Haemodialysis (jugular access)

Peritoneal dialysis

Renal transplant

7. COMORBIDITY

DIABETES

SYSTEMIC HYPERTENSION

CORONARY HEARTDISEASE

CEREBROVASCULAR ACCIDENT

PULMONARY TUBERCULOSIS

BRONCHIAL ASTHMA/ COPD

CHRONIC PULMONARY DISEASE

EPILEPSY

CHRONIC LIVER DISEASE

8. SMOKING :

9. ALCOHOL USE :

10. MAJOR SURGERY :

11. MAJOR TRAUMA :

12. DRUG INTAKE :

EXAMINATION

BLOOD PRESSURE

- SYSTOLIC BLOOD PRESSURE :
- DIASTOLIC BLOOD PRESSURE :
- PULSE PRESSURE :
- MEAN ARTERIAL PRESSURE :

PULSE RATE :

CARDIOVASCULAR SYSTEM :

RESPIRATORY SYSTEM :

GASTROINTESTINAL SYSTEM :

CENTRAL NERVOUS SYSTEM :

PALLOR :

ICTERUS :

CLUBBING :

CYANOSIS :

PEDAL EDEMA :

SIGNIFICANT LYMPHADENOPATHY :

HEIGHT :

WEIGHT :

BODY MASS INDEX :

BODY SURFACE AREA :

WAIST CIRCUMFERENCE :

HIP CIRCUMFERENCE :

WAIST HIP RATIO :

INVESTIGATIONS

COMPLETE BLOOD COUNT

- Total count :
- Differential count :
- Haemoglobin :
- Platelet count :
- Erythrocyte sedimentation rate :

RENAL FUNCTION TEST

- Random blood sugar :
- Blood urea :
- Serum creatinine :

URINE EXAMINATION

- Albumin :
- Sugar :
- Deposits :
- Urine spot PCR :
- 24 hours proteinuria :
- 24 hour creatinine clearance :

LIVER FUNCTION TEST

- Total protein :
- Serum albumin :
- Serum globulin :
- Serum alkaline phosphatase :
- Serum bilirubin :

LIPID PROFILE

- Serum total cholesterol :
- Serum triglycerides :

SERUM PHOSPHORUS :

ELECTROCARDIOGRAM :

eGFR :

K/ DOQI STAGING :

ECHOCARDIOGRAM

- INTERVENTRICULAR SEPTAL THICKNESS IN DIASTOLE (IVSDd)
- LEFT VENTRICULAR INTERNAL DIAMETER IN DIASTOLE (LVIDd)
- LEFT VENTRICULAR INTERNAL DIAMETER IN SYSTOLE (LVIDs
- LEFT VENTRICULAR POSTERIOR WALL THICKNESS IN DIASTOLE (LVPWDd)
- EJECTION FRACTION (EF)
- FRACTIONAL SHORTENING (FS)
- LEFT VENTRICULAR MASS (LVM)(Devereux formula)
- LEFT VENTRICULAR MASS INDEX (BSA)
- LEFT VENTRICULAR MASS (HEIGHT)
- RELATIVE WALL THICKNESS (RWT)
- CONCENTRIC/ ECCENTRIC LVH
- SYSTOLIC DYSFUNCTION
- DIASTOLIC DYSFUNCTION

MASTER CHART

NO	NAME	AGE	SE	Du	DM	SHT	SBP	DBP	Sr.Alb	Hb	Sr. AL	CHOL	TGL	B. UR	B.CR	24CrCl	ECrC	MDRD	stage	Ur.PCR	24 pro	LV MASS	BSA	LVMI
1	pooncholai	35	F	3	no	no	118	84	3.2	9	200	118	100	29	0.8	98	93	87	1	0.76	762	67.4693	1.34629	50.11
2	Rajendran1	46	M	2	yes	yes	140	86	3	8	220	273	153	42	1	97	85	86	1	0.57	571	95.0356	1.7756	53.52
3	madurai	45	M	3	yes	yes	138	90	2.8	9.5	210	320	157	52	1.1	91	72	77	2	0.85	855	80.4922	1.4699	54.87
4	Subramani	39	M	1	yes	yes	128	80	2.6	8.4	180	278	297	68	0.9	90	78	76	2	0.68	682	100.01	1.6586	60.30
5	kaliammal	32	F	5	no	no	116	80	2.4	7.5	200	120	125	100	1.2	87	84	76	2	0.86	857	99.8191	1.6278	61.32
6	rathnammal	56	F	3	yes	yes	134	84	3.4	6	240	167	218	34	0.9	90	72	69	2	1.18	1200	105.502	1.6431	64.21
7	Sarada	45	F	1	yes	no	118	86	2.5	9.5	280	247	188	210	1.1	88	67	67	2	1.21	1200	109.838	1.64766	66.66
8	subaidha	54	F	4	yes	no	136	86	3.5	8	360	216	260	39	1.2	83	64	70	2	1.35	1300	116.845	1.7076	68.43
9	Meena	24	F	4	no	no	114	80	3.4	9.5	400	120	145	130	1.5	80	68	65	2	1.44	1400	103.621	1.4977	69.19
10	Manickam	54	M	4	yes	yes	132	84	3.5	8.4	280	169	162	40	1.1	82	71	74	2	1.67	1700	96.2175	1.3579	69.77
11	Ponraj	46	M	5	yes	yes	138	88	3.2	8.4	250	223	119	58	1.4	78	75	71	2	1.58	1600	129.888	1.786	72.73
12	vembu	30	F	4	no	no	132	80	3	6.4	290	127	165	28	1.5	70	65	60	2	1.64	1600	91.2614	1.2402	73.59
13	vijayakumar	25	M	2	no	no	100	70	2.8	7.5	310	150	80	110	1.5	72	74	60	2	0.8	800	124.83	1.678	74.39
14	hazira begur	48	F	3	yes	no	110	76	2.8	7	380	284	218	80	1.9	65	64	60	2	1.06	1100	134.283	1.791	74.98
15	Meera	24	F	2	no	no	106	70	3	6	420	145	150	46	1.8	62	65	57	2	1.5	1500	122.729	1.4896	82.39
16	rajendran2	34	M	5	yes	no	118	78	2.8	8.4	240	280	210	61	2	56	68	60	2	1.9	1900	150.627	1.732	86.97
17	Srinivas	35	M	4	yes	no	120	80	3.2	10	350	301	169	87	2.1	53	65	58	3	1.45	1400	165.556	1.8643	88.80
18	swarnam	54	F	3	yes	yes	136	86	3.5	8.4	360	378	137	27	2	50	50	48	3	1.16	1200	150.484	1.6456	91.45
19	veerammal	32	F	4	no	no	108	74	2.8	8.4	330	120	120	180	2.3	50	46	46	3	1.75	1700	138.414	1.47381	93.92
20	Vananakshat	45	F	3	yes	no	140	90	3.2	8	420	217	178	39	2.2	51	46	40	3	1.85	1800	168.179	1.7643	95.32
21	amaresan	50	M	4	yes	yes	102	78	2.4	9.8	410	213	274	120	2.4	48	60	55	3	2.69	2700	161.488	1.57759	102.36
22	zarina	54	F	3	yes	yes	114	74	2.1	8.2	190	196	168	180	2.5	48	44	45	3	2.88	2900	178.405	1.736	102.77
23	Surendar	36	M	3	no	yes	136	84	3	9.6	200	200	188	100	2.6	42	50	54	3	2.33	2300	154.443	1.4643	105.47
24	Pitchai	50	M	4	no	yes	124	82	2.5	8.4	220	140	135	58	2.5	39	48	45	3	2.6	2600	180.483	1.6989	106.23
25	desamma	40	F	5	no	no	132	80	2.8	9.4	240	180	168	58	2.4	38	43	35	3	2.67	2700	147.458	1.3462	109.54

26	Mariappan	36	M	3	no	yes	130	90	2.4	8.6	260	229	130	80	2.6	41	45	45	3	3.56	3600	176.633	1.5678	112.66
27	annakilli	52	F	4	yes	yes	140	86	3.2	9.2	280	249	174	90	2.9	35	38	40	3	3.57	3600	192.801	1.6832	114.54
28	Srimathi	27	F	3	no	no	120	80	3.4	8.8	300	136	140	110	3	34	40	42	3	4	3900	161.735	1.40786	114.88
29	amsa	48	F	4	yes	yes	116	78	2.7	8	320	298	178	120	3.5	32	35	34	3	3.75	3800	197.469	1.71656	115.04
30	Mohana	50	F	5	no	yes	134	84	2.6	9.6	420	185	140	70	3.1	30	35	32	3	3.6	3600	208.443	1.7857	116.73
31	Selvarani	36	F	1	yes	no	126	82	3	9.4	400	200	150	145	3.2	32	34	30	3	3.59	3600	186.36	1.5851	117.57
32	James	45	M	5	no	yes	136	86	2.4	8	380	216	88	80	2.8	40	40	42	3	3.25	3300	160.876	1.3676	117.63
33	Mary	21	F	2	no	no	104	74	2.8	7.8	360	120	150	150	3.2	24	21	20	4	3.64	3600	159.057	1.3365	119.01
34	mani	38	M	5	no	yes	126	80	3	8.4	240	189	164	40	2.9	36	38	38	3	3.52	3500	194.702	1.6309	119.38
35	Sumangali	56	F	4	yes	yes	132	82	3.1	8	280	219	163	56	3.5	21	18	20	4	3.31	3300	162.548	1.3583	119.67
36	mariammal	24	F	2	no	no	110	80	2.5	7	220	145	180	90	3.7	19	18	20	4	4.2	4200	179.635	1.4432	124.47
37	velu	43	M	5	no	yes	130	90	2.6	9	230	160	155	56	4.1	39	34	36	3	4.09	4100	212.129	1.7029	124.57
38	Marudhamm	51	F	3	yes	yes	140	90	2.6	8.4	340	171	316	84	4	15	14	18	4	4.1	4100	207.364	1.6527	125.47
39	sampoornan	45	F	5	yes	yes	110	74	2.4	6.9	220	215	118	91	4.7	14	14	15	4	5.1	5100	211.174	1.6733	126.20
40	Sangeetha	34	F	2	no	no	106	80	2.5	8.1	240	159	158	53	4.6	14	15	15	4	5.56	5600	221.539	1.74922	126.65
41	Vimala	37	F	3	no	no	104	74	2.5	5.7	290	246	128	65	4.2	15	16	15	4	5.23	5200	242.965	1.83301	132.55
42	Latha	35	F	4	yes	no	110	76	3	6.4	320	152	114	39	4.4	16	16	15	4	5.76	5800	193.66	1.4585	132.78
43	Pooranam	54	F	5	yes	yes	140	86	3.4	8.4	250	183	226	86	4.6	13	14	14	4	6.14	6100	253.184	1.8637	135.85
44	Palaniamma	26	F	3	no	no	98	70	3.2	9.6	190	100	110	70	4.9	13	15	14	4	6.07	6100	181.734	1.33746	135.88
45	ArivudaiNan	32	M	4	no	yes	124	82	3.1	10	260	187	150	110	4.9	37	28	30	3	7	5000	256.044	1.87057	136.88
46	Kalyani	26	F	2	no	no	110	74	2.5	9.4	270	120	106	75	5	11	14	11	5	7.76	7800	182.59	1.3225	138.06
47	Sheela	45	F	1	yes	no	128	80	2.6	8.8	300	168	118	85	5.2	11	13	11	5	8.75	7100	242.983	1.75098	138.77
48	Iqbal Basha	46	M	3	no	yes	138	86	2.7	9.5	280	176	250	80	5.3	35	30	32	3	6.74	6700	257.818	1.84763	139.54
49	john peter	48	M	2	no	yes	140	84	2.8	8.8	290	210	124	105	5.4	30	25	31	4	8.86	7900	230.281	1.6062	143.37
50	Manohar	46	M	2	no	yes	134	80	2.8	9	200	187	150	100	5.5	32	28	34	3	8.55	8200	200.777	1.3856	144.90

51	Sambanthan	42	M	3	no	yes	130	78	2.1	8.8	300	152	114	98	5.7	30	25	24	4	8.5	8500	299.523	2.05646	145.65
52	Jeganathan	47	M	5	yes	yes	128	76	2.4	8.4	280	220	106	140	5.8	25	28	26	4	9.57	9600	252.111	1.73094	145.77
53	Jeyakumar	25	M	2	no	no	108	80	2.6	8.6	310	100	180	200	6	24	26	20	4	9.72	9700	263.146	1.80249	145.99
54	Suresh	47	M	5	yes	no	116	80	2.7	9.4	210	189	264	80	6.2	22	20	24	4	11.25	10500	242.532	1.66129	145.99
55	Parveen Ban	43	F	4	yes	yes	140	86	2.7	9.5	260	219	163	78	6.5	14	12	12	5	9.375	9600	239.902	1.61051	148.96
56	Chandra	50	F	5	yes	yes	134	80	3	9.6	320	173	218	60	6.5	14	10	10	5	9.23	10300	267.442	1.78342	149.96
57	Ganga	43	F	1	no	yes	130	80	3.2	8	220	160	155	68	6.9	12	10	10	5	9.6	10600	242.276	1.5854	152.82
58	Rajkumari	56	F	5	yes	no	128	84	3.4	9	240	171	316	70	7	10	8	8	5	9.736	11500	263.403	1.7019	154.77
59	Sahul Hamee	28	M	4	no	no	110	76	3.5	9	330	128	159	80	7.2	18	18	15	4	13.39	10000	219.968	1.42025	154.88
60	Kolandaivel	48	M	4	no	yes	140	86	2.4	7.6	230	273	153	38	7.4	17	15	13	4	13.75	10850	228.151	1.4583	156.45
61	kuppan	45	M	6	no	yes	138	84	2.8	6.5	340	320	157	102	7.8	19	15	11	4	14.44	11000	244.351	1.5365	159.03
62	eswaran	49	M	6	yes	yes	126	80	2.4	8	240	278	297	130	8	20	14	10	5	16.67	10800	253.125	1.5585	162.42
63	Deenadayala	39	M	2	yes	no	136	84	2.6	8.4	350	190	219	65	8.2	16	18	15	4	17.83	11200	270.147	1.64744	163.98
64	Raman	37	M	3	no	yes	118	72	2.4	9	220	167	162	43	8.1	12	10	12	5	18.41	11500	222.528	1.3458	165.35
65	Subramani	52	M	6	no	yes	100	76	2.8	6.8	250	226	118	48	8.5	14	10	10	5	18.18	12100	284.656	1.71605	165.88
66	Ganesh	29	M	4	no	no	120	78	3	7.4	360	320	150	80	8.7	13	12	11	5	17.5	12000	209.886	1.24567	168.50
67	Dorairaj	48	M	6	yes	yes	116	74	3.12	6.1	200	265	267	110	9	10	9	8	5	18.91	12450	313.247	1.77096	176.88
68	Palani	22	M	2	no	no	120	80	3.2	8.4	370	98	110	62	9.4	9	10	10	5	17.5	12500	293.538	1.6585	176.99
69	Vasu	25	M	2	no	no	110	70	3.4	8.6	260	101	120	120	9.5	9	10	9	5	18.18	12000	239.862	1.3484	177.89
70	Chinnasamy	56	M	8	yes	no	138	80	2.8	9	380	184	182	58	9.8	8	8	7	5	18.91	12800	279.741	1.5432	181.27
71	Ravi	56	M	7	no	yes	140	90	2.5	9.4	190	378	137	180	10	7	8	7	5	20	13000	329.794	1.7492	188.54
72	Chelladurai	37	M	5	yes	no	118	74	2.6	9.6	390	223	119	145	11	7	8	7	5	20.91	13100	337.547	1.77227	190.46
73	Dilli Babu	51	M	6	no	yes	124	80	2.4	9.2	270	301	169	110	12	6	7	6	5	18.96	13200	264.329	1.3856	190.77
74	ameerudin	19	M	2	no	no	100	78	2.8	8.4	420	223	119	150	13	4	4	4	5	20.45	13500	261.244	1.3693	190.79
75	Sheik Mujibu	48	M	3	yes	yes	120	86	3	8.4	400	247	188	120	13	3	4	4	5	21	14000	278.579	1.4567	191.24

Dur - Duration

DM - Diabetes Mellitus

SHT - Systemic Hypertension

B.U - Blood Urea (mg/dL)

B.Cr - Blood Creatinine (mg/dL)

24CrCl - 24 hour Creatinine Clearance (ml/min)

ECrCl - Estimated Creatinine Clearance using Cockcroft Gault Formula (ml/min)

MDRD - Estimated Creatinine Clearance using Modified Diet in Renal Disease formula (ml/min)

Ur.PCR - Urine Spot Protein Creatinine Ratio

24 pro - 24 hours proteinuria (mg/dL)

LVmass - Left Ventricular Mass (g)

BSA - Body Surface Area (m2)

LVMI - Left Ventricular Mass Index (g/m2)

ABBREVIATIONS

ABBREVIATIONS

CKD	Chronic Kidney Disease
GFR	Glomerular Filtration Rate
PCR	Protein Creatinine Ratio
LVMI	Left Ventricular Mass Index
NFK	National Kidney Foundation
KDOQI	Kidney Disease Outcomes Quality Initiative
ESRD	End Stage Renal Disease
DM	Diabetes Mellitus
HT	Hypertension
CVD	Cardio Vascular Disease
LVH	Left Ventricular Hypertrophy

CAD	Coronary Artery Disease
mTOR	Mammalian Target Of Rapamycin
2D/3D	2 Dimensional/ 3 Dimensional
CT	Computed Tomography
CMRI	Cardiac Magnetic Resonance Imaging
NTproBNP	N Terminal Prohormone Brain Natriuretic Peptide
Trop T	Troponin T
ACE	Angiotensin Converting Enzyme
ARB	Angiotensin Receptor Blocker
RAS	Renin Angiotensin System
LDL	Low Density Cholesterol
Na+ K+ ATPase	Sodium Potassium Adenosine TriPhosphatase
PI3K	Phospho – inositide 3 Kinase
PPAR	Peroxisome Proliferator Activated Receptor

ERK	Extracellular signal- Related Kinases
CTS	Cardio tonic Steroids
ET 1	Endothelin 1
PTH	Parathormone
IL 1α	Interleukin 1-alpha
IL 6	Interleukin 6
TNFα	Tumour Necrosis Factor – alpha
AT II	Angiotensin II
HDL	High Density Cholesterol
LV	Left Ventricle
TGF	Transforming Growth Factor

MDRD formula - Modification of Diet in Renal Disease formula

ETHICAL COMMITTEE

CLEARANCE CERTIFICATE

INSTITUTIONAL ETHICAL COMMITTEE
GOVT.KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Ref.No.2318/ME-1/Ethics/2012 Dt:04.04.2013
CERTIFICATE OF APPROVAL

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "A Study on eGFR and Proteinuria – Predictors of left ventricular mass in chronic kidney disease" – For Research Work.submitted by Dr.M.Jeniffer Sinekalatha, MD (GM), PG Student, Govt. Royapettah Hospital, Chennai-14.

The Proposal is APPROVED.

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

29/5/13.

CHAIRMAN,
Ethical Committee
Govt.Kilpauk Medical College,Chennai

GOVT. KILPAUK MEDICAL COLLEGE * Kilpauk, Chennai-10. * 29 MAY 2013

A

PATIENT CONSENT FORM

நோயாளி ஒப்புதல் படிவம்

ஆராய்ச்சியின் விவரம்:

ஆராய்ச்சி மையம்: அரசு கீழ்பாக்கம் மருத்துவக் கல்லூரி மருத்துவமனை

நோயாளியின் பெயர்: நோயாளியின் வயது:

பதிவு எண்:

1. மேற்குறிப்பிட்டுள்ள ஆராய்ச்சியின் நோக்கத்தையும் பயனையும் முழுவதுமாக புரிந்துகொண்டேன். மேலும் எனது அனைத்து சந்தேகங்களையும் கேட்டு அதற்கான விளக்கங்களையும் தெளிவுபடுத்திக் கொண்டேன்.
2. மேலும் இந்த ஆராய்ச்சிக்கு எனது சொந்த விருப்பத்தின் பேரில் பங்கேற்கிறேன் என்றும், மேலும் எந்த நேரத்திலும் எவ்வித முன்னறிவிப்புமின்றி இந்த ஆராய்ச்சியிலிருந்து விலக முழுமையான உரிமை உள்ளதையும், இதற்கு எவ்வித சட்ட பிணைப்பும் இல்லை என்பதையும் அறிவேன்.
3. ஆராய்ச்சியாளரோ, ஆராய்ச்சி உதவியாளரோ, ஆராய்ச்சி உபயத்தாரோ, ஆராய்ச்சி பேராசிரியரோ, ஓழுங்குநெறி செயற்குழு உறுப்பினர்களோ எப்போது வேண்டுமானாலும் எனது அனுமதியின்றி எனது உள்நோயாளி பதிவுகளை இந்த ஆராய்ச்சிக்காகவோ அல்லது எதிர்கால பிற ஆராய்ச்சிகளுக்காகவோ பயன்படுத்திக்கொள்ளலாம் என்றும் மேலும் இந்த நிபந்தனை நான் இவ்வராய்ச்சியிலிருந்து விலகினாலும் தகும் என்றும் ஒப்புக்கொள்கிறேன். ஆயினும் எனது அடையாளம் சம்பந்தப்பட்ட எந்த பதிவுகளும் (சட்டபூர்வமான தேவைகள் தவிர) வெளியிடப்படமாட்டது என்ற உறுதிமொழியின் பெயரில் இந்த ஆராய்ச்சியிலிருந்து கிடைக்கப்பெறும் முடிவுகளை வெளியிட மறுப்பு தெறிவிக்கமாட்டேன் என்று உறுதியளிக்கின்றேன்.

4. இந்த ஆராய்ச்சிக்கு நான் முழுமனதுடன் சம்மதிக்கின்றேன் என்றும் மேலும் ஆராய்ச்சிக் குழுவினர் எனக்கு அளிக்கும் அறிவுரைகளை தவறாது பின்பற்றுவேன்

என்றும் உறுதியளிக்கின்றேன்.

5. இந்த ஆராய்ச்சிக்குத் தேவைப்படும் அனைத்து மருத்துவப் பரிசோதனைகளுக்கும் ஒத்துழைப்பு தருவேன் என்று உறுதியளிக்கின்றேன்.
6. இந்த ஆராய்ச்சிக்கு யாருடைய வற்புறுத்தலுமின்றி எனது சொந்த விருப்பத்தின் பேரிலும் சுயஅறிவுடனும் முழுமனதுடனும் சம்மத்திக்கின்றேன் என்று இதன் □ லம் ஒப்புக்கொள்கிறேன்.

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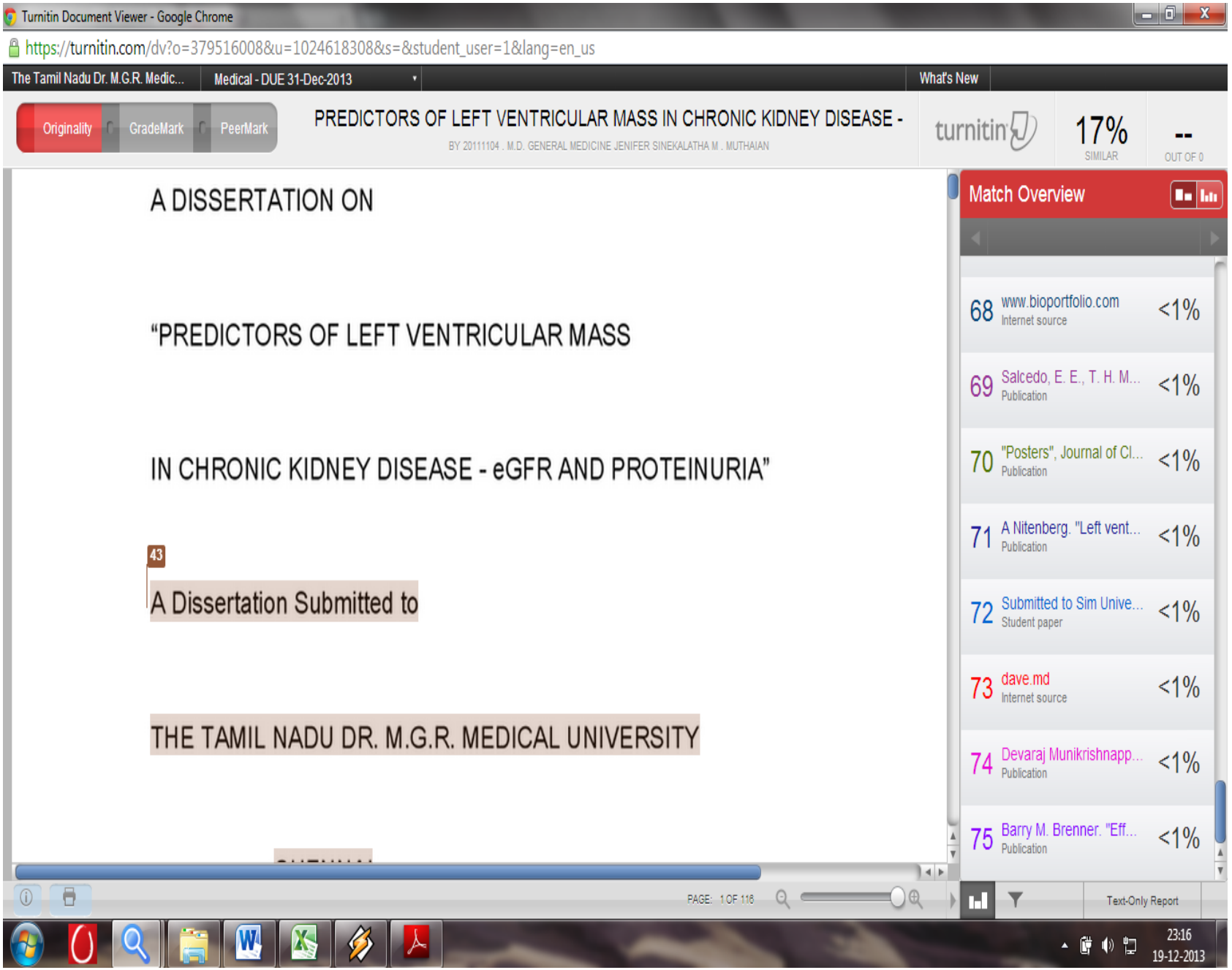
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