# DISSERTATION ON

# A STUDY OF ELECTROCARDIOGRAPHIC CHANGES IN PATIENTS WITH CHRONIC KINDEY DISEASE

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# CERTIFICATE

This is to certify that this dissertation entitled "**A STUDY OF ELECTROCARDIOGRAPHIC CHANGES IN PATIENTS WITH CHRONIC KINDEY DISEASE**" is the bonafide original work of **Dr. VIMAL RAJ .A** in partial fulfillment of the requirements for M.D Branch -I (General Medicine) Examination of the Tamilnadu Dr. M.G.R. Medical University to be held in APRIL - 2015. The period of study was from January– 2014 - August 2014.


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**DECLARATION**

I, **Dr. VIMAL RAJ.A** , solemnly declare that the dissertation titled DISSERTATION ON **"A STUDY OF ELECTROCARDIOGRAPHIC CHANGES IN PATIENTS WITH CHRONIC KINDEY DISEASE"** is a bonafide work done by me at Thanjavur Medical College, Thanjavur during January 2014 – August 2014 under the guidance and supervision of **Prof .Dr .K.NAGARAJAN, M.D.,** Unit Chief M-2, Thanjavur Medical College, Thanjavur.

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

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# CONTENTS


| SL. NO. | TITLE | PAGE NO. |
|---|---|---|
| 1 | INTRODUCTION | 1-2 |
| 2 | OBJECTIVE OF THE STUDY | 3 |
| 3 | REVIEW OF LITERATURE | 4-69 |
| 4 | MATERIALS AND METHODS | 70-73 |
| 5 | RESULTS AND OBSERVATION | 74-99 |
| 6 | DISCUSSION | 100-103 |
| 7 | CONCLUSION | 104-105 |
| 8 | ANNEXURE –I BIBLIOGRAPHY | |
| 9 | ANNEXURE –II PROFOMA | |
| 10 | ANNEXURE –III MASTER CHART | |
| 11 | ANNEXURE –IV ABBREVIATIONS | |
| 12 | ANNEXURE –V CONSENT FORM | |

# ABSTRACT

**Background and objectives:**

Cardiovascular disease(CVD) is the leading cause of morbidity and mortality in patients with Chronic kidney disease(CKD). The mortality due to cardiovascular disease is 15-30 times higher in dialysis patients. Our aim is to study Electrocardiographic changes in patients with CKD.

**Materials and methods:**

75 consecutive patients of CKD admitted in thanjavur medical college hospital were taken up for the study. Patients were evaluated with history, general examination, systemic examination, Blood investigations, ECG, etc.,

**Results:**

In our study changes in ECG among CKD patients constituted to around 71% of the study population. The commonest ECG finding was Left ventricular hypertrophy constituting to 29% of study population. Ischemic changes in ECG were found to be in 23%, Conduction disturbances were found to be in 17%, Left atrial enlargement in ECG was found in 12%, Hyperkalemic ECG changes were found in 12% of our study population. The overall changes in ECG significantly (p value <0.05) correlated with the increasing age & presence of

dyslipidaemia. The ischemic changes in ECG correlated significantly (p value<0.05) with the low HDL and high Triglyceride levels.

**Conclusion**

CVD poses a major threat to patients with CKD. In the context of CKD aim of evaluating CVD is warranted. The changes in ECG of patients with CKD can aid in detection of CVD and should be carried out in all patients with CKD.

**Key words**

Chronic kidney disease (CKD), Cardiovascular disease (CVD), Electrocardiography (ECG).

# 1. INTRODUCTION

The epidemicity of chronic kidney disease, full spectrum of which ranges from asymptomatic state to obvious kidney failure is being increasingly noted. Kidney failure being the most visible aspect of this spectrum, it represents only a minimal of total population affected by kidney disease [1].

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in patients with CKD. This risk of cardiovascular disease may begin in early stages of CKD much before the onset of kidney failure. This high burden of CVD mortality is well illustrated by comparing CVD mortality in dialysis population to general population. The mortality due to Cardiovascular disease is 15-30 times higher in dialysis patients [1,2,3]. National Kidney Foundation (NKF) in their clinical guideline for CVD in dialysis patients recommended baseline electrocardiogram and echocardiograph at the onset of dialysis and at annual interval.

The clinical manifestation of CKD and CVD overlap substantially and often missed on clinical examination, hence these abnormalities has to be evaluated by noninvasive, easily available diagnostic method to prevent morbidity and mortality.

Even in this modern era of sophisticated investigations the use of cost effective non invasive modalities of investigations hold good for many disorders. One such investigation being electrocardiography for cardiovascular diseases. It is a very widely available investigation that can aid in the detection of ischemia to myocardium, conduction abnormalities of the heart, chamber enlargements & can even provide clues regarding the electrolyte abnormalities. The importance of this inevitable investigatory modality should be never neglected.

## 2. OBJECTIVE OF THE STUDY

To study Electrocardiographic changes in patients with chronic kidney disease and to determine whether there is a correlation between the Electrocardiographic changes and duration of illness, stage of the illness or to any other potential factors.

## 3. REVIEW OF LITRETURE

Atrophied Kidney a fatal consequence of chronic renal inflammation seen in early inhabitant of Nile valley was noticed by Dawson, Buffex and Smith. Charaka explained different urinary affection in 2nd century. Hipppocrates has given the detailed description of renal disease. He diagnosed certain affection of kidney by urinary examination. Soliceto, the Italian surgeon pointed out the association of dropsy, scanty urine and hardened kidneys.

The term "Uremia" originally used to imply retention of urine in the blood by the Piorry and Lheritter. Jacobe Henly showed urinary casts under microscope. Fredrick Akabar Mohammed found relation between hypertension and renal disease. Herman and Straus described blood urea estimation in kidney disease. Fredrich Wholer synthesized the urea in laboratory.

**PHYSIOLOGY OF KIDNEYS**

The kidneys are paired organs in the shape of been seeds placed bilaterally and are located in the retroperitoneal space one on each side of the vertebral column. Each kidney weighs hundred and fifty grams and is about eleven cm length, six cm in width and three cm in thickness. Kidneys have a cortex which constitutes the outer segment and a medulla which constitutes the inner segment. The medullary portion of kidney has approximately 12 pyramids.

Each of the pyramid and the cortex overlying it together forms the renal lobe. The pyramids have two zones. 1)INNER ZONE also known as papilla & 2)OUTER ZONE. This inner zone drains into the calyces which then drain into the renal pelvis. Renal pelvis further empties into the ureter.

BLOOD VESSELS

Kidneys receive around 20 to 25% of the cardiac output. This blood supply is derived from the branches of abdominal aorta, the renal arteries through its anterior and posterior branches. After a series of successive divisions the afferent arterioles arise, each arteriole provides blood supply to a glomerulus.

Capillaries are formed by the branching of efferent arteriole which drains the glomeruli. These capillaries either form the vasa recta or provide blood supply to the renal cortex.

Functional unit of the kidneys is known as the nephrons. It is composed of

- The glomeruli
- The tubules &
- Collecting system

GLOMERULI

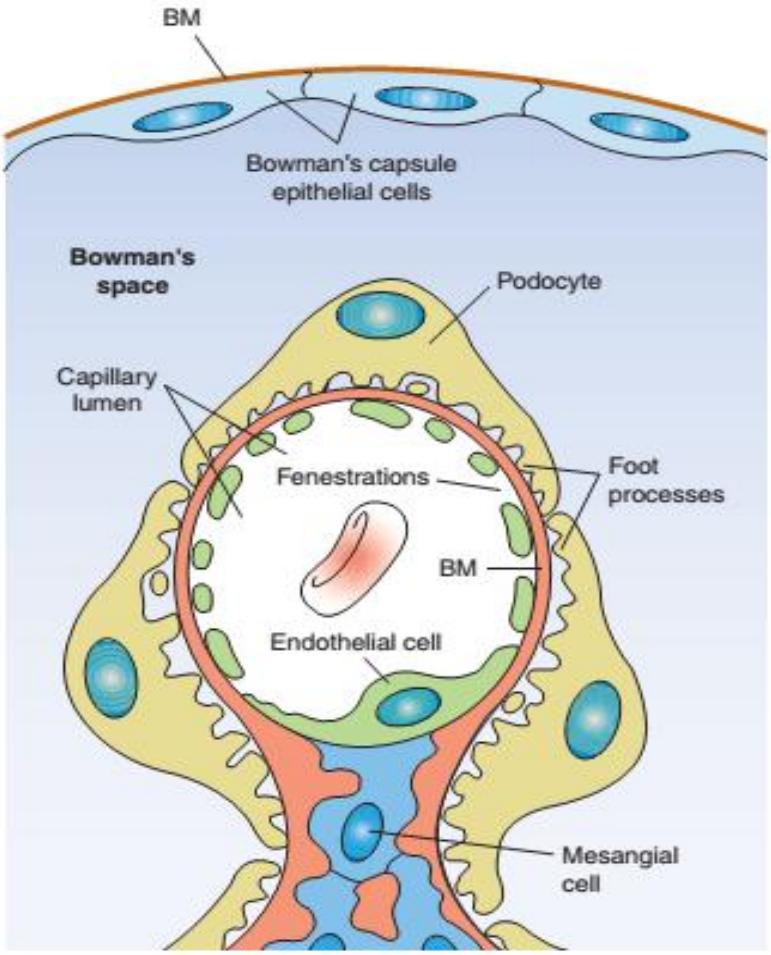



**Figure depicting the glomerulus**

The glomeruli consist of capillary network which is covered by the epithelial cells and interspersed with mesangial cells. The afferent arteriole after entering the glomeruli divides into capillaries, forming a tuft and then converges into the efferent arteriole leaving the glomeruli. Capillary endothelium lies on basement membrane. On its other surface the membrane is covered by podocytes. The

Bowman space is the space between podocytes and the epithelium of the malphigian capsule.

THE GBM

The Glomerular Basement Membrane varies from other basement membranes in its composition and function. It is around 350 nm in thickness and has 3 laminae.1)Lamina densa 2)Laminarara interna3)Laminarara externa. The GBM contains glycosaminoglycans abundant in heparin sulfate, which provides a negative charge to the GBM. The negative charge of the GBM facilitates filtration of neutral and positive charged molecules and relative exclusion of substances like albumin which are negatively charged.

GLOMERULAR ENDOTHELIUM

The Glomerular endothelium is 50 nm in thickness has pores in 60-100nm size. Membrane proteins in the endothelium, prostaglandins and nitric Oxide produced by the endothelium have a major role in much glomerular pathology.

PODOCYTES

Podocytes rest on the Glomerular basement membrane. Over the externa layer of the GBM(Glomerular basement membrane) the podocytes extend processes similar to that of feet which gives them the name foot process. The slit

diaphragm separates these projections. These podocytes provide a defense against proteinuria. Mutations in the various components of podocytes result in proteinuria and nephrotic syndrome.

MESANGIUM

Mesangial cells are basically specialized smooth muscle cells that occupy the central area of glomeruli interspersed with the capillaries. Some of the function of mesangium:

■ Endocytosis of immune complexes and many other proteins

■Production of prostaglandins & cytokines.

■acting as a matrix for glomerulus thus provides support.

■Contractility of mesangial cells Modulates GFR.

TUBULES

They are the

- Proximal convoluted tubule
- Distal convoluted tubule and
- Loop of Henle.

The proximal convoluted tubule lined by tall columnar cells with microvilli forming the so called brush border. The proximal convoluted tubule then straightens into the thick descending limb of the loop of Henle. This thick limb thins to form the thin limb of the loop of Henle .the thin limb then becomes the thick ascending limb. Here it lies close to the glomeruli forming the ‘ juxta glomerular apparatus ’, Then the distal tubule arises from the thin ascending limb. Collecting duct is formed by the union of many distal tubules. ‘ Duct of Bellini ’ is formed by the union of collecting ducts . These ducts drain into the calyx via the papilla.

THE JUXTAGLOMERULAR APPARATUS (JGA)

The JGA consists of:

■Macula densa

■Extraglomerular mesangial cells

■Terminal portion of the afferent arteriole and proximal portion of the efferent arteriole.

This JGA is responsible for the production and release of rennin and angiotensin.

THE INTERSTITIUM

The renal interstitial cell not only provides structural support, but also has some secretory function as of its cortical cells produce erythropoietin and medullary cell produce prostaglandins.

FUNCTIONS OF KIDNEY

The kidneys are the major organs in maintaining the homeostasis of the body by controlling excretion of various substances. Few of the functions of kidneys are as follows

- They increase the excretion of ions when their levels reach a higher level beyond a threshold. They Conserve ions by increasing the re absorption when they are in lower levels than normal. Thus they control the ionic concentration of body. Ions regulated by kidneys include sodium, potassium, phosphate, magnesium , calcium & chloride.
- The kidneys conserve bicarbonate ions, the important blood pH buffer. They also excrete the hydrogen ions in excess. Thereby monitoring and regulation of hydrogen ion levels and bicarbonate ion levels, regulates the pH of the blood.

- Kidneys maintain osmolality of the blood by regulating the quantity of water excreted through the urine. When water is consumed in larger quantities, there is reduction in the reabsorption of water facilitating the excretion of excess water, producing a diluted urine .By the process of reabsorption, highly concentrated urine can be formed in response to dehydration. These changes are controlled by the anti-diuretic hormone.
- Kidneys regulate the blood pressure. When blood pressure is high, kidneys by decreasing the blood volume normalizes the blood pressure. Conversely during times of hypotension, the kidneys secrete renin and there's activation of the renin-angiotensin system to cause constriction of blood vessels and produce concentrated urine, thereby allowing the plasma volume to expand.
- Kidneys produces Calcitriol, the active form of vitamin D. Calcitriol along with parathormone regulates the level of calcium ions in the blood. During times of hypocalcaemia parathormone is released from, the parathyroid glands. The parathormone stimulates the kidneys to produce calcitriol. This vitamin D3 promotes the gut to absorb calcium avidly. There's stimulation of osteoclasts causing the release of calcium ions in bloodstream.
- Production of the Erythropoietin (EPO), the erythropoietic hormone. The kidney monitors oxygen-carrying capacity of the blood passing through its capillaries.

During times of hypoxia the peritubular fibroblasts produce erythropoietin & releases into the blood. Erythropoietin stimulates hematopoietic cells in the marrow to increase production of RBCs, thus tries to improve the hemoglobin concentration so as to correct hypoxia.

- Kidneys produce the renin to favor the activation of the renin-angiotensin system (RAS). The renin-angiotensin system during periods of hypotension, blood loss or dehydration expands the blood volume and increases the blood pressure. Renin converts the angiotensinogen produced in the liver to form angiotensin I. Angiotensin I is converted by angiotensin converting enzyme to form the Angiotensin II.
- Angiotensin II is involved in varied mechanisms, one of them being the secretion of aldosterone by stimulation of adrenal cortex. Aldosterone in turn increases blood volume and increases the blood pressure by increasing the sodium and water reabsorption by the kidneys. There is a negative feedback mechanism based on this system to regulate levels of blood pressure.

**CHRONIC KIDNEY DISEASE**

**Definition:** Kidney damage for ≥3 months, defined as functional or structural Renal abnormality, along with or without reduced GFR, irrespective of the cause, manifest by *either*:

1. Abnormal pathology;

2. Markers of renal damage that includes abnormal composition of the blood or urine, or abnormal imaging studies.

3. GFR less than 60 ml/min/1.73 m2 for ≥3 months, along with or without renal damage.

**Staging of CKD based on GFR**

| Stage | GFR (mL/min/1.73 $m^2$) | Description |
|---|---|---|
| 1 | ≥90 | Normal or increased glomerular filtration rate (GFR), with other evidence of kidney damage |
| 2 | 60–89 | Slight decrease in GFR with other evidence of kidney damage |
| 3A<br>3B | 45–59<br>30–44 | Moderate decrease in GFR with or without other evidence of kidney damage |
| 4 | 15–29 | Severe decrease in GFR with or without other evidence of kidney damage |
| 5 | <15 | Established renal failure |

*Note*: The suffix 'P' can be applied to the stage of CKD if the patient has significant proteinuria, defined as a urinary albumin:creatinine ratio >65 mg/mmol or protein:creatinine ratio >100 mg/mmol.
*Source:* NICE Clinical guidance 73. Chronic kidney disease. 2011.

## Risk Factors for Chronic Kidney Disease

### Established risk factors

Age

Gender (male predilection)

Race (African American, Hispanic, Native American)

High blood pressure

Diabetes mellitus

Obesity

Metabolic syndrome

Proteinuria

Family history of kidney disease

Smoking

Atherosclerosis

Exposure to nephrotoxins such as analgesics, heavy metals

Dyslipidemia

Reduced nephron number at birth

Recurrent urinary tract infection

**Emerging risk factors**

Oxidative stress

Elevated plasma homocysteine level

Anemia

Prothrombotic factors (e.g., plasminogen inhibitor activator-1).

**PREVELANCE:**

The Third National Health and Nutrition Examination Survey (NHANESIII) showed the following observations related to CKD.

- 6.2 million people had serum creatinine ≥ 1.5 mg/dL, showing that there is 30-fold increased prevalence of reduced kidney function when compared with that of the treated ESRD during the same time period.
- 2.5 million people were having serum creatinine ≥ 1.7 mg/dL.
- 800,000 people had a serum creatinine ≥ 2.0 mg per dL.
- 70% of the people with elevated serum creatinine levels had hypertension.
- Only three fourth of patients received treatment despite having both hypertension and elevated serum creatinine levels, with only 27% having

Reduced their blood pressure lower than 140/90 mm Hg and 11% having their BP reduced to lower than 130/85 mm Hg [4].

**Estimation of Glomerular Filtration Rate:**

GFR is the preferred method for assessing kidney function and staging CKD for the purpose of diagnosis, prognosis, and management. There are several methods for measuring and estimating GFR. Each method has particular strengths, weaknesses, and limitations. Inulin clearance remains the gold standard. For clinical purposes, creatinine and cysC are good markers for measuring GFR [5]. For clinical management, serum creatinine-based estimates of GFR, including the Cockcroft Gault and MDRD equations, are the preferred methods. For research purposes, inulin and iothalamate clearances are accurate, reliable, and reproducible measures of GFR.

**Cockcroft – Gault Equation**

$$CrCl = \frac{(140 - age) \times weight(kg)}{SerumCr(mg/dl) \times 72}$$

The above equation calculates the creatinine clearance. It must be multiplied by the factor 0.85 in case of females. It is done because this formula's assumption that when compared with males, females will have a low creatinine clearance by fifteen percentage.

**Modification of Diet in Renal Disease Equation.**

$$\text{GFR in ml/min/1.73 m}^2 = 170 \times \text{serum creatinine}^{-0.999} \times 0.762(\text{if female}) \times 1.180(\text{if black}) \times \text{BUN}^{-0.180} \times \text{Albumin}^{+0.318}$$

**Etiology of CKD.**

| Renal Disease | Total % |
|---|---|
| Diabetes mellitus | 43.9 |
| Hypertension | 26.2 |
| Glomerulonephritis | 9.1 |
| Interstitial nephritis/pyelonephritis | 3.8 |
| Cystic/hereditary/congenital diseases | 3.2 |
| Secondary glomerulonephritis/vasculitis | 2.2 |
| Neoplasms/tumors | 1.9 |
| Miscellaneous | 4.1 |
| Unknown | 5.7 |
| Total | 100 |

## CAUSES OF CKD

Diabetic glomerulosclerosis
Hypertensive nephrosclerosis

Glomerular disease
- Glomerulonephritis
- Amyloidosis,
- light chain disease
- Systemic lupus erythematosus,
- Wegener's granulomatosis

Tubulointerstitial disease
- Reflux nephropathy (chronic pyelonephritis)
- Analgesic nephropathy
- Obstructive nephropathy
- Myeloma kidney

Vascular disease
- Scleroderma
- Vasculitis
- Renovascular renal failure (ischemic nephropathy)
- Atheroembolic renal disease

Cystic diseases
- Autosomal dominant polycystic kidney disease
- Medullary cystic kidney disease

## PATHOPHYSIOLOGY OF CKD:

The kidneys amounts to 1% of total body weight, but the blood flow to kidneys constitutes to 20% of the total cardiac output, which is required for ultrafiltration. The volume of urine excreted represents the total of two

opposite physiological process namely, ultrafiltration of 180L/24hrs or more of plasma water and reabsorption by transport process in the renal tubules by which 99% of the above said filtrate is reabsorbed[6].

The pathophysiological of chronic renal failure involves two varied type of etiologies:

• Initiating mechanisms which are brought about by varied causes e.g., in various types of glomerulonephritis via the immune complexes and various inflammatory mediators, or toxin exposure in certain cases of interstitial and tubular diseases of the kidney and

• A set of progressive mechanisms, causing nephronal hypertrophy and hyper filtration, which are caused by over a longer durational decrease in the renal mass.

Vasoactive hormones, cytokines, and growth factors mediate the response to reduction of renal mass and number of nephrons.

As time progresses, the short lived compensations of nephronal hypertrophy and hyper filtration turns out in vain as the increase in the glomerular pressure and increased flowing leads to sclerosis and the remaining nephrons then get damaged. The initial part of short lived compensations of nephronal hypertrophy and hyper filtration is brought about by the raise in the

activity of renin –angiotensin system (RAS) within the kidney. Following this in the transforming growth factor (TGF-β) stimulation carries out the same activities during later stages. For these reasons there may be renal mass reduction following a single episode of insult to the kidney and may cause a continuous reduction in the function of the kidneys even over the decades [6].

In chronic kidney disease, compensatory and adaptive mechanisms maintain acceptable health until the GFR is about 10-15ml/min and life sustaining the renal excretory and homeostatic function continue until the glomerular filtration rate is less than 5ml/hr [7].

The metabolic product of protein and amino acids depends primarily on the kidneys for excretion unlike fats and carbohydrates, which are eventually metabolized to Co2 and water substance, which are readily excreted even in uremic subjects via lungs and skin.

The pathophysiology of the uremic syndrome is divided into those sets of abnormalities consequent to the accumulation of end products of protein metabolism and the abnormalities consequent to the loss of fluid and electrolyte homeostasis and synthesis of certain hormones{e.g.:- erythropoietin EPO, 1.25-dihydroxycholecalciferol}.

The kidney normally catabolizes a number of circulating plasma proteins and polypeptide which is reduced in renal failure. Furthermore, plasma levels of parathyroid hormone {PTH}, Insulin, Glucagon, Luteinizing hormone and prolactin hormone rise with renal failure-not only because of renal catabolism but also because of enhanced glandular secretion. PTH is an important toxin because of its adverse effect of elevating cellular cytosolic Ca2+ levels in several tissue and organs [8].

**CLINICAL AND BIOCHEMICAL MANIFESTATION OF CKD.**

The symptoms of uraemia may develop insidiously and late. The most common and dominant symptoms are fatigue, dyspnoea, ankle swelling, Anorexia, vomiting, pruritus and inability to concentrate. Physically sign in chronic kidney disease depends on its degree of chronicity and its likely complication. Signs of chronicity include pallor, yellow brown skin discoloration and nail dystrophy.

Other manifestation of chronic kidney disease includes hypertension, cardiomegaly, congestive cardiac failure and pericarditis. The florid manifestation of uraemia has largely disappeared because of chronic dialysis, which reduces the incidence and severity of disturbance in the function of every organ system secondary to uraemia[ 9].

**Anaemia**

Anaemia is common in CKD stages III through IV and Is due to the apparent deficiency of the hormone erythropoietin (EPO), and also iron deficiency, reduced RBC life span ,vitamin deficiency of folate or cyanocobalamine , and chronic inflammation are frequent contributors. Anaemia may contribute to cardiac dysfunction by increasing cardiac output and there by exacerbate left ventricular hypertrophy [10].

Although reversal of anaemia with erythropoietin has can cause the left ventricular hypertrophy to regress, there is currently no evidence that treatment is associated with an improved longer term cardiac prognosis, although its use may be associated with better quality of life. Debate remains as to the optimal target range of haemoglobin concentrations, with most guidelines recommending a level of 11 to 13 g/dl. Partial correction of anaemia does not accelerate the decline of renal function but may necessitate increases in antihypertensive therapy [10].

**Water homeostasis**

Inability to concentrate urine is often the first symptom of CKD, resulting in polyuria, nocturia and thirst, when glomerular filtration rate is about is 30ml/min or less. Diseases such as pyelonephritis, interstitial nephritis and

medullary cystic disease, which show their predominant effect on the medulla, may present with concentration defect at an earlier stage of CKD. This is due to increased solute load in serving nephrons. As obligatory water loss is increased there is need for careful attention to fluid balance in the presence of anorexia, fever, surgery and other sources of extra renal loss that leads to dehydration and hypertension [11].

**Sodium homeostasis**

As the renal function decreases sodium balance and extracellular fluid volume are maintained until GFR is less than 10ml/min. The extent of this adaption such that 1% or less of filtered sodium excreted by normal subject increases to 30% in late CKD. In most patients with stable CKD the total body contents of Na+ and H2o are increased modestly, but may not be clinically evident. The major consequence of sodium and fluid excess is hypertension, present in 80% of patient in late CKD [11].

**Potassium homeostasis**

Hyperkalemia may develop in CKD stages 4 and 5 and can be managed by dietary restriction to less than 60mg potassium daily. Patients with CKD may tolerate higher levels of potassium, and may not show change in ECG or may not develop arrythmia than those with acute kidney injury (AKI), but this is not

a consistent feature, and hyperkalemia should always be actively managed. Acute reductions in serum potassium are best achieved by glucose and insulin infusion; sodium bicarbonate is less effective in the setting of impaired renal function. Oral Resins (such as Kayexalate with sorbitol) are widely used in some countries but May cause gastrointestinal upset and can raise blood pressure because of sodium retention. Dialysis may be required acutely if the serum potassium concentration is markedly elevated (levels > 6.5 mmol/l). For chronic management of hyperkalemia, dietary potassium restriction and loop diuretics may be required. Haemodialysis patients with hyperkalemia may not exhibit the usual ECG changes possibly due to fluctuation in serum calcium [11].

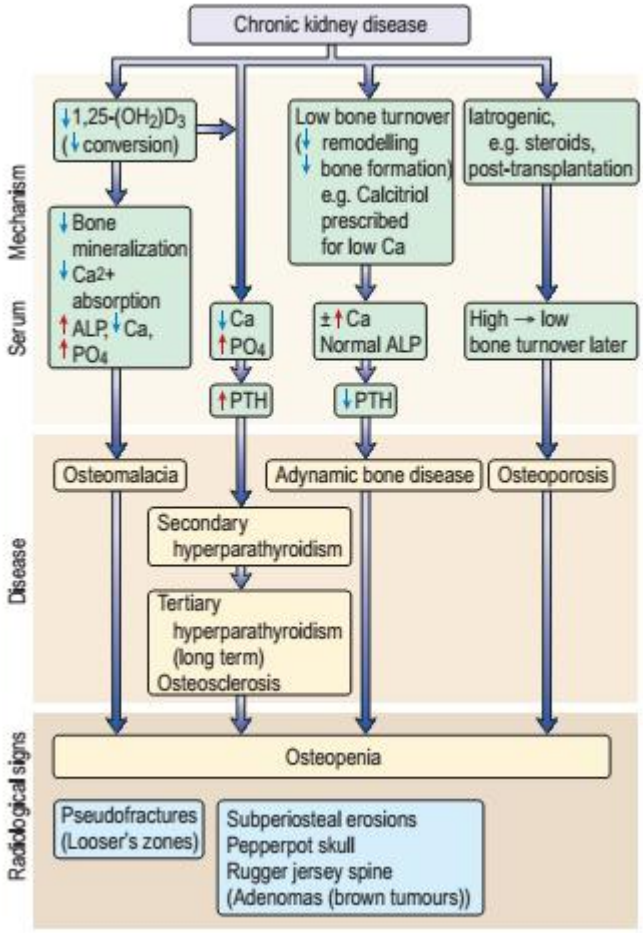
**Acid base balance**

The metabolic acidosis associated with CKD is caused by failure of hydrogen ion excretion and may be compounded by bicarbonate loss, particularly in interstitial kidney diseases and the accumulation of organic acids. Clinical symptoms from acidosis are rare until patients reach CKD stage 5, when dyspnea may occur.

Acidosis causes increase in the serum level of potassium, decreases production of protein, and tends to increase the rate of resorption of calcium

from bones as the ionic hydrogen is being buffered in the bones. There is also emerging evidence that correction of metabolic acidosis slows progression of renal disease. Severe metabolic acidosis (e.g., serum bicarbonate < 20 mmol/l) associated with symptoms in a patient with CKD stage 5 is an indication to start dialysis. If dialysis is not immediately available, oral sodium bicarbonate in a dose up to 1.2 g four times daily may be considered, but sodium loading may aggravate hypertension [11].

**Bone, Phosphates, Calcium abnormalities**



Two principle types of bone disease observed in patient with ESRD:-

1. High turnover-osteodystrophy {osteitis fibrosa cystica}

2. Low turnover- osteodystrophy characterized initially by osteomalacia and subsequently by dynamic bone disease [12].

The High turnover-osteodystrophy is associated with elevated parathyroid hormone. The main factor responsible for deranged PTH synthesis in CKD is related to

1. Altered Vitamin D metabolism and resistance to calcitriol

2. Hypocalcemia

3. Hyperphosphatemia

4. Altered degradation of PTH hormone by the kidney

Low-turnover bone disease can be grouped into two categories

• **Adynamic bone disease**:

Adynamic bone disease is increasing in prevalence, especially among diabetics and elderly. It manifests as a decrease in mineralization and volume of the bone and may result from excessive suppression of PTH production. Its complication can lead to pathological fractures and may lead to calcifications in the heart as well as blood vessels

• **Osteomalacia:**

The bone matrix which gets deposited is largely unmineralised which is brought about by Reduced levels of vitamin D ,Increased accumulation of aluminium or even metabolic acidosis.

Cardiovascular morbidity and mortality increases proportionally with the increased levels of phosphate. This mechanism is effected not only in end stage diseases but also in patients with lower stages of chronic renal failure. There is excess calcification of blood vessels in proportion to increased levels of calcium and phosphate but there is uncertainty concerning the causation of excessive mortality by this mechanism. There can also be calcification in the valves of the heart. The level of calcification increases with advancing age. The possible mechanism of this excessive calcification is

1) Deposition of calcium in sites other than bone because of the defective mineralization of bone

2) There is change in the genetic expression that causes the vascular endothelium to react as osteoblast like mechanism. The later mechanism is brought about by the hyperphosphatemia.

**CARDIOVASCULAR COMPLICATION OF CHRONIC KIDNEY DISEASE**:

Cardiovascular diseases is the most important and largely the cause of death in chronic kidney disease largely due to the increase in the number of patients with end stage renal disease and a wide variety of factors which affect the functions of the heart. This increased risk of cardiovascular disease may begin even before the onset of renal failure in the beginning stages of chronic kidney disease. Patients with chronic kidney disease will have largely the traditional risk factors of CVD together with the presence of certain nontraditional risk factors that causes the increased burden of CVD.

Cardiovascular disease is the important and largely the cause of death, accounting for nearly 45% of deaths; approximately 20% of cardiac deaths are attributed directly to acute myocardial infarction. At all ages in both men and women, deaths due to CVD is 10 to 30 fold increased in patients with CKD dependent on dialysis comparing to general population[13].

The anatomic and hemodynamic alteration of cardiovascular system in CKD is

• Increased total body and vascular volume.

• Increased blood pressure.

• Left ventricular hypertrophy.

• Increased pulmonary capillary permeability.

• Increased cardiac index.

• Increased left ventricular chamber size.

• Increased serosal membrane permeability.

• Increased total peripheral resistance [14].

• Impaired left ventricular contractile function {decreased ejection fraction}.

**Cardiac risk factors in chronic kidney disease.**

TRADITIONAL RISK FACTORS

Advanced age

Male sex

Systemic hypertension

Diabetes

Dyslipidemia

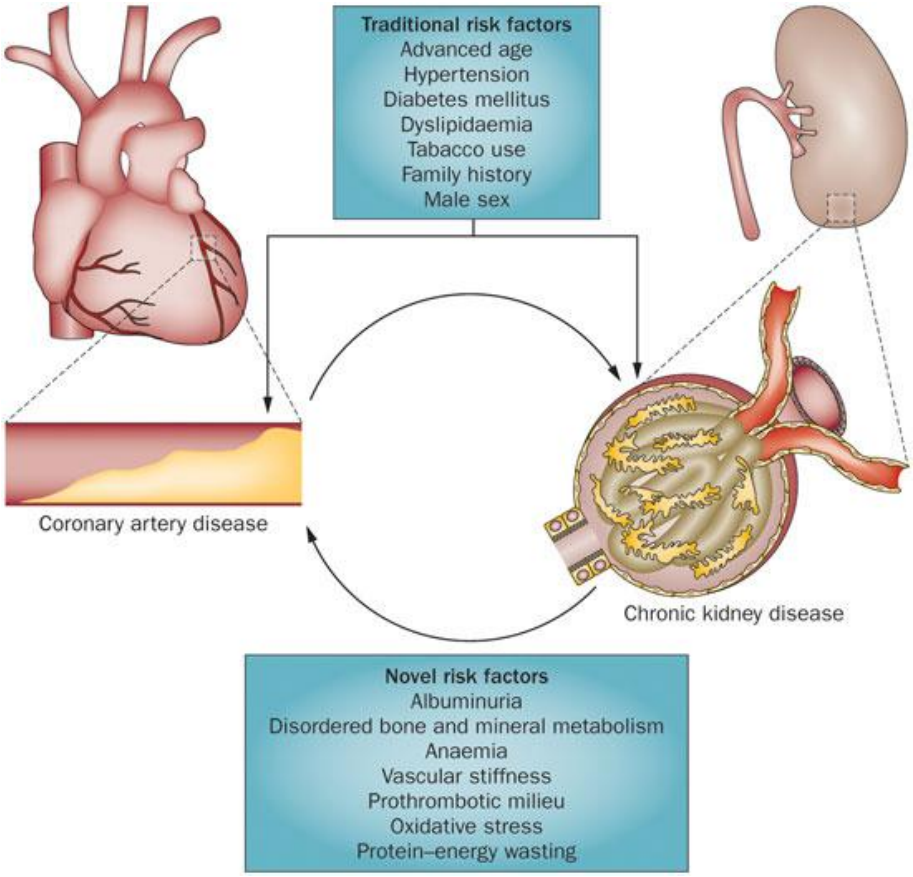
Menopause

Insulin resistance

Sedentary life style

Family history of cardio vascular disease

LVH




RISK FACTORS CAUSED BY CKD

Albuminuria

Homocysteine

Lipoprotein (a) and apo (a) isoforms

Lipoprotein remnants

Anemia

Disordered bone /mineral metabolism

Increase in the volume of extracellular fluid

Electrolyte imbalance

Oxidative stress

Increase in Inflammatory mediators

Protein energy wasting

Prothrombotic mileu

Endothelial dysfunction

Toxins of uremia

Hypotension related to dialysis

Sympathetic activation

**Hypertension**

Hypertension is one of the most serious complications of chronic kidney disease. It occurs in more than three fourth of patients with end stage renal disease and constitutes in major for the emergence of ischemic heart disease and congestive heart failure [15].

Factor contributing hypertension in uremia

1. Salt and water retention

2. Enhanced activity of renin angiotensin system

3. Excess aldosterone secretion

4. Increased sympathetic tone

5. Diminished production of vasodepressor hormone

6. Excess release of vasoconstrictor natriuretic factors.

7. Stiffening of the arteries because of sclerosis of the tunica media

8. Erythropoietin therapy.

In patients with CKD, GFR and albuminuria are proportionate to the increase in the systolic blood pressure. High levels of blood pressure in dialysis dependent patients is seen in patients who are young, who are having lesser adherence to the advised dialytic regime or who have increased weight gain in between the dialysis sessions [16,17,18,19]. Hypertension is also prevalent among post transplant patients. Apart from all the usual factors associated with CKD causing hypertension post transplant patients have an increased risk due to therapy with calcineurin inhibitors which exert a vasoconstriction mechanism

Hypertension is foremost cause of left ventricular hypertrophy in patients with chronic kidney disease. Left ventricular hypertrophy and myocardial fibrosis can also be caused by non hemodynamic factors like angiotensinogen II, paratharmone, endothelin, aldosterone, increased sympathetic discharge. Left

ventricular hypertrophy is consistent with hypertension, ventricular arrhythmia probably reflecting that the most likely mechanisms are either due to subendocardial ischaemia, alterations in vasodilator reserve or structural changes in coronary micro circulation.

**Hyperglycemia**

In general population with CKD, CVD is more prevalent among individuals with diabetes those without diabetes. However it is not known hyperglycemia per se causes CVD in either population. Approximately 30% of all patients who begin maintenance dialysis therapy have diabetes.

The American Diabetic association recommends lower blood glucose levels to normal or near normal in patient with type1 and type2 diabetes to reduce the risk for development and progression of renal, retinal and neurologic disease and to improve dyslipidemia. In the CKD patients with micro albuminuria, strict glycemic control may slow the progression of renal disease. The most significant factor contributing for CVD, in diabetes is Coronary Artery Disease {CAD}. In patients with advanced complication like CAD, intensive glycemic control may not be effective [20].

## Hyperlipidaemia

The prevalence of hyperlipidaemia in CKD is greater than in general population even though the type of abnormality varies. Hypertriglyceridemia is the most common lipid abnormality in ESRD patient and is often found in association with a low HDL-C. Elevated total or LDL cholesterol levels are associated with CVD in CKD. There is also elevation in levels of other lipids such as IDL-C, VLDL-C, Lipoprotein-a[Lp(a)]. Patients with elevated levels of Lp(a) are at an increased risk of CVD mortality.

In patients on hemodialysis, lower levels of serum total cholesterol are associated with unfavorable outcomes. The lower levels of cholesterol in these patients are accounted by malnutrition and inflammation.

## Proteinuria

The ratio of albumin to creatinine in urine is an important factor linked with the cardiovascular disease and events. Studies have found out not only micro–albuminuria but also low grade albuminuria (even lesser amount than microalbuminuria) is associated with cardiovascular disease. Albuminuria is a documented risk factor also for the progression of CKD. This dual effect of albuminuria is actually the marker of widespread dysfunction of the endothelium. Chronic kidney disease is defined as cardiovascular disease risk

equivalent, and all the stages of chronic kidney disease are considered in the highest risk group [4, 21].

**Insulin resistance**

Insulin resistance is a part of the metabolic syndrome which is an important factor associated with increased CVD risk. In CKD owing to the presence of inflammation it is suggested that metabolic syndrome is linked in patients with varying stages of CKD [22]. The insulin resistance is particularly documented in the beginning stages of CKD.

**Homocysteine**

Elevated Homocysteine levels appear to increase the risk of development of cardio vascular disease in general population. Homocysteine levels are elevated in most patients with CKD. As per studies elevated homocysteine appears to be associated with risk factor for cardiovascular morbidity and mortality in patient with ESRD. But larger studies are needed for confirmation. It is proposed that elevated levels of homocysteine may cause injury to vascular endothelium and may cause a hypercoagulable state.

**Increase in the volume of ECF**

Increase in Plasma volume owing to sodium and water retention can occur in every stage of CKD particularly in ESRD or dialysis dependent patients. This volume expansion leads to hypertrophy and dilatation of the left ventricle. The importance of this lies mainly in dialysis patients whom the inter-dialytic weight gain affected mainly by this volume expansion is responsible for the blood pressure to rise. In a study it was shown that rate of fluid removal by dialysis was an independent factor affecting survival of the patients[23].

**Reduced levels of albumin**

Hypoalbuminemia is seen as predictor of outcomes in dialysis dependent patients. This relationship is even more evident in patients undergoing peritoneal dialysis rather than hemodialysis. The reduced levels of albumin are associated with the left ventricular enlargement, and there is increased incidence of cardiac failure and coronary artery disease[24]. In post transplant individuals the levels of albumin alone particularly hypoalbuminemia is an independent risk factor for cardiovascular diseases.

**Increase in inflammatory markers**

In patients with CKD, the inflammatory marker- C- reactive protein is been seen as an important risk factor in development of atherosclerosis. C-reactive protein (CRP)

- Is an effective stimulator of monocytes to produce tissue factor.
- Can activate the complement system
- Binds and causes aggregation of LDL and VLDL by a calcium dependent mechanism

The causes for CRP elevation are of debate. The proposed sources include

- Sub clinical or unidentified infections
- Dialysate fluid's bio-incompatibility
- Endotoxins back filtered in the process of dialysis

It is studied that CRP has as an independent association with the number of atherosclerotic plaque in HD patients. It is also associated with the thickness of intima & media of arteries in pre dialysis population. In a particular group of patients who were on hemodialysis it has been studied that patients with higher levels of C- reactive protein have 5 times increased risk of CVD death [ 25].

**Oxidative stress**

It occurs due to alteration in balance between production of reactive oxygen species and radical anti oxidative processes. The important free radicals include

Superoxide

Hydrogen peroxide and

Hydroxyl ions

These molecules provide protection against various neoplastic cells and pathogenic agents [26, 27]. The neutralization of these molecules are done either by

Enzymatic elements

- Glutathione peroxidase
- Superoxide dismutase

Or by non enzymatic elements namely

- VitaminE
- VitaminC
- Se
- Zn

The increased oxidative stress is due the increase in lipid peroxidation, reduction in substances enhancing resistance against oxidation and reduced levels of reducing substances. Dialysis also can increase the level of stress because the anti oxidant molecules may get removed and or due to the stimulation of the free radicals via the dialytic components.

**Prothrombotic mileu**

Even though patients with CKD will have reduced platelet aggregation and prolongation of bleeding time, elevated levels of many pro thrombotic factors particularly increased levels of fibrinogen is also seen in them and is associated with increased coronary events[ 28, 29] . This leads to increased risk of CVD in such patients.

**Physical inactivity**

Physical activity is reduced among the patients with CRF especially patients with ESRD. As in general population exercise appears to improve the well being in patients with CKD. The association of physical activity and CVD in CKD has not been carefully studied.

**Hyperparathyroidism**

Secondary hyperparathyroidism is virtually universal in dialysis patient. The Pathophysiological mechanism due solely to high serum phosphorus levels. The risk of vascular and soft tissue calcification rises sharply with higher levels of serum phosphorus. Calcification can occur in coronary and peripheral arteries and in the myocardium [30]. In the order of strong association with mortality it

has been studied and shown that high serum phosphorus levels and the presence of elevated levels of calcium – phosphate product were strong predictors, while hypocalcemia alone constituted an intermediate risk and high levels of parathyroid hormone alone carried the lowest risk.

**Hemodialysis related hypotension**

HD therapy can lead on to hypotension and subsequent hypoperfusion in around one-tenth to one-third of the patients. Hypotension during dialysis is either reduction of systolic BP less than 100 mm of Hg or a symptomatic lowering of systolic BP more than twenty mm of Hg. The complications include cerebral hypoperfusion and or ischemia to myocardium. In a study it was found that patient groups who had lowered their systolic BP less than 110 mm of Hg were at twice the risk of mortality compared with group having systolic BP of 140mm of Hg to 149 mm of Hg post dialysis.

The mechanism underlying this scenario is the altered balance between the volume of fluid that is been removed and vascular compartment's refilling capacity.

## PATHOPHYSIOLOGY OF CARDIOVASCULAR ABNORMALITY

### Left ventricular hypertrophy

LVH is highly prevalent in CKD through stages III to V and it represents adaptative mechanism that occurs in response to a chronic increments in myocardial work requirement [30].

### Pathogenesis

LVH may be thought of as resulting from one or the other, the LV pressure overload or the volume overload to the left ventricle. Pressure overload or systolic overload occurs often due to hypertension, aortic stenosis, due to higher after load to the heart and reduced arterial compliance from arteriosclerosis. Volume overload or diastolic overload is often caused by anaemia, which results as the counteractive mechanism of the heart to increase the delivery of oxygen to peripheral tissues [31, 32].

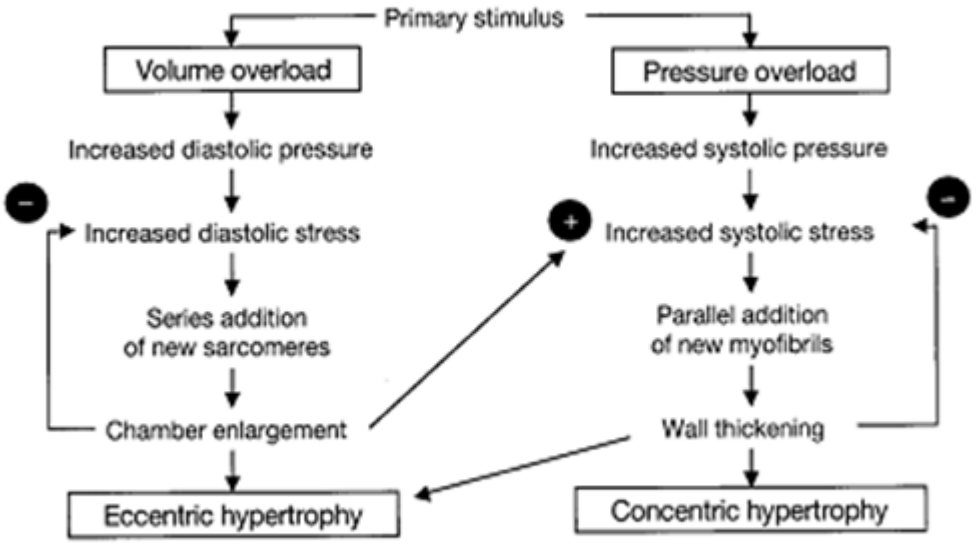



**FIGURE : PATHOGENESIS OF LVH.**

Initially the effect of LVH seems to be useful. Even though there is either higher intraventricular pressure or volume overload or both, there will be structural alterations in the heart that permits an increased work capacity while preserving the tensile strength of the ventricular wall which enables to conserve energy favorably [33]. This can be compared to physiological changes that occur in pregnant women in last trimester, athletes and in normal development of children through adolescence.

As the course of the disease progresses the benefits turns out as detrimental as there is loss of myocytes because of the chronic mismatch

between the production and utilization of energy leading to energy deficit over a long term [34, 35]. Pathogenesis of this energy deficit is caused by various factors such as

- Reduction of capillaries in myocardium
- Decreased blood supply to sub endocardium [36].
- Increased aortic and large to medium arterial stiffness [37].

The papillary muscles get lengthened and along with myocyte rearrangements, apoptosis there is also impairment of the myocardium to generate adequate force. There is increased expression of certain proto oncogenes that favor the fibroblastic activity leading to fibrosis of myocardium [34, 38]. All these changes promote the diastolic dysfunction and various electrophysiological derangements. The myocardial fibrosis, which predisposes to conduction abnormalities along with the decelerated sarcoplasmic reticular calcium ion reuptake predispose to arrythmogenic potential. The above said factors along with stiffening of ventricular wall predisposes to diastolic dysfunction.

An Indian study in the year 2003 done by Dhangri P and his colleague in 60 patients divided into 2 groups of 30 each into mild to moderate chronic

kidney disease (S.Creatinine 1.5-6.0 mg/dl) and advanced chronic kidney disease (S. Creatinine >6.0mg/dl) found in mild to moderate group 40% patient had LVH, and in advanced group 97% of patients had LVH [32].

Another study done in India by SA Kale and his friends in a prospective study including 161 patients from 1997-1999 with mean age group of patient being found left ventricular disease was found in 105(65.2%) patients. Systolic dysfunction was noticed in 42(37.8%) patients. Left ventricular hypertrophy was seen in 88 (54.7%) patients [39].

Zocalli in his study found LVH in ESRD patients is a multifactorial origin like hypertension, anaemia, hyperparathyrodism, chronic volume expansion, inflammation, hyperhomocysteinemia, increased sympathetic activity [ 40].

**Cardiac failure**

**Systolic dysfunction**

The systolic function of patients with excessive volume overload and patients with pre existing cardiac disease is reduced. Approximately fifteen percent of patients during the initiation of dialysis have systolic dysfunction [41]. One of the causes of this systolic dysfunction is the overload cardiomyopathy which causes reduced contractility of the cardiac musculature. This overload cardiomyopathy has a poor prognosis when compared with the

concentric LVH or the left ventricular dilatation without systolic dysfunction [42].

Another important mechanism contributing to systolic dysfunction in patients with CKD includes the uremia which causes reversible myocardial dysfunction. As the level of uremia increases the force of contraction of the myocyte is proportionally reduced. The renal transplantation can reverse the systolic dysfunction in dialysis patients.

**Impaired Diastolic function**

Patients with CKD particularly patients on HD mostly will have some degree of diastolic dysfunction. The degree of diastolic dysfunction is not high as seen with cardiomyopathy but higher than the diastolic dysfunction seen with hypertensive heart disease [43, 44, 45]. This dysfunction causing the impaired filling of LV is caused by the intra mural fibrosis. This causes stiffening of the left ventricular wall which in turn can precipitate pulmonary edema even when there is a mild change in the volume status [46]. This stiffening per se can cause the hypotension and hypoperfusion when there is volume depletion leading on to reduced left ventricular filling.

In a study done in Canada using echocardiographic evaluation twice in dialysis patients one year apart it was found that increased LV mass is an

independent predictor of cardiac failure and mortality. There is also evidence that the management of hemodynamic factors can reduce the left ventricular hypertrophy and death.

## Ischemic heart disease

### Atheromatous coronary disease

Ischemic heart disease is frequently present in patients with end stage renal disease. The development of atherosclerosis in patients with CKD is multifactorial and begins before kidney failure. There is a higher occurrence of critical stenosis in coronary vessels in patients with CKD. Vessel wall damage predisposing to the development of atherosclerosis is caused by a variety of factors

- Activation of endothelium and injury caused by chronic uremia [ 47, 48]
- Endothelial activation brought about by the increased shear stress [49].
- Endothelial activation brought increased tensile stress of the vessel wall [49].
- Production of the various growth factors in response to the stress

All these factors finally contribute to the cellular death of endothelium, extracellular matrix production and deposition. Apart from the activation and injury of the endothelium certain other factors predispose to the alteration in coronary arteries in patients with CKD. They are

- Increase in the levels of procoagulant factors
- Increase in the oxidative stress effected by the reduced anti oxidant and increased reactive oxygen molecules.
- Various lipid abnormalities promoting atherosclerosis.
- Increased insulin resistance and irreversible changes in extracellular substrates effected by elevated blood sugar levels
- Imbalance between inflammatory mediators & inhibitors
- Endothelial effects of elevated homocysteine levels.
- Elevated levels of CRP
- Calcium deposition in the wall of vessels.

**Non-Atheromatous coronary disease**

Patients with this type of coronary artery disease tend to have ischemic symptoms even without having critical coronary disease. The origin of

these symptoms is likely to be because of the cardiomyopathy and microvascular pathology. The left ventricular hypertrophy predisposes to this kind of heart disease in dialysis patients. The hypertrophy is responsible for the increase in the myocardial oxygen demand which requires further dilatation of the coronary vasculature to effect adequate blood flow. As this process is not amenable if there is pathology in large or small vessels, there is occurrence of ischemia. Few other factors have been implicated in this type of heart disease are.

- Cardiac Myocyte-capillary mismatch
- Small vessel muscle hypertrophy and abnormalities in endothelium associated with LVH and uremia [ 50, 51]
- Predisposition to ischemia brought about by the improper regulation of phosphate compounds.

S patrick et al in their study found 28 to 41% of patients have ischemic heart disease [42].

| |
|---|
| **Increased myocardial oxygen demand** |
| Increased myocardial mass |
| Increased systolic & diastolic wall stress |
| **Decreased oxygen supply** |
| Decreased capillary / myocyte density |
| Increased diffusion distances |
| Abnormal diastolic relaxation |
| Compression of myocardial circulation |
| Fibrous replacement of microcirculation |
| Small vessel disease |
| Abnormal vasomotor tone |
| Coronary artery disease |
| Anemia |

**TABLE 3: FACTORS CONTRIBUTING TO ISCHEMIC HEART DISEASE**

Lintrine et al described that among stage 5 CKD cardiac failure is common. The reciprocal causation between the renal failure and cardiac failure is a cyclical event and also occurs due to the common risk factors that exists. The cardiac failure imparts a poorer prognosis in stage 5 CKD and dialysis patients, even subtle dys function of the heart is an independent predictor of mortality in renal transplant patients. Few of the factors causing cardiac failure

in these patients like uremia, anaemia and volume overload could be improved by renal transplantation therapy [53].

**Arrhythmias**

In patients with CKD, particularly patients with ESRD and dialysis, there can be high occurrence of arrhythmia and sudden cardiac deaths. Factors predicting higher incidence and severity of arrhythmia include

- Advancing age
- History of cardiac disease
- LVH
- Treatment with digoxin

The other important factor associated with the arrhythmias in patients on dialysis is the dialysis hypotension[54]. As far as for various dialysis procedures there is a study showing reduced occurrence of arrhythmias in people undergoing peritoneal dialysis rather than HD. It was stated that these effects may be due to absence of post dialysis hypotension & reduced occurrence of hyperkalemia in peritoneal dialysis.

The presence of left ventricular hypertrophy & coronary artery disease as well as the alterations in the various serum electrolyte concentrations occur in

the context of CKD, providing the basis for arrhythmias. Various studies have found out various atrial and ventricular arrhythmias can occur. Some of the high grade arrhythmias prevalent in a study include

- Ventricular tachycardia
- Ventricular couplet&
- Multiple ventricular ectopics[55].

These arrhythmias's presence indicates high chance of sudden death and mortality.

**Valvular heart disease**

There can be valvular leaflet and annular calcifications in the mitral and aortic valves due to the dystrophic calcifications [56]. The occurrence of aortic valvular calcification occurs a decade or two earlier. The aortic sclerosis is considered to be related to high CVD mortality. The valvular calcifications are associated with the conduction disturbances, rhythm disturbances, regurgitant lesions and peripheral vessel disease. The reduced survival because of valvular calcifications can be brought about by

- ❖ LV systolic dysfunction
- ❖ Severe calcification[56].
- ❖ Mitral valve insufficiency.

## LARGE VESSEL DISEASE

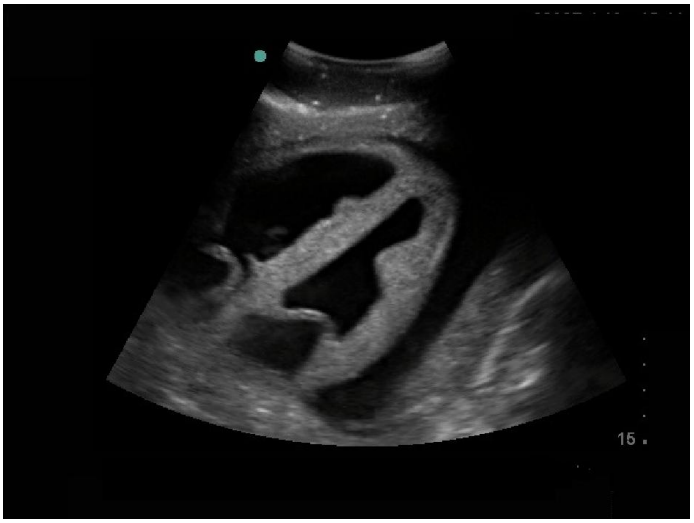
The increased LV after load is linked with higher incidence of the CVD burden [57, 58]. The reasons for the increased after load include increased vessel stiffening, increased sympathetic tone & autonomic derangements.

In chronic kidney disease there is an accelerated ageing process of the vessels leading to arteriosclerosis and vascular dilatation. These changes predispose to the so called faster pulse wave velocity and systolic hypertension. Even in patients on dialysis tend to have a normal peripheral resistance, thus reducing the chances of diastolic hypertension. So as a result there is widened pulse pressure which is also associated with the development of LVH [59].

**Pericardial disease**

Pericardial disease in CKD is generally associated with stage 5 CKD. Pericarditis is the consequence of an inflammation of the pericardium, the serous membrane enclosing the heart and the root of the great blood vessels. Pericarditis occurs in both acute and chronic renal failure patient. Over the past 40 years with the advent of dialysis therapy the incidence of clinically apparent pericarditis has decreased from 50% --60%. The reason for occurrence of this entity is thought to be because of the increase in various toxins of uremia. This

thought originated as the pericarditis resolves with intensive dialysis regimen. Pericarditis is frequently seen in peritoneal dialysis patient than it occurs in haemodialysis patient. The difference has been attributed to a higher clearance of 'middle molecule' in peritoneal dialysis. Pericardial effusion frequently complicates pericarditis but cardiac tamponade is rare. Constrictive pericarditis is rare in dialysis patient. Small pericardial effusion is found in 15-20% of patient of stable asymptomatic patient .It most commonly manifests as acute uremic or dialysis-associated pericarditis although chronic constrictive pericarditis may also be seen.




**Transthoracic echocardiogram showing pericardial effusion.**

Dialysis pericarditis describes patients who develop clinical manifestations of pericarditis after 8 weeks of initiation of this kidney replacement therapy [60]. It is associated with the poor response even with the

intense dialysis regime. Avoidance of heparin is done during dialysis in order to prevent cardiac tamponade.

## INFECTIVE ENDOCARDITIS

Infective endocarditis (IE) is a relatively common complication of hemodialysis when compared to rates in the general population. This likely reflects several factors, including

- the relatively high incidence of bacteremia,
- common use of dialysis catheters, and
- the high prevalence of pre-existing valvular abnormalities.

The bacteremia in patients undergoing HD is mainly because of the catheter access site infection. The left sided valves are more involved, among them mitral valve is the most commonly affected there should be a suspicion of infective endocarditis when there is

- ❖ Indication of persistent infections beyond catheter removal/antibiotics
- ❖ Occurrence of metastatic abscesses
- ❖ Positive blood culture for staph aurues

Trans oesophageal echo is very sensitive as high as hundred percent. Therapy of IE should be based on culture reports and should be continued for at least 1 month in HD patients. However the death rate is higher in ESRD[61] patients.

## AUTONOMIC DYSFUNCTION

In patients with CKD particularly among stage 5 CKD, there is some degree of resistance in baroreceptors. This manifests in the exercise ECG as a restriction in maximum pulse rate and limited exercise ability. The cause for this may be attributed to

- Increasing age
- Hypertension
- Volume overload

Increased sympathetic activity is common in patients with stage 5 CKD. The relationship is proved by the nephrectomy of diseased kidneys. There is downregulated vasopressor response to sympathetic activity which is an important factor that accounts for dialysis-hypotension.

## INVESTIGATING CARDIAC DISEASE IN CKD

LVH associated ECG changes are prevalent in CKD patients, thus making the ST segment depression in routine ECG less predictable of CAD. Many electrolyte and fluid alterations take place that produce diagnostic dilemma in ECG. Particularly HD causes the prolongation of $QT_c$, QT dispersional increase and QRS segment abnormalities.

Troponins, the cardiac biomarkers are moderately increased in CKD. However their importance is felt when there is a rise from the baseline. High levels of troponin-t are a potent marker of adverse events. Apart from these BNP can be used as a reliable predictor for outcomes.

| |
|---|
| Uremic myopathy |
| Expression of fetal cardiac troponins in the skeletal muscle |
| Altered protein clearance |
| Abnormal protein metabolism |
| Silent myocardial injury, microinfarctions |
| Uremic mileau-uremic toxins, nonischemic damage to the myocardium |
| Left ventricular hypertrophy |
| Inflammatory condition |

**TABLE 4: CAUSES OF ELEVATED CARDIAC TROPONIN IN CKD PATIENTS.**

## ECHOCARDIOGRAPHY

Echocardiography in both Two-dimensional and M mode gives idea about the left ventricular hypertrophy & systolic dysfunction. The amount of LVH is detected by increased free wall thickness of left ventricle or via the Left Ventricular mass index calculation. Echocardiography is also useful in valvular and pericardial pathologies.

The mass index of Left Ventricular before the dialysis is higher than mass index measured after the dialysis even though the actual Left Ventricular mass remains the same .this due to the removal of fluid during dialysis causing a decrease in the Left ventricular internal diameter. For this reason echocardiography must be done after achieving the so called ‘ base weight ’.it it is the minimum weight which the patient can be in without muscular cramp or dialysis associated hypotension.

Diastolic dysfunction can be assessed via Doppler analysis of diastolic flow across the mitral valve. Physiologically after the opening of the valve, there is relaxation of ventricle, with sudden rise in flow causing the E peak or the early peak, than atrial systole occurs causing the A peak or the atrial peak. The stiffening of the hypertrophied Left Ventricle causes a small E peak, and a large

A peak, when the function of the left atrium is normal. Diastolic dysfunction is represented by a reduced E/A ratio.

Stress echocardiography using Dobutamine can be used for screening CKD individuals to find out CAD. It is used to find out the underlying systolic reserve even in patients with systolic dysfunction. This investigation has a good specificity and sensitivity exception being female sex and older age[62]. For patients who cannot tolerate exercise it is preferred over scintigraphy. For patients undergoing dialysis this investigation has shown to have a very high negative predictive value [63].

**NUCLEAR SCINTIGRAPHY**

Systolic function and ischemic changes can be detected by nuclear scintigraphy. For the proper evaluation via this technique the valvular insufficiency should not be there. With normal valvular function estimation of systolic dysfunction during exercise and rest can be done accurately.

Either by the use of $^{99m}$Tc-labelled thalium, methoxyisbutylisonitrile,‘ MIBI ’, or metiodobenzylguanidine ‘ MIBG ’ or exercise it is used in screening prior to transplantation and in cases of uncertain diagnosis of CAD. Hypotension, very high blood pressures, LVH causing reduced perfusion , blunting of tachycardia

response because of autonomic neuropathy are significant obstacles to this type evaluation[64], and may cause improper evaluation or may cause adverse results.

**Coronary Angiography**

This technique is gold standard for the diagnosis of CAD. There is always the risk of contrast nephropathy with this procedure which offers hindarance. The risk of cholesterol embolism is also there. As there is more occurrence of asymptomatic CAD, the American society of transplants physicians suggests the screening can be avoided only in the patients who are at lowest risk for CAD [65].

**EBCT**

EBCT, Electron-beam ultrafast computed tomography is used to determine the coronary atherosclerosis with the help of coronary arterial calcification. This technique takes into account that coronary calcification is an important marker of atherosclerosis but in CKD patients there is a vascular calcification widespread and severe in degree. But the use of this technique is very useful due to the fact that the higher the accumulation of calcium in atheroma or vessel wall poorer the prognosis according to the recent evidences [66, 67].

## Duplex Ultrasonography and Doppler Flow Imaging

The different vessel beds have different waveforms, pathology is indicated by the change of the normal waveform.. Generally pathological arterial segment show spectral broadening of waveforms, the increased velocity of flow at the site of vessel stenosis and there will be pre stenotic waveforms above and post stenotic waveforms below the obstructed segment.

## Ankle Brachial Index

The ankle brachial index provides useful screening test for arterial disease of the lower limbs. The procedure uses continuous-wave Doppler interpretation of the arm's blood pressure and ankle blood pressure. The ankle brachial index is calculated by

Ankle brachial index = ankle systolic BP ÷ arm systolic BP

The index is usually taken twice before and after exercise. Absence of pain throughout the exercise period rules out pathology in vessels of lower limb vascular claudication. Ankle-brachial index ranges from 1.0 to 1.1 in normal individuals at rest. Progressive decrements indicate worsening, often multi level,

arterial stenosis. A resting level of ≤ 0.25 indicates severity of disease [68] but the important predictor is the post exercise reduction in the index.

**MRI and Angiography**

These techniques are particularly important in dissection of arteries and imaging the vascular morphology. These techniques are much useful in the imaging of renal vasculature and mesenteric vasculature when there is risk of contrast nephropathy or cholesterol embolism.

**Intravascular Ultrasonography**

It is mostly used to determine the morphology of the vessel and morphology of the plaque used in adjunction with intervention technique of vessels. The vascular lumen can be displayed using 3-dimensional re-construction methods. As there is reduced interference from the inter positioned structures and vascular calcification this technique is more sensitive than the routine ultrasonography.

**Electrocardiogram**

Muirhead and others demonstrated electrical activity of the heart during later period of 19th century, following which there was direct recording of cardiac potentials by Waller in 1886 [69].

William Einthoven first introduced the term “electrocardiogram” by the year 1893 which is used till date worldwide for the recording of electric activity of the heart. String Galvanometer which was invented by William Einthoven in 1901 provided a consistent and direct method for registering electrical activity of the heart [69].

**String galvanometer which was used to record ECG initially**

After the year 1910 string galvanometer become very popular in clinical practice. Subsequent ECG became the first and most common bioelectric signal to be computer processed and most commonly used cardiac diagnostic test.

## ELECTROCARDIOGRAPHIC CHANGES IN CKD

The abnormal resting ECG and exercise ECG are brought about by the ever so increased occurrence of LVH among CKD patients. ST-T changes along with the increase in the PR interval and QRS duration are seen in patients who are dialysis dependent. These patients also exhibit more ECG changes during dialysis due to changes in electrolyte transfer between intra and extra cellular compartments. However the occurrence of classical ECG changes of acute coronary ischemia indicate occurrence of MI and unstable angina.

The risk of arrhythmia, sudden cardiac arrest and death is higher in patients undergoing maintenance HD. The factors that are associated with the occurrence of arrhythmias in these patients include

- The alteration in the serum electrolytes
- Alteration in the volumeic status
- Blood pressure
- Underlying CVD
- various medicational usage

There is a markedly increased rate of cardiac events and decreased event free survival rate in non diabetic dialysis patients than general population [70].

At the time of initiation of dialysis, many of CKD patients will have ischemic heart disease. ESRD patients with coronary artery disease either symptomatic or asymptomatic are at increased risk for arrhythmias and Sudden Cardiac Death. The risk is exaggerated in the presence of anaemia and left ventricular hypertrophy, which are commonly encountered in patients with ESRD and dialysis dependant.

The occurrence of ECG abnormalities and the occurrence of new arrhythmias and silent ischemia to myocardium are related to the presence of Coronary artery disease, and is related to the duration of dialysis. Serious, life threatening ventricular arrhythmias and silent ischemia of myocardium has been noted in patients on dialysis [71].

Factors contributing to increased occurrence of arrhythmias include

- compromised myocardium

  (Because of either underlying Coronary Artery disease, decreased coronary blood flow, or the effects of uraemia on myocardium),

- increased QTc interval or dispersion,
- Abnormalities in levels of electrolytes,
- Dialysis hypotension,

- presence of LVH (present in most of the patient on dialysis), and
- Autonomic dysfunction (with or without diabetes). [25]

Patients on Dialysis have frequent electrolyte abnormalities like fluctuation in the levels of potassium, ionized calcium, magnesium, and other divalent ions.

Patients on HD have wide fluctuating levels of potassium and bicarbonate. These fluctuations are due to

- Intermittent nature of procedure, promoting high interdialytic variation
- the level of potassium and calcium in the dialysate fluid used and
- Incomplete adherence to dietary regimes directed towards the control of calcium-phosphate product. [72].

Soman and his colleague divided 9,554 patients into 5 groups based on creatinine clearance, where mean age group of patients being 63.4±13.8 years and they observed atrial fibrillation in 4.1 to 9.4%, complete heart block in 0.7-3.5%, RBBB in 3.5-7.1%, LBBB in 3.6-8.3% and LVH in 7.1-18.5%. Unstable angina was documented 33.2%-39.9% in different groups of chronic kidney disease [73].

Graham in his study in 2004 on 296 patients found by ambulatory ECG recording higher prevalence of supraventricular tachycardia, ventricular tachycardia and ectopics. The chronic renal insufficiency cohort study done by Soliman and his friend in on 3,267 patients with mean estimated glomerular filtration rate of 43.6±13.0 found atrial fibrillation as the most common arrhythmia in CKD patients, nearly one in every five participants had evidence of atrial fibrillation [74].

Abe in his study on 221 patients noticed 72 patients had sinus rhythm, 2 patients had atrial fibrillation, 29 patients had ventricular premature complex, ST-T changes seen in 43 patients [75].

In a study done by A.S Menon et al [9] and Krivosheiv[76] et al the commonest electrocardiographic abnormality was lateral wall ischemia, left axis deviation with left ventricular hypertrophy, prolonged QT interval, p.mitrale and intraventricular conduction defect.

**The Electrocardiographic manifestation of the left ventricular hypertrophy due to systolic overload [77]**.

1. Abnormalities of the QRS complex

· Increased magnitude of QRS deflection.

· Attenuation of the small q wave in left oriented leads.

· An increased time in left ventricular activation time.

· A small equiphasic complex in lead AVF.

· Counter clockwise electric rotation.

2. Abnormalities of ST segments and t waves

T wave may be inverted in lead V5, V6 lead I and AVL, upright in

right oriented leads. The associated ST segment in the left oriented leads is usually minimally depressed. This is an indication of hypertrophied left ventricular strain, probably the expression of relative ischemia.

3. left sided chest leads showing inverted u waves.

4. Left atrial enlargement.

5. Abnormality of the QRS and T wave.

Early and uncomplicated left ventricular hypertrophy causes no change in the direction of the mean plane QRS vector. With relatively long standing left

ventricular hypertrophy, the QRS axis begin to deviate to the left side.

The mean frontal T wave vector is directed to the right reflecting very

compromised left ventricle.

**The Electrocardiographic manifestation of diastolic overload**.

Left oriented leads showing

1. Increase in the R wave voltage.
2. Deep Q waves.
3. Relatively tall symmetrical T wave.
4. Minimally elevated S-T segment.
5. Inverted U waves in the left precordial leads.

**The Electrocardiographic manifestation of the cardiomyopathy**

They include

- Sinus tachycardia
- Ventricular arrhythmia
- Left atrial enlargement
- Non specific ST-T wave changes
- Intra ventricular conduction defects
- Low voltage

**Effect of electrolyte disturbance on ecg.**

Uraemia presents with manifestation of hypocalcaemia and associated with hyperkalaemia and or acidosis. The hypocalcaemia causes a prolong ST segment and there by the QT interval. The hyperkalaemia causes tall T waves.

The prolongation of QT interval is inversely proportional to the level of serum calcium. QT interval in hyperkalaemia is either normal or actually decreased. If the hyperkalaemia is associated with hypocalcaemia the QT interval may be prolonged.

The QT interval is the interval beginning from the Q wave to the end of T wave. The QT interval shortens with tachycardia and prolong with bradycardia. It is thus evident that QT interval cannot be viewed in absolute term but must be corrected to the effect of associated heart rate.

Drechsler Christiane et al in his study found atrial fibrillation in 8 to 12% of patients, signs of MI in 13 to 17%, LVH in 12 to 14%, ventricular conduction defect in 7 to 8% of patients in CKD patients with different ranges of HBA1c[78].

Graham27 with his collegue observed prolongeded $QT_c$ duration and increased QT dispersion was associated with reduced kidney function [79].

# 4. MATERIALS AND METHODS

**Study design:**

This study is a single center non randomized prospective study meant to study the electrocardiographic changes in patients with chronic kidney disease.

**Study period:**

75 Consecutive patients of chronic kidney disease admitted in thanjavur medical college hospital during the period of 8 months between January 2014 to august 2014 were taken up for the study.

**Inclusion Criteria**

• Chronic kidney disease for more than 3 months.

• Reduced Kidney size bilaterally.

**Exclusion Criteria**

- Documented ischemic heart disease.
- Congenital heart disease.
- Valvular heart disease.
- Age less than 18 years.

**Study centre:**

This study was carried out in Department of Medicine, Thanjavur Medical college Hospital, Thanjavur, Tamil Nadu.

All cases were admitted and examined in detail in the wards and clinical data was recorded in the proforma annexed herein. All cases were followed till discharge or death.

**Clinical details:**

Personal particulars like age, sex, duration of illness, presenting complaints, relevant history, past history, treatment history, clinical signs and symptoms were recorded.

**Clinical examination:**

Examination was done in a detailed manner and vital signs, weight, were recorded and systemic examination was carried out.

**ECG monitoring:**

ECG was taken in all cases after admission. Routine conventional limb leads, chest leads and long strips were recorded. Continuous cardiac monitoring was done in some needful patients.

**Lab investigations:**

1. a. Urine

PH,

Specific gravity,

Protein,

Sugar,

Microscopy

2. Blood

- COMPLETE BLOOD COUNT
- Random blood sugar,
- FBS/PPBS,
- Blood Urea,
- Serum Creatinine,
- serum sodium ,
- serum potassium
- Serum fasting lipid profile

2. Ultrasound Abdomen

3. Transthoracic echocardiography (ECHO)

These investigations were carried out in all patients.

eGFR calculation done using cockraft and gault equation.

**Data Analysis**

The patients' data were collected prospectively and entered in the proforma (annexure). The data was digitalized in Microsoft excel software. Statistical analysis was done using SPSS 21 software.

The categorical variables have been described as proportions and percentages. The continuous variables have been expressed as mean and standard deviation, as well as range.

The effect of various factors on presence of ECG changes and no ECG changes was analysed by unpaired ‘t’ test for continuous data. Chi – square test was used to compare the categorical data. P value $< 0.05$ was considered significant in this study.

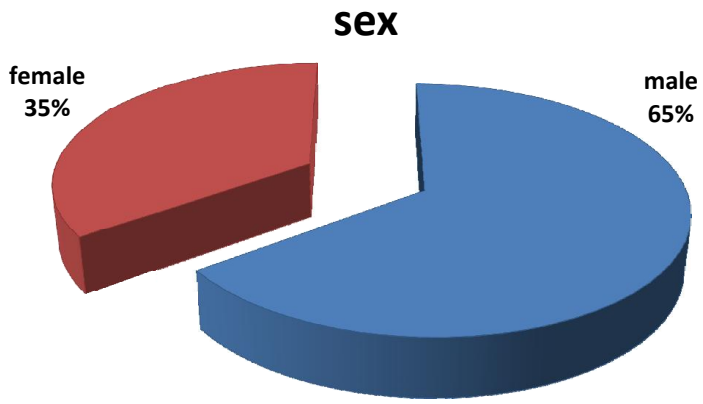
# 5. RESULTS

The present study comprises 75 consecutive proven chronic kidney disease patients admitted to thanjavur medical college and hospital during January 2014 to august 2014.

SEX DISTRIBUTION

TABLE: SEX DISTRIBUTION OF 75 CASES OF CKD

| SEX | Number | Percentage |
|---|---|---|
| Male | 49 | 65% |
| Female | 26 | 35% |

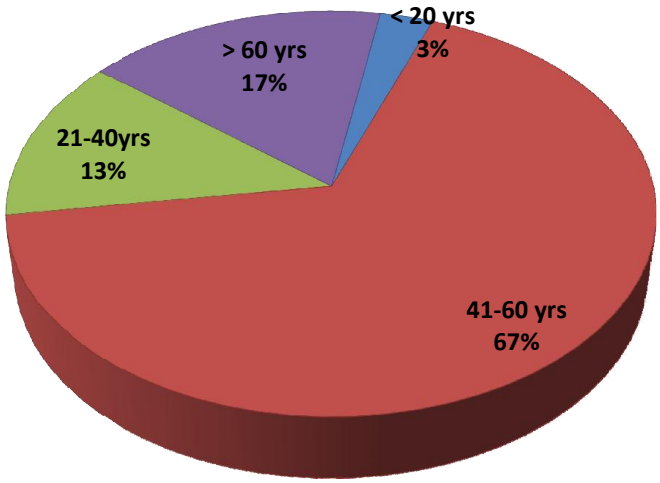



In the present study 49(65%) persons were males and 26(35%) the sex distribution among males: females was approximately 1.8:1.

AGE DISTRIBUTION

TABLE: AGE DISTRIBUTION OF 75 CASES OF CKD

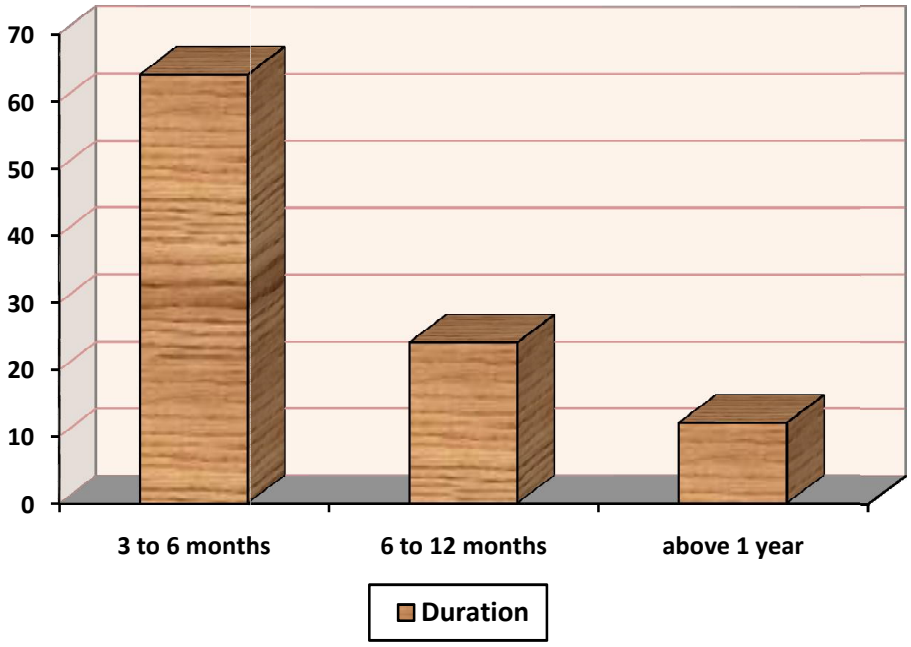
| S.no | Age distribution | Number | Percentage |
|---|---|---|---|
| 1 | Below 20yrs | 2 | 3% |
| 2 | 21 to 40yrs | 10 | 13% |
| 3 | 41 to 60yrs | 50 | 67% |
| 4 | 61yrs & above | 13 | 17% |




In the present study the age variation was from 18 to 76 years. Majority of the patients were in the age group of 41-60 years, which included 50 patients (67%). The mean age of the study group was 50.3±11.5 years.

TABLE : DISTRIBUTION OF 75 CASES OF CKD BASED ON DURATION OF ILLNESS

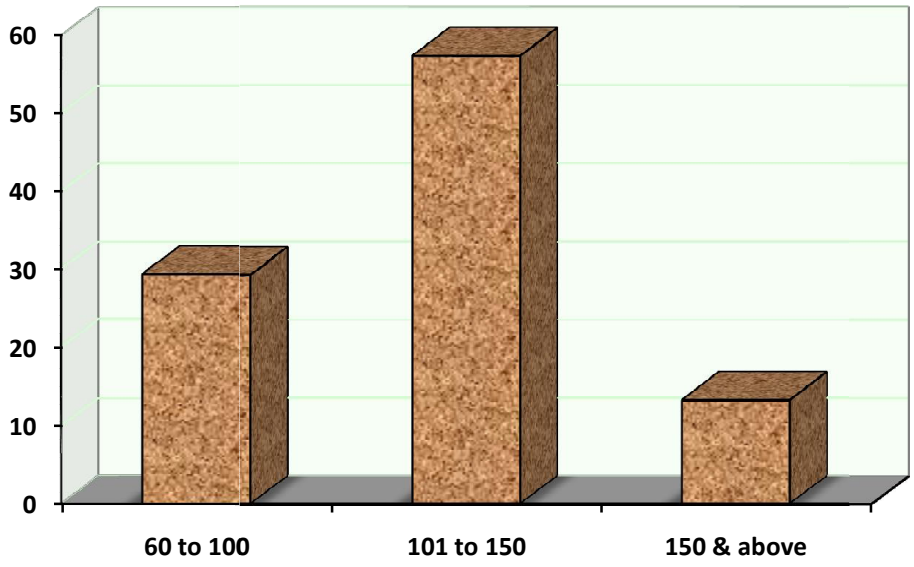
| Particulars | Number | Percentage |
|---|---|---|
| 3 to 6months | 48 | 64.0% |
| 6 to 12months | 18 | 24.0% |
| Above 1year | 9 | 12.0% |




The duration of the renal failure in our study group ranges from 3 months to 6 years. The mean duration of renal failure in the group was 6.9 months.

TABLE : DISTRIBUTION OF 75 CASES OF CKD BASED ON LEVELS OF BLOOD UREA

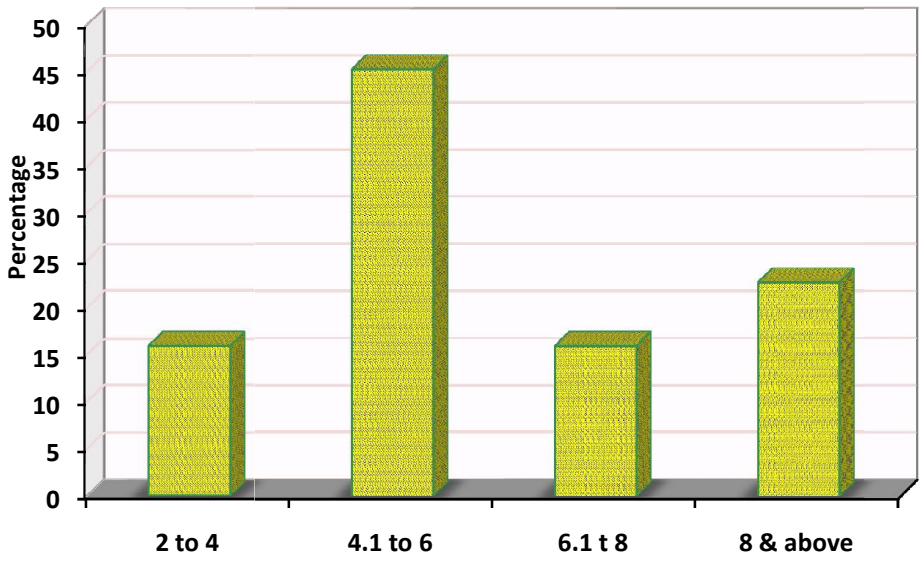
| **Blood urea (in mg/dl)** | **No.of patients (n=75)** | **Percentage** |
|---|---|---|
| 60 to 100 | 22 | 29.3% |
| 101 to 150 | 43 | 57.3% |
| 150 & above | 10 | 13.3% |




The blood urea levels of patients with CKD enrolled in our study ranges from62-180 mg%. Maximum number of patients (43 patients) (57%)had their blood urea levels in the range101-150mg% the mean value of the study group was 120.5±28mg%.

TABLE: DISTRIBUTION OF 75 CASES OF CKD BASED ON LEVELS OF SERUM CREATININE.

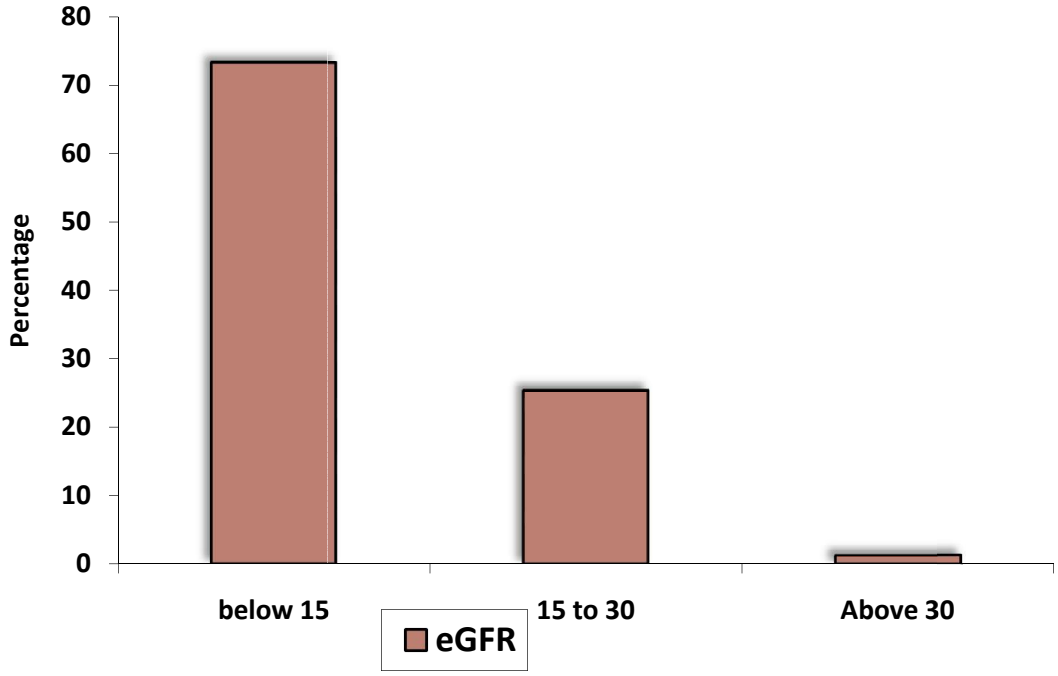
| **Serum creatinine (in mg/dl)** | **No.of patients** | **Percentage** |
|---|---|---|
| 2 to 4 | 12 | 16.0% |
| 4.1 to 6 | 34 | 45.3% |
| 6.1 to 8 | 12 | 16.0% |
| 8 & above | 17 | 22.7% |




The serum levels of creatinine of patients in our study ranges from2.2-20.2 mg%. The mean value for serum creatinine levels was 6.2±3mg% with maximum number of patients(34 patients) i.e.(45%) were in the range of 4.1 to 6.0 mg%.

TABLE: DISTRIBUTION OF 75 CASES OF CKD BASED ON eGFR.

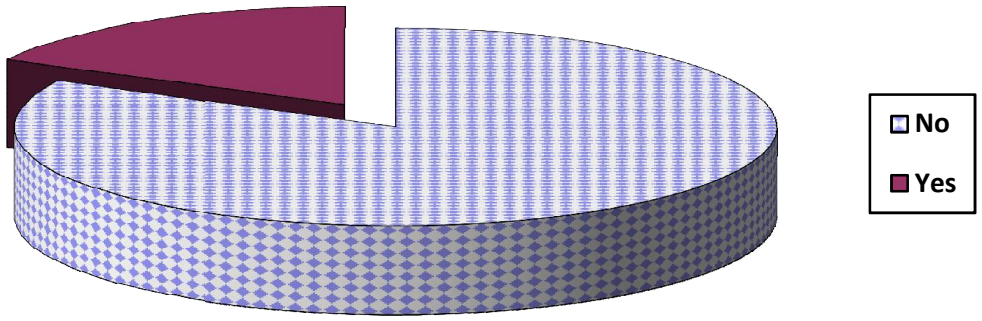
| **eGFR (in ml/min)** | **No.of patients** | **Percentage** |
|---|---|---|
| Below 15 | 55 | 73.3% |
| 15 to 30 | 19 | 25.3% |
| 30 to 60 | 1 | 1.3% |




The eGFR of CKD patients enrolled in our study ranges from4ml/ min t0 33ml/min. maximum number of patients(55 patients) (73%)had eGFR<15 ml/min. the mean eGFR of the study group was 12.8±5.4 ml/ min. The eGFR calculation was done using cockraft and gault formula

TABLE: NUMBER OF PATIENTS UNDERGOING REGULAR HEMODIALYSIS .

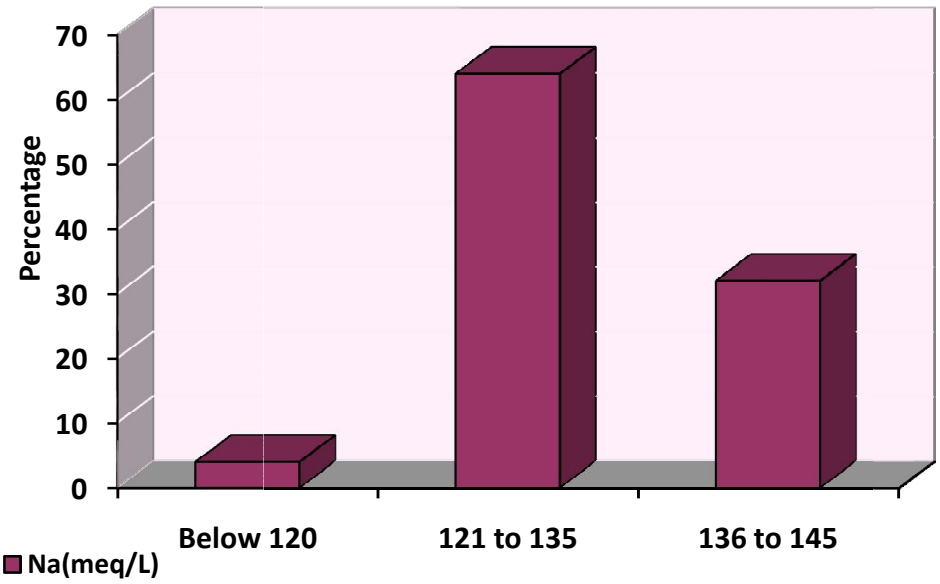
| THERAPY | No. of patients | Percentage |
|---|---|---|
| No | 62 | 82.7% |
| HD | 13 | 17.3% |




In our study group among the 75 cases of CKD enrolled there were about 13 patients undergoing regular hemodialysis. These patients in regular hemodialysis constituted around 17% of the total study patients.

TABLE: DISTRIBUTION OF 75 CASES OF CKD BASED ON LEVELS OF SERUM SODIUM.

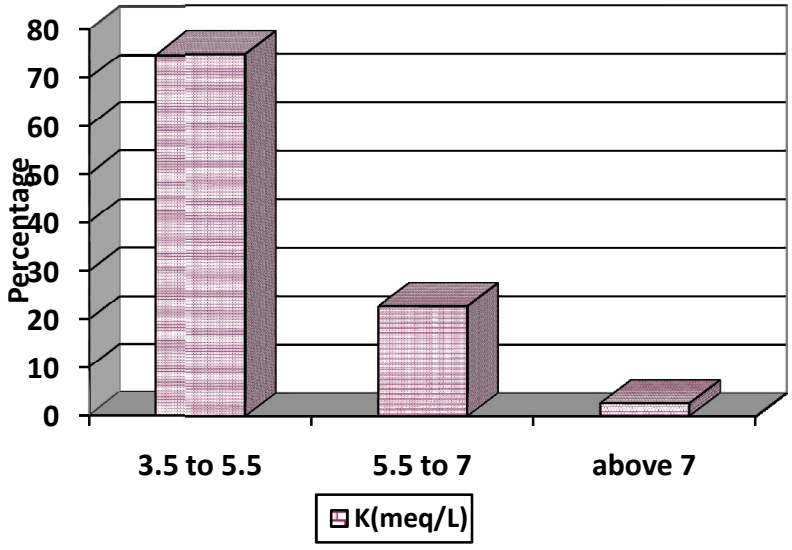
| **Serum Na(meq/L)** | **No. of patients** | **Percentage** |
|---|---|---|
| Below 120 | 3 | 4.0% |
| 121 to 135 | 48 | 64.0% |
| 136 to 145 | 24 | 32.0% |




In our study group patients were having serum sodium in the range of 117-145 meq/L. the mean for this study group is 132.3±5.9 meq/L. the maximum number of patients (48 patients)were in the range 121 to 135 meq/L constituting to 64% of group.

TABLE: DISTRIBUTION OF 75 CASES OF CKD BASED ON LEVELS OF SERUM POTASSIUM.

| **Serum K+ (in meq/L)** | **No.of patients** | **Percentage** |
|---|---|---|
| 3.5 to 5.5 | 56 | 74.7% |
| 5.5 to 7 | 17 | 22.7% |
| Above 7 | 2 | 3.4% |

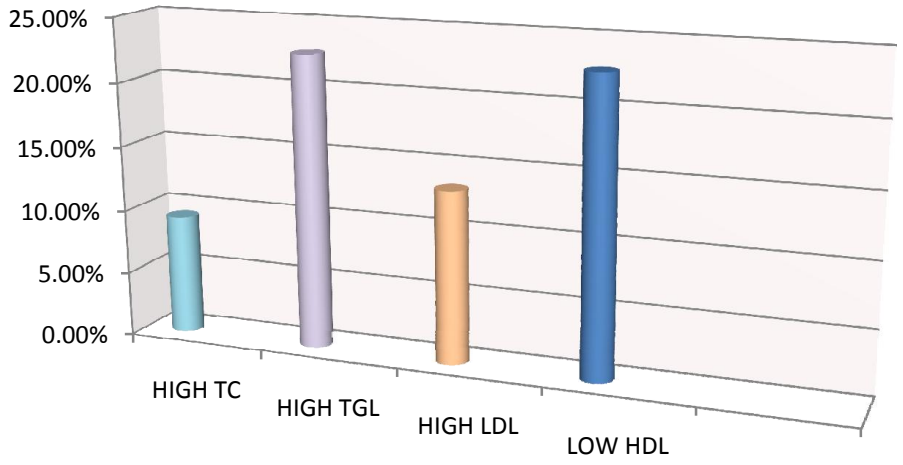



The levels of potassium in CKD patients enrolled in our study ranges from 3.5 to 8meq/L. maximum number of patients(56 patients) (75%)had serum potassium within the normal range . the mean potassium value was5.1 ± 0.9 meq/L.

TABLE: DISTRIBUTION OF 75 CASES OF CKD BASED ON LIPID LEVELS.

| Lipid | MEAN | S.D. |
|---|---|---|
| Total cholesterol | 183.4 | 21.3 |
| Triglycerides | 181.1 | 29 |
| HDL | 45.7 | 6.2 |
| LDL | 94.3 | 17.6 |

| Lipid abnormality | No. of patients | percentage |
|---|---|---|
| High TC | 7 | 9.3% |
| HIGH TGL | 17 | 22.7% |
| High LDL | 10 | 13.3% |
| Low HDL | 17 | 22.7% |

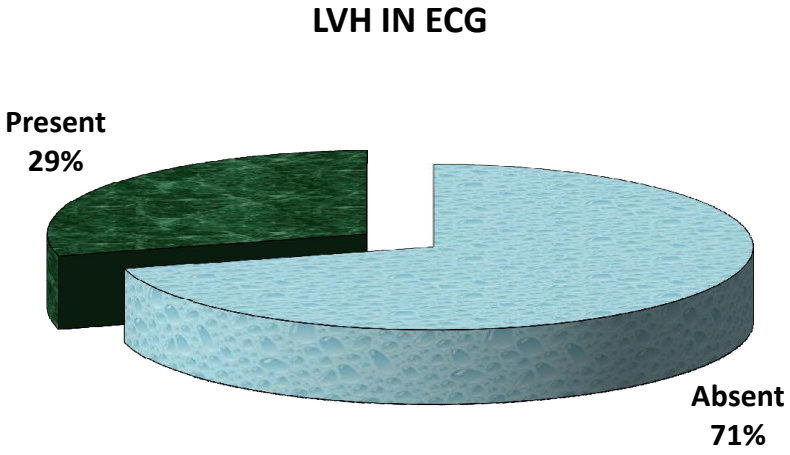



In our study population 40% of patients had abnormal lipid profile with elevated TGL and Reduced HDL as the commonest abnormalities, both of them accounting to 23% individually.

TABLE : CASES OF CKD with LVH in ECG.

LVH

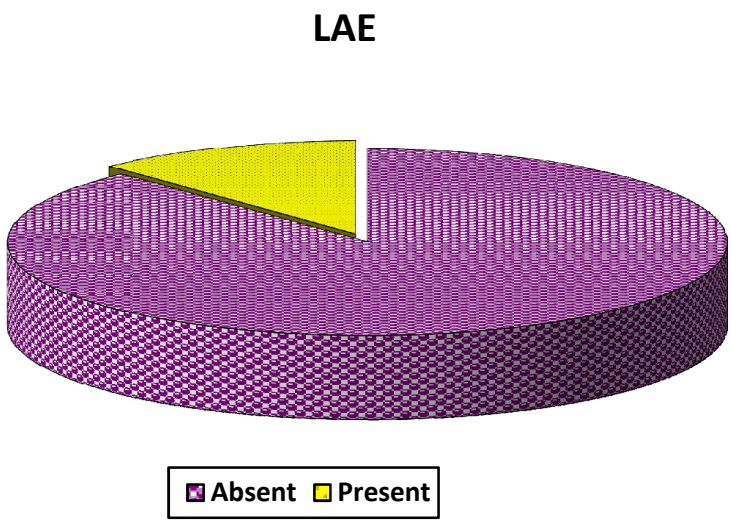
| LVH in ECG | No.of patients | Percentage |
|---|---|---|
| Absent | 53 | 70.7% |
| Present | 22 | 29.3% |




In our study group patients having LVH in ECG were 22 in number out of the total 75 patients, constituting to 29% of study population.

TABLE: CASES OF CKD WITH LEFT ATRIAL ENLARGEMENT IN ECG..

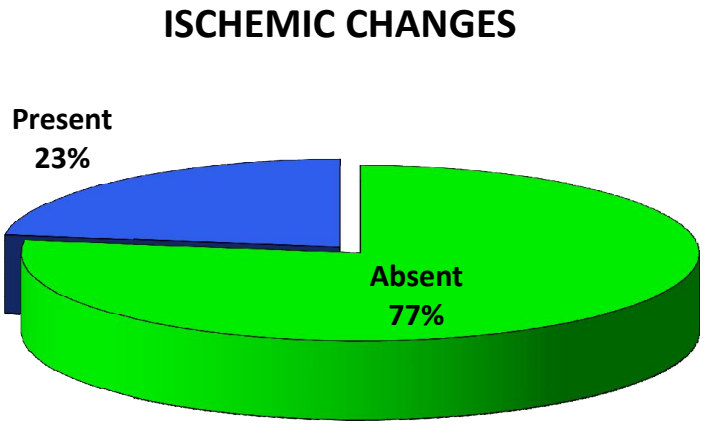
| LAE in ECG | No.of patients (n=75) | Percentage |
|---|---|---|
| Absent | 66 | 88.0% |
| Present | 9 | 12.0% |




In our study group patients having Left atrial enlargement in ECG was present 9 in number out of the total 75 patients, constituting to 12% of study population. 66 out of 75 patients did not have the Left atrial enlargement in ECG.

TABLE: CASES OF CKD WITH CHANGES OF CORONARY ARTERY DISEASE IN ECG

| Ischemic changes | No.of patients (n=75) | Percentage |
|---|---|---|
| Absent | 58 | 77.3% |
| Present | 17 | 22.75 |

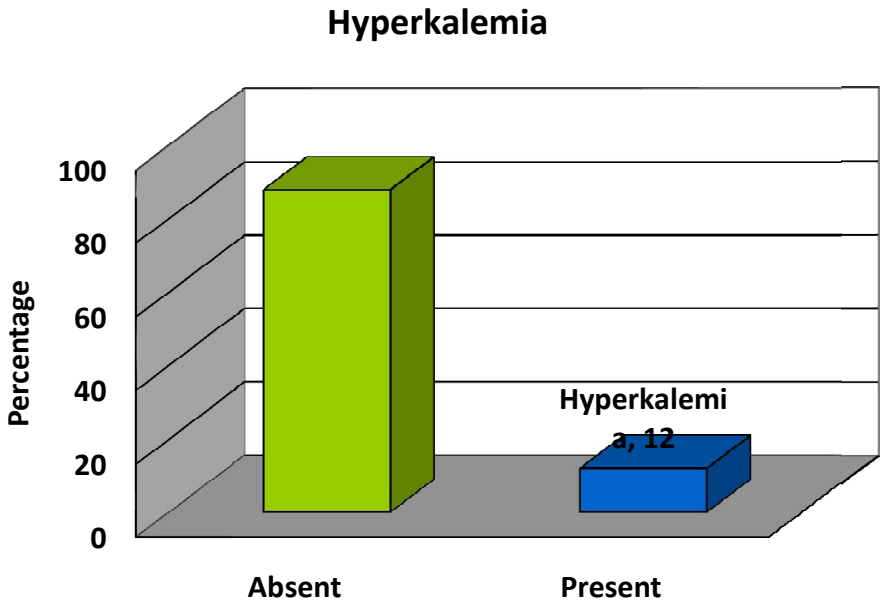



In our study group patients having ISCHEMIC CHANGES in ECG was present 17 in number out of the total 75 patients, constituting to 23% of study population. 58 out of 75 patients did not have the ischemic changes in ECG.

TABLE: CASES OF CKD HAVING ECG FINDINGS OF HYPERKALEMIA

HYPERKALEMIA.

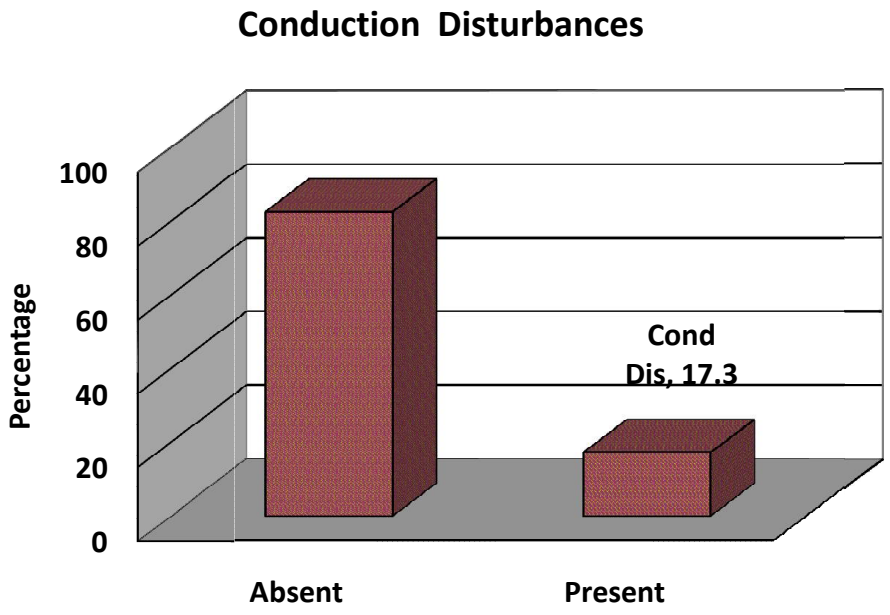
| **Hyperkalemic changes** | **No.of patients (n=75)** | **Percentage** |
|---|---|---|
| Absent | 66 | 88.0% |
| Present | 9 | 12.0% |




In our study group patients having ECG changes pertaining to hyperkalemia was present 9 in number out of the total 75 patients, constituting to 12% of study population. 66 out of 75 patients did not have the ECG changes pertaining to hyperkalemia.

TABLE: CASES OF CKD HAVING CONDUCTION DISTURBANCES.

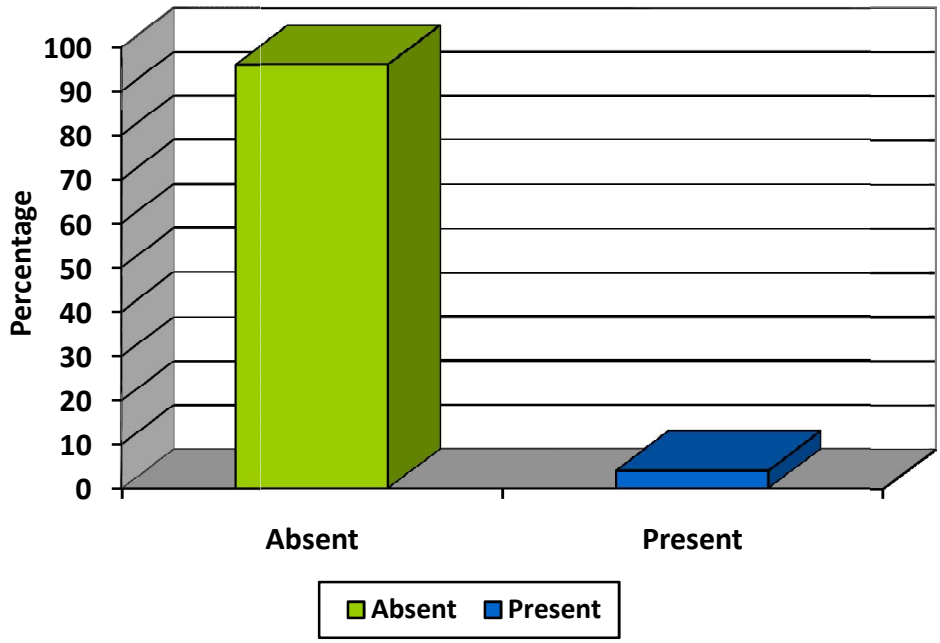
| Conduction disturbances | No. of patients | Percentage |
|---|---|---|
| Absent | 62 | 82.7% |
| Present | 13 | 17.3% |




In our study group patients, conduction disturbances in ECG was present 13 out of the total 75 patients, constituting to 17% of study population. 62 out of 75 patients did not have the conduction disturbances in ECG. Conduction disturbances included intraventricular conduction delay and QTc prolongation.

TABLE: CASES OF CKD HAVING ARRHYTHMIA ON ECG

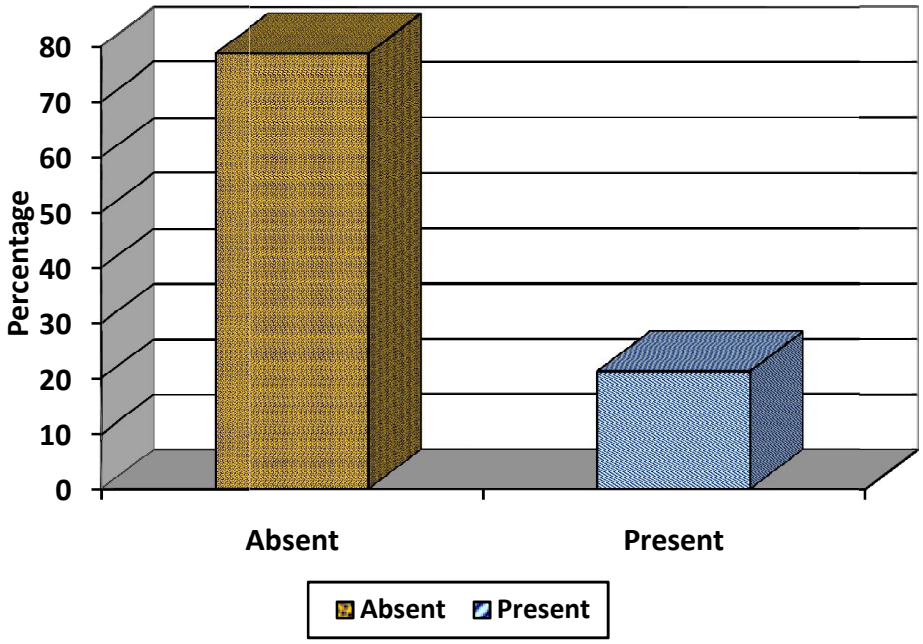
| Arrhythmia | No.of patients (n=75) | Percentage |
|---|---|---|
| Absent | 72 | 96.0% |
| Present | 3 | 4.0% |




In our study group patients, arrythmia in ECG was present in 3 out of the total 75 patients, constituting to 4% of study population. 72 out of 75 patients did not have arrythmia in ECG. Two patients had premature ventricular contractions and one patient had atrial fibrillation.

TABLE: CASES OF CKD WITH ECHOCARDIOGRAPHIC CHANES OF CORONARY ARTERY DISEASE.

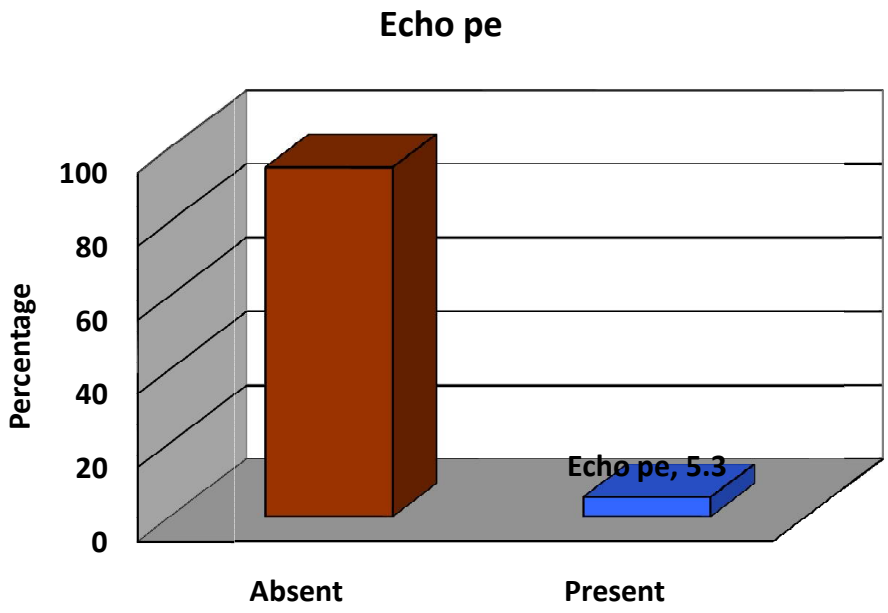
| **Cad In ECHO** | **No. of patients** | **Percentage (100%)** |
|---|---|---|
| Absent | 59 | 78.7 |
| Present | 16 | 21.3 |




In our study group patients echocardiographycally detected coronary artery disease was present 16 out of the total 75 patients, constituting to 21% of study population. 59 out of 75 patients did not have echocardiographycally detected coronary artery disease.

TABLE: CASES OF CKD HAVING PERICARDIAL EFFUSION ON ECHOCARDIOGRAPHY.

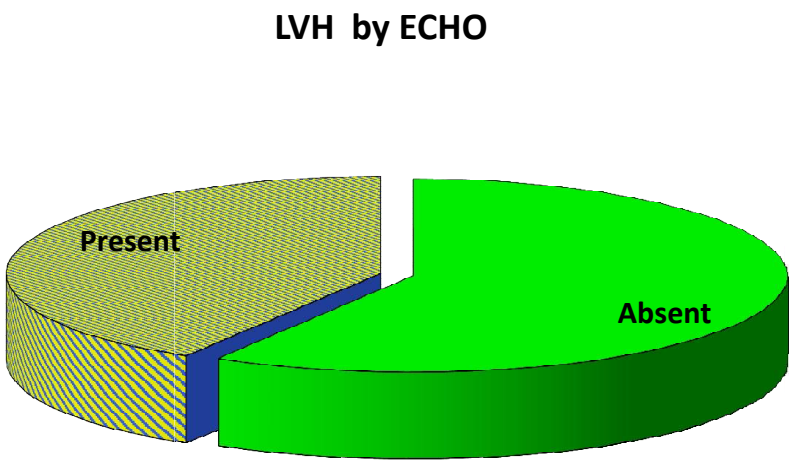
| **Pericardial Effusion** | **No. of patients (n=75)** | **Percentage** |
|---|---|---|
| Absent | 71 | 94.7 |
| Present | 4 | 5.3 |




In our study group patients pericardial effusion in echocardiography was present 4 out of the total 75 patients, constituting to 5% of study population. 70 out of 75 patients did not have echocardiographycally detected pericardial effusion.

TABLE: CASES OF CKD WITH LEFT VENTRICULAR HYPERTROPHY IN ECHOCARDIOGRAPHY

| **Lvh in Echo** | **No. of patients (n=75)** | **Percentage** |
|---|---|---|
| Absent | 44 | 58.7 |
| Present | 31 | 41.3 |




The eGFR of CKD patients enrolled in our study ranges from4ml/ min t0 33ml/min. maximum number of patients (55 patients) (73%) had eGFR<15 ml/min. the mean eGFR of the study group was 12.8±5.4 ml/ min.

**TABLE: SUMMARY OF ECG CHANGES**

| CHANGE | NO.OF PATIENTS | PERCENTAGE |
|---|---|---|
| LVH | 22 | 29.3 |
| LAE | 9 | 12 |
| ISCHEMIA | 17 | 22.7 |
| HYPERKALEMIA | 9 | 12 |
| CONDUCTION ABNORMALITY | 13 | 17.3 |
| ARRYTHMIA | 3 | 4 |
| NO CHANGES | 22 | 29.3 |

In our study group the observed ECG changes were LVH in 29%, left atrial enlargement in 12%, CAD in 23%, hyperkalemia in 12%, conduction abnormalities in 17%, arrhythmia in 4% of the total study population.

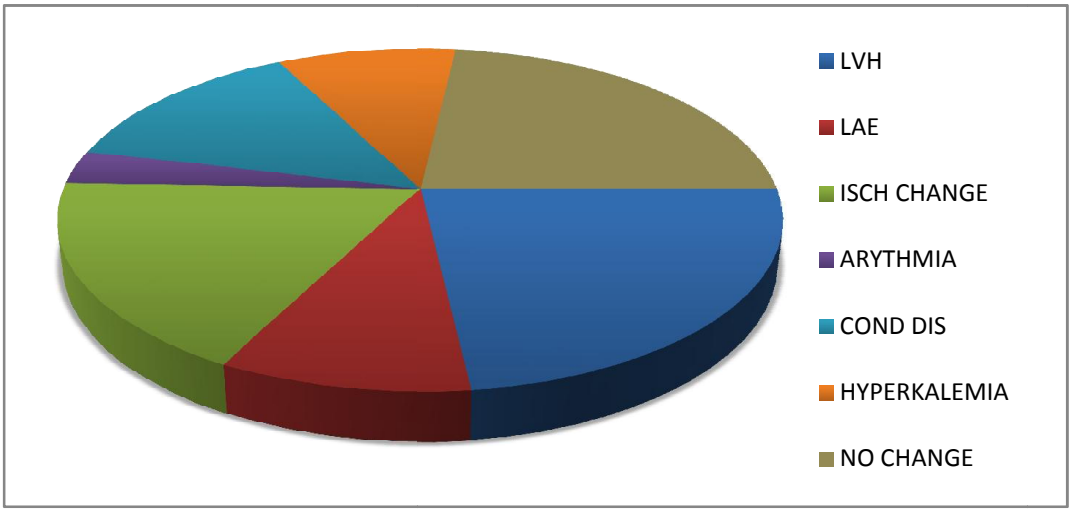
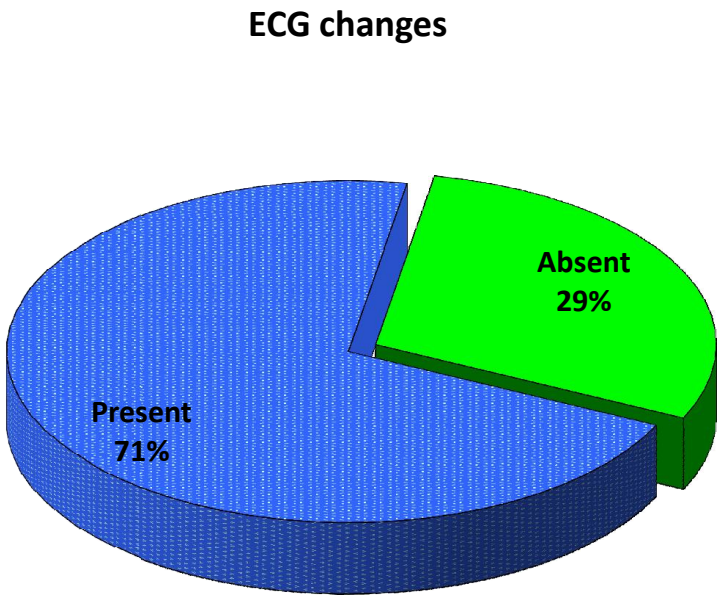


TABLE: TOTAL NUMBER OF PATIENTS WITH ECG CHANGES.

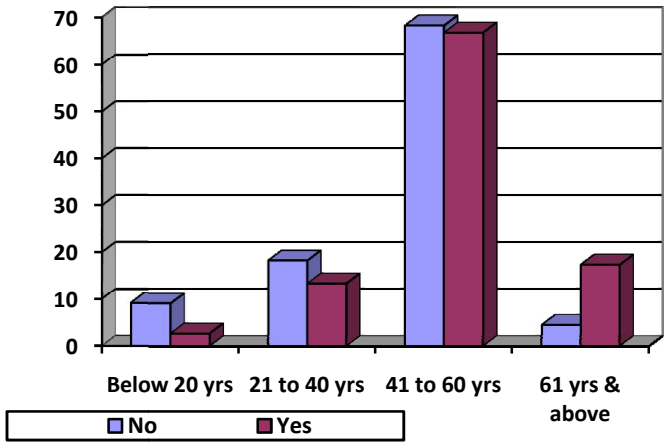
| **Particulars** | **No. of respondents (n=75)** | **Percentage (100%)** |
|---|---|---|
| No | 22 | 29.3 |
| Yes | 53 | 70.7 |




Among the 75 patients with CKD only 29% of the study population had a normal ECG. The rest of the study group constituting 71% had abnormalities which were mentioned above.

**Chi-square test comparing ECG changes with age**

| AGE | ECG Changes | | | | | | Statistical inference |
|---|---|---|---|---|---|---|---|
| | No | | Yes | | Total | | |
| | *(n=22)* | *(100%)* | *(n=53)* | *(100%)* | *(n=75)* | *(100%)* | |
| Below 20yrs | 2 | 9.1% | 0 | .0% | 2 | 2.7% | $X^2$=8.315 Df=3 P value <0.05 Significant |
| 21 to 40yrs | 4 | 18.2% | 6 | 11.3% | 10 | 13.3% | |
| 41 to 60yrs | 15 | 68.2% | 35 | 66.0% | 50 | 66.7% | |
| 61yrs & above | 1 | 4.5% | 12 | 22.6% | 13 | 17.3% | |




Based on the statistical analysis there was a correlation between the age and the Changes in ECG . With advancing age the changes in ECG were evident in patients with CKD (p value=0.04).

**Chi-square test comparing ECG changes with duration of CKD & eGFR**

| DURATION | ECG Changes | | | | | | Statistical inference |
|---|---|---|---|---|---|---|---|
| | No | | Yes | | Total | | |
| | *(n=22)* | *(100%)* | *(n=53)* | *(100%)* | *(n=75)* | *(100%)* | |
| 3 to 6months | 11 | 50.0% | 37 | 69.8% | 48 | 64.0% | Pvalue >0.05 |
| 6 to 12months | 7 | 31.8% | 11 | 20.8% | 18 | 24.0% | Not |
| Above 1year | 4 | 18.2% | 5 | 9.4% | 9 | 12.0% | significant |

| eGFR | ECG Changes | | | | | | Statistical inference |
|---|---|---|---|---|---|---|---|
| | No | | Yes | | Total | | |
| | *(n=22)* | *(100%)* | *(n=53)* | *(100%)* | *(n=75)* | *(100%)* | |
| <15 | 14 | 63.6% | 41 | 77.4% | 55 | 73.3% | P value>0.05 |
| 15-30 | 8 | 36.4% | 11 | 20.8% | 19 | 25.3% | Not |
| > 30 | 0 | .0% | 1 | 1.9% | 1 | 1.3% | Significant |

Based on the statistical analysis the changes in ECG were compared with eGFR and duration of CKD. Both the analysis only showed an insignificant association (p values >0.05).

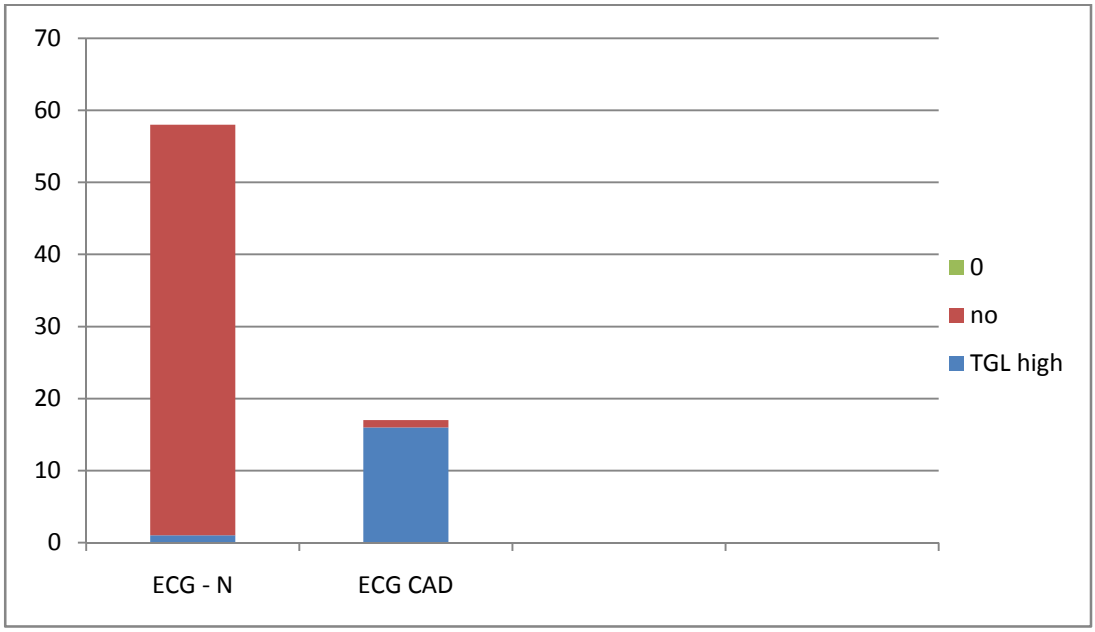
**Chi-square test comparing ECG changes with blood urea, serum creatinine, & dyslipidemia**

| | ECG Changes | | | | | | Statistical inference |
|---|---|---|---|---|---|---|---|
| | No | | Yes | | Total | | |
| | *(n=22)* | *(100 %)* | *(n=53)* | *(100%)* | *(n=75)* | *(100%)* | |
| **BL.UREA** | | | | | | | |
| 60 to 100 | 5 | 22.7% | 17 | 32.1% | 22 | 29.3% | $X^2$=.681 Df=2 P value >0.05 Not Significant |
| 101 to 150 | 14 | 63.6% | 29 | 54.7% | 43 | 57.3% | |
| 150 & above | 3 | 13.6% | 7 | 13.2% | 10 | 13.3% | |
| **Sr.Cr** | | | | | | | |
| 2 to 4 | 4 | 18.2% | 8 | 15.1% | 12 | 16.0% | $X^2$=1.029 Df=3 P value >0.05 Not Significant |
| 4.1 to 6 | 8 | 36.4% | 26 | 49.1% | 34 | 45.3% | |
| 6.1 to 8 | 4 | 18.2% | 8 | 15.1% | 12 | 16.0% | |
| 8 & above | 6 | 27.3% | 11 | 20.8% | 17 | 22.7% | |
| **Dyslipidemia** | | | | | | | |
| Absent | 17 | 77.3% | 28 | 52.8% | 45 | 60.0% | $X^2$=3.870 Df=1 P value <0.05 Significant |
| Present | 5 | 22.7% | 25 | 47.2% | 30 | 40.0% | |

The statistical analysis comparing the levels of blood urea with the changes in ECG didn't correlate significantly. The levels of serum creatinine were also compared with the ECG changes. The correlation was found to be insignificant in our study. The presence of dislipidemia was found to be associated with changes in ECG with a significant p value of 0.049. The association of dyslipidemia with CAD changes in ECG was not statistically significant.

**Chi-square test comparing CAD changes with levels of TGL**

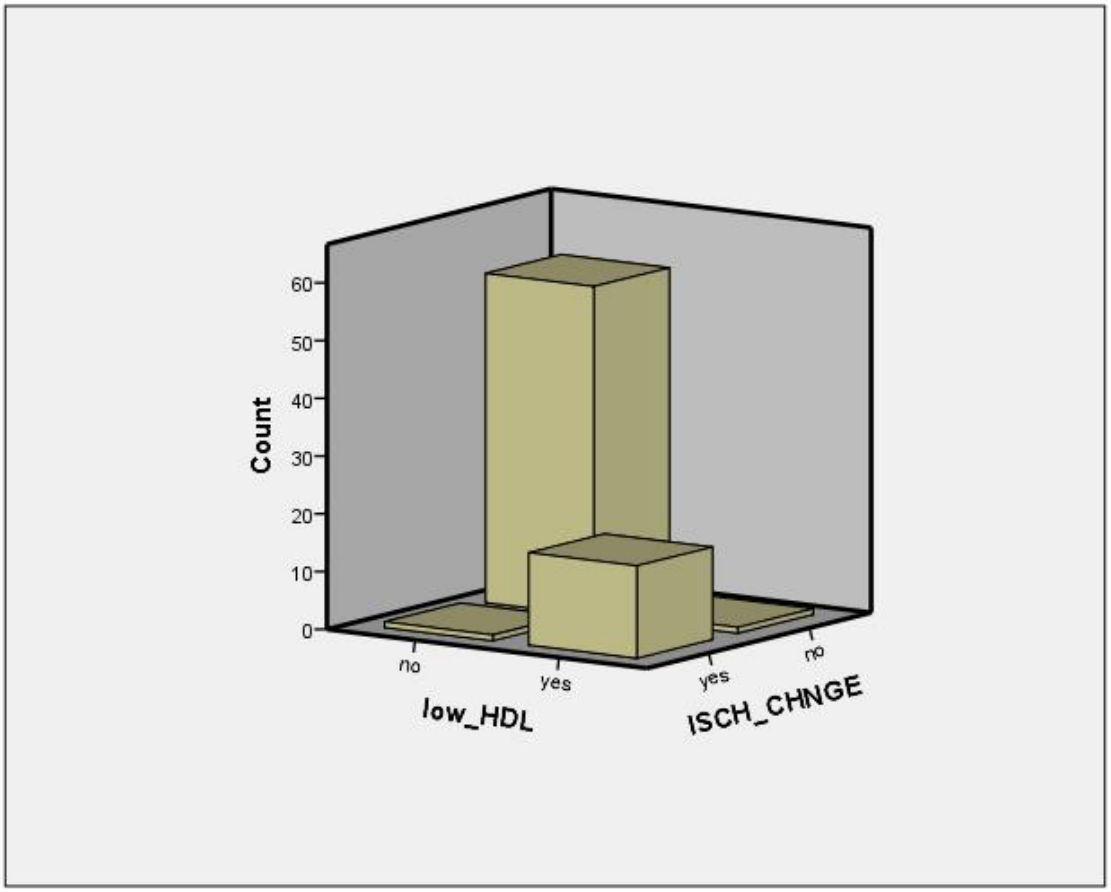
| Count | | ISCH_CHNGE | | Total | |
|---|---|---|---|---|---|
| | | No | Yes | | |
| High TGL | no | 57 | 1 | 58 | P value<0.05 |
| | yes | 1 | 16 | 17 | |
| Total | | 58 | 17 | 75 | |




The changes of ischemia in ECG didn't correlate significantly with elevated total cholesterol and elevated LDL, but ischemic changes correlated significantly with elevated levels of serum triglycerides with p value< 0.05.

**Chi-square test comparing CAD changes with levels of HDL**

| Count | | ISCH_CHNGE | | Total | P value<0.05 |
|---|---|---|---|---|---|
| | | No | Yes | | |
| lowHDL | no | 57 | 1 | 58 | |
| | yes | 1 | 16 | 17 | |
| Total | | 58 | 17 | 75 | |




In our study the lower level of HDL correlated with the presence of coronary artery changes in ECG with statistical significance with a p value < 0.05.

# 6. DISCUSSION

CKD is associated with high cardio-vascular mortality and morbidity. As the detrimental effects of CKD commences from early stages of CKD. Preventive strategies must also start at a very early stage. But the asymptomatic nature and the dilemmas in the detection of renal failure in early stages costs the valuable time of patients and a proper consultation is hampered .The mean age of patients in our study was 50.4±11.5years. Earlier studies also show that the prevalence of CKD in 3rd, 4th & 5th decades. In the studies from developed countries it has been shown to be beyond the 6th decade of life there is prevalence of CKD.

In this present study comprising of 75 patients of CKD, the ECG change of Left ventricular hypertrophy was present in 29.3%. Previously done studies by soman [73] showed LVH in 18% of study group, A.S.Menon's study[9] showed 12% and the study done by Krivoshiev[76] showed 34%, chijoke et al [80] study showed LVH in 28%. Our result was comparable to the study done by Krivoshiev et al, & chijoke et al. The presence of LVH in our study group was limited only to 29.3% even though maximum numbers of patients were hypertensive. This brings into account that not only hypertension but also some

other factors are involved in the pathogenesis of LVH. Possible factors include the presence of volume overload & anemia. But the emphasize on controlling the blood pressure should not be taken lightly as proper control can aid in regression of LVH or even prevent its development. The regression in LVH can considerably reduce the mortality from cardiac arrhythmias and sudden cardiac death.

The left atrial enlargement on ECG in our study was seen in 9 out of 75 patients comprising 12% of the patients. In the study made by A.S.Menon et al [9] a similiar proportion of patients i.e. 12% had the same changes. The study done by chijoke et al [80] showed 17% of his population with left atrial enlargement.

The changes pertaining to coronary artery disease was found in 17 out of 75 patients constituting to around 23%. The previously done studies by A.S.Menon [9] showed that 20% of his study population had changes pertaining to CAD. In Krivosheiv's study [76] the percentage of CAD changes was 29% and the study made by soman [73] showed that 32% of his study group had changes pertaining to CAD. Our study results pertaining to ischemic changes can be compared to that of A.S.Menon's study. The statistical analysis showed the significant correlation of ECG changes of ischemia with the elevated serum

triglyceride levels and the reduced HDL levels. This emphasizes that statins should be used in patients with CKD to prevent the occurrence of CAD.

Conduction abnormalities in ECG were found in 13 0f our 75 patients. The percentage was 17%. Previous study done by soman et al[73] described a similar percentage of people with 15% having conduction disturbances in the ECG. The study done by Krivoshiev [76] showed the percentage of conduction disturbances to be 11% in his study. A.S.Menon's study [9] showed intraventricular conduction disturbances in 8% of his study population.

Hyperkalemic changes in ECG were found to be present in 9 of the total 75 patients constituting to around 12% of our patients. Arrhythmia was found in 3 of our patients thus constituting to around 4% of our study population. Study made by soman et al [73] showed a similar percentage of people (5%) having arrhythmia.

Overall ECG changes were found to be present in 53 out of 75 patients constituting to around 71%. 29% of the study population (22 patients) had a normal ECG. In the study done by Krivoshiev [76] et al 19% of his study population had a normal ECG and 81% had abnormal ECG changes. In the study done by chijoke [80] et al 86% of his study population had changes in ECG. These overall changes correlated significantly with advancing age and

dyslipidaemia. The changes pertaining to coronary artery disease were significantly correlated with increased Triglycerides levels and reduced HDL levels.

# 7. CONCLUSION

1. The changes in ECG among CKD patients were frequent and constituted to around 71% in our study.
2. The commonest ECG finding was Left ventricular hypertrophy constituting to 29%.
3. Ischemic changes in ECG were found to be in 23% of our study population.
4. Conduction disturbances in ECG were found to be in 17% of our study population.
5. Left atrial enlargement in ECG was found to be in 12% of our study population.
6. Hyperkalemic changes in ECG were found to be in 12% of our study population.
7. With the advancing age changes in ECG becomes evident in patients with CKD and it has been shown with statistical significance.
8. The presence of Dyslipidemia is significantly associated with the presence of changes in ECG.

9. The presence of high levels of serum triglycerides and low levels of High Density lipoprotein are statistically correlated with the presence of changes of coronary artery disease in ECG.

10. The changes in ECG didn't correlate with either eGFR, the duration of illness, blood urea or serum creatinine levels.

Cardiovascular diseases propose a major threat to patients with CKD. In the context of CKD aim of evaluating CVD is warranted. The changes in ECG of patients with CKD can aid in detection of CVD and should be carried out in all patients with CKD.

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# ANNEXURE II - PROFORMA

Name :
Age :
Sex :
I.P. No :
**Presenting Complaints**

**Past History**

| | Present | Absent | Duration |
|---|---|---|---|
| 1 Similar complaints | | | |
| 2 Diabetes Mellitus | | | |
| 3 Hypertension | | | |
| 4 Ischemic / Valvular / Pericardial heart disease | | | |
| 5 Tuberculosis | | | |

**Treatment history**

**Family history**

**Personal History**

| | |
|---|---|
| **Appetite** | **Normal / Increased / Decreased** |
| **Sleep** | **Normal / Increased / Decreased** |
| **Bowel** | **Regular / Irregular** |
| **Bladder Frequency** | **Normal / Increased / Decreased** |
| **Volume** | **Normal / Increased / Decreased** |

## General Examination

| | |
|---|---|
| Built | Well / Moderate / Poor |
| Nutrition | Good / Moderate / Poor |
| Pallor | Present / Absent |
| Nails | clubbing / pallor/ koilonoichyia |
| Cyanosis | Present / Absent |
| Edema | NO /Generalized / Facial/ Pedal |
| Skin | Smooth / Dry/ |
| Lymphadenopathy | Present / Absent |
| Weight | Kg |
| Height | Cm |
| Pulse | / Min |

| | |
|---|---|
| BP | mmHg |
| RR | / Min |
| Temperature | |

## Systemic examination

**Cardiovascular system**

**Respiratory system**

**Per Abdomen**

**Nervous system**

## Investigations

**1. Urine**

| | |
|---|---|
| Albumin | Present / Absent |
| Sugar | Present / Absent |
| Microscopy | Casts / Pus cells / EP cells / RBC |

**2. Blood**

| | |
|---|---|
| HB | gm% |
| RBS | mg/dl |
| FBS | mg/dl |
| PPBS | mg/dl |
| Blood Urea | mg / dl |
| Serum Creatinine | mg / dl |
| Electrolytes | |
| $Na^+$ | m Eq / L |
| $K^+$ | m Eq / L |

**LIPID PFOFILE**

| | |
|---|---|
| Total cholesterol | mg/dl |
| Triglycerides | mg/dl |
| HDL | mg/dl |
| LDL | mg/dl |

**3 .Ultrasound abdomen**

***ECG***

Rate
Rhythm
P wave
PR interval
QRS duration
QT /QTc
ST segment
T wave
U wave
Chamber hypertrophy
Others
**Inference**

**Echocardiography**

# ANNEXURE III – MASTER CHART

# Master chart

| *IP.NO* | *SEX* | *AGE* | *DURATION* | *UREA* | *creati* | *eGFR* | *HD* | *Na+* | *K+* | *HDL* | *TGL* | *LDL* | *T.C.* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 41871 | m | 55 | 3 months | 153 | 7.3 | 8 | no | 128 | 4.6 | 44 | 189 | 91 | 184 |
| 42717 | M | 31 | 5 months | 180 | 20.2 | 5 | no | 135 | 5.1 | 43 | 192 | 93 | 192 |
| 42050 | m | 50 | 6 months | 178 | 20.2 | 4 | no | 124 | 5.3 | 46 | 176 | 97 | 179 |
| 41491 | f | 40 | 2 years | 166 | 5.7 | 7 | no | 136 | 3.8 | 42 | 222 | 90 | 167 |
| 42570 | f | 50 | 4 months | 110 | 7.7 | 7 | no | 131 | 5.9 | 51 | 156 | 96 | 167 |
| 42434 | f | 60 | 8 months | 80 | 2.5 | 17 | no | 135 | 5.5 | 50 | 173 | 88 | 163 |
| 42274 | f | 50 | 4 months | 142 | 8.3 | 7 | YES | 138 | 5 | 53 | 156 | 78 | 198 |
| 41767 | m | 55 | 4 months | 88 | 3.9 | 13 | no | 136 | 6.2 | 36 | 176 | 132 | 165 |
| 42683 | m | 38 | 3 months | 69 | 2.6 | 33 | no | 126 | 3.5 | 46 | 184 | 90 | 157 |
| 41758 | f | 55 | 6 years | 130 | 8.8 | 6 | no | 139 | 3.9 | 57 | 165 | 92 | 154 |
| 41955 | m | 35 | 1 YR | 148 | 8.7 | 12 | no | 144 | 6 | 44 | 178 | 93 | 173 |
| 41105 | m | 70 | 6 months | 62 | 2.2 | 23 | no | 130 | 5.7 | 34 | 212 | 95 | 232 |
| 41742 | m | 62 | 3 months | 84 | 5 | 14 | no | 128 | 4.5 | 38 | 243 | 142 | 185 |
| 41738 | m | 49 | 3 months | 135 | 9.3 | 9 | YES | 117 | 4.6 | 45 | 145 | 90 | 184 |
| 41714 | m | 76 | 4 months | 100 | 3.4 | 17 | no | 132 | 3.8 | 43 | 146 | 81 | 195 |
| 41989 | m | 55 | 1 YR | 92 | 5 | 18 | no | 140 | 4.2 | 42 | 193 | 83 | 186 |
| 41309 | M | 48 | 4 months | 110 | 6.2 | 14 | YES | 134 | 5.6 | 46 | 254 | 85 | 167 |
| 41432 | m | 61 | 6 months | 80 | 2.8 | 23 | no | 128 | 5.2 | 45 | 164 | 128 | 256 |
| 41422 | m | 67 | 1 YR | 79 | 4 | 14 | no | 136 | 4.8 | 37 | 205 | 79 | 157 |
| 41555 | F | 65 | 3 months | 120 | 5.2 | 9 | YES | 132 | 4.6 | 50 | 185 | 83 | 185 |
| 41128 | F | 63 | 9 months | 134 | 7 | 7 | no | 129 | 5.4 | 40 | 235 | 84 | 185 |
| 41673 | M | 55 | 4 months | 130 | 4.3 | 17 | no | 144 | 5.9 | 42 | 138 | 85 | 189 |
| 42784 | M | 52 | 4 months | 98 | 4.8 | 17 | no | 136 | 7.1 | 38 | 260 | 87 | 168 |
| 41347 | M | 23 | 1 YR | 104 | 6.2 | 16 | YES | 126 | 5.6 | 46 | 187 | 126 | 187 |
| 41346 | m | 58 | 6 months | 96 | 3.8 | 19 | no | 135 | 5.3 | 43 | 158 | 86 | 160 |
| 41357 | M | 45 | 5 months | 102 | 5.7 | 15 | yes | 145 | 4.3 | 44 | 147 | 99 | 248 |
| 41366 | f | 52 | 3 months | 126 | 9 | 7 | no | 134 | 4.3 | 46 | 208 | 75 | 186 |
| 41386 | m | 44 | 4 months | 104 | 3 | 28 | no | 138 | 6 | 42 | 186 | 94 | 167 |
| 42010 | M | 52 | 1 YR | 124 | 4.5 | 19 | YES | 129 | 4.8 | 50 | 156 | 83 | 184 |
| 41394 | M | 54 | 5 months | 110 | 6.2 | 12 | no | 136 | 5.5 | 38 | 212 | 84 | 169 |
| 42023 | F | 19 | 4 months | 156 | 4.6 | 15 | no | 126 | 3.7 | 56 | 145 | 86 | 156 |
| 41456 | M | 60 | 3 YR | 84 | 4.5 | 13 | no | 136 | 6.8 | 56 | 182 | 146 | 176 |
| 41412 | M | 60 | 4 months | 162 | 5.6 | 10 | no | 135 | 4.8 | 51 | 164 | 95 | 185 |
| 42035 | M | 54 | 6 months | 140 | 5.2 | 13 | no | 134 | 5.2 | 50 | 165 | 88 | 212 |
| 41403 | M | 65 | 7 months | 112 | 6.4 | 9 | YES | 128 | 4.9 | 48 | 197 | 79 | 169 |
| 42047 | M | 43 | 3 months | 156 | 9.4 | 10 | no | 136 | 4 | 40 | 225 | 86 | 154 |
| 41427 | F | 45 | 10 months | 142 | 7.5 | 8 | no | 143 | 5.6 | 54 | 154 | 90 | 178 |
| 42060 | M | 48 | 8 months | 136 | 8.6 | 10 | no | 140 | 5.7 | 48 | 169 | 93 | 187 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 41438 | F | 55 | 6 months | 140 | 4.6 | 12 | no | 132 | 4.8 | 46 | 246 | 94 | 198 |
| 42072 | M | 45 | 4 months | 96 | 5.2 | 14 | YES | 126 | 5.8 | 45 | 154 | 95 | 164 |
| 41447 | M | 53 | 4 months | 118 | 8.8 | 8 | no | 138 | 4.5 | 42 | 176 | 132 | 194 |
| 42083 | M | 24 | 2 YR | 100 | 5.7 | 17 | no | 126 | 4.4 | 43 | 146 | 140 | 230 |
| 41461 | F | 60 | 3 months | 80 | 4.6 | 10 | no | 128 | 5.4 | 43 | 239 | 97 | 172 |
| 42095 | F | 60 | 4 months | 130 | 7.2 | 7 | no | 138 | 4.3 | 47 | 218 | 93 | 182 |
| 41475 | F | 41 | 6 months | 140 | 9.3 | 7 | YES | 140 | 4.6 | 52 | 192 | 87 | 184 |
| 42177 | F | 65 | 1 YR | 176 | 5.4 | 8 | no | 134 | 6.4 | 53 | 183 | 86 | 193 |
| 41483 | M | 18 | 1 1/2 YR | 125 | 3.9 | 21 | no | 128 | 5.4 | 43 | 163 | 89 | 190 |
| 42163 | M | 34 | 5 months | 140 | 4.2 | 22 | no | 134 | 5.3 | 45 | 156 | 98 | 187 |
| 41492 | M | 61 | 3 months | 108 | 5.8 | 11 | no | 140 | 5 | 40 | 159 | 87 | 179 |
| 42175 | M | 48 | 6 months | 114 | 5.3 | 14 | no | 130 | 5.5 | 41 | 164 | 76 | 175 |
| 41506 | M | 52 | 4 months | 126 | 4 | 19 | no | 124 | 5 | 42 | 164 | 79 | 188 |
| 42157 | M | 54 | 4 months | 112 | 5.9 | 13 | no | 128 | 5.2 | 36 | 214 | 129 | 191 |
| 41520 | F | 65 | 6 months | 148 | 9.2 | 5 | no | 126 | 3.5 | 54 | 149 | 85 | 177 |
| 42148 | F | 34 | 3 months | 82 | 3.4 | 19 | no | 130 | 3.9 | 56 | 158 | 84 | 194 |
| 41536 | M | 42 | 4 months | 160 | 4.9 | 18 | YES | 134 | 6.3 | 43 | 164 | 94 | 175 |
| 42137 | F | 63 | 6 months | 138 | 6.6 | 8 | no | 128 | 5.4 | 53 | 176 | 93 | 173 |
| 41549 | M | 66 | 1 YR | 110 | 5.4 | 12 | no | 130 | 4.6 | 34 | 184 | 97 | 177 |
| 42123 | F | 42 | 4 months | 143 | 4.9 | 12 | no | 126 | 4.7 | 54 | 195 | 88 | 189 |
| 41560 | M | 53 | 3 months | 140 | 6 | 13 | no | 135 | 4 | 43 | 176 | 86 | 157 |
| 42112 | M | 48 | 3 months | 134 | 5.6 | 14 | no | 120 | 4.5 | 42 | 173 | 76 | 246 |
| 41573 | F | 42 | 6 months | 138 | 6 | 11 | no | 138 | 5.5 | 38 | 210 | 83 | 186 |
| 41892 | M | 38 | 4 months | 94 | 9 | 10 | no | 126 | 5.1 | 44 | 162 | 84 | 182 |
| 41582 | F | 40 | 3 months | 116 | 7.1 | 8 | no | 129 | 4.7 | 56 | 173 | 97 | 192 |
| 41883 | M | 46 | 4 months | 100 | 8.2 | 10 | YES | 132 | 4.3 | 32 | 248 | 90 | 183 |
| 41592 | M | 53 | 1 YR | 78 | 4.2 | 19 | no | 134 | 5.2 | 48 | 172 | 79 | 184 |
| 41871 | F | 43 | 6 months | 128 | 4.8 | 13 | no | 128 | 5.7 | 54 | 169 | 86 | 165 |
| 41599 | F | 54 | 4 months | 138 | 8.4 | 6 | no | 126 | 6.9 | 56 | 168 | 147 | 179 |
| 41848 | M | 52 | 2 YR | 170 | 5.3 | 13 | no | 134 | 5.6 | 48 | 164 | 92 | 172 |
| 41624 | M | 58 | 4 months | 123 | 4.2 | 18 | no | 136 | 5.3 | 53 | 182 | 87 | 178 |
| 41823 | M | 56 | 6 months | 138 | 6.8 | 10 | no | 138 | 3.8 | 44 | 160 | 96 | 195 |
| 41617 | M | 54 | 8 months | 106 | 8.9 | 7 | no | 120 | 4.3 | 46 | 154 | 98 | 241 |
| 41812 | F | 42 | 8 months | 142 | 8.3 | 8 | no | 140 | 8 | 53 | 148 | 78 | 179 |
| 41636 | F | 48 | 6 months | 98 | 4.3 | 13 | YES | 132 | 4.8 | 33 | 164 | 76 | 169 |
| 41809 | M | 58 | 5 months | 88 | 4.2 | 15 | no | 126 | 5.5 | 44 | 174 | 88 | 162 |
| 41642 | f | 46 | 7 months | 99 | 4.6 | 15 | no | 128 | 4.2 | 54 | 186 | 136 | 167 |

# ECG and ECHO findings

| *IP.NO* | *LVH* | *LAE* | *ISCHEMIA* | *hyperkalemia* | *conduction abn* | *arrythmia* | *echo-CAD* | *echo-PE* | *echo-LVH* |
|---|---|---|---|---|---|---|---|---|---|
| 41871 | yes | no | no | no | no | no | no | no | yes |
| 42717 | no | no | no | no | no | no | no | no | no |
| 42050 | no | no | no | no | no | no | no | no | no |
| 41491 | no | no | yes | no | no | no | yes | no | no |
| 42570 | yes | no | no | yes | no | no | no | no | yes |
| 42434 | no | no | no | no | no | no | no | no | no |
| 42274 | no | no | no | no | no | no | no | no | no |
| 41767 | no | no | no | yes | no | no | no | no | no |
| 42683 | yes | no | no | no | no | no | no | no | yes |
| 41758 | no | no | no | no | no | no | no | yes | no |
| 41955 | no | no | no | yes | no | no | no | no | no |
| 41105 | no | no | yes | no | no | no | yes | no | no |
| 41742 | no | no | yes | no | yes | no | yes | no | no |
| 41738 | no | yes | no | no | yes | no | no | yes | no |
| 41714 | yes | yes | no | no | no | no | no | no | yes |
| 41989 | yes | no | no | no | no | no | no | no | yes |
| 41309 | no | no | no | no | yes | no | no | no | no |
| 41432 | yes | yes | no | no | yes | yes | no | no | yes |
| 41422 | yes | no | yes | no | no | yes | yes | no | yes |
| 41555 | yes | yes | no | no | yes | no | no | no | yes |
| 41128 | yes | no | yes | no | no | no | yes | no | yes |
| 41673 | no | no | no | no | no | no | no | no | no |
| 42784 | yes | no | yes | yes | no | no | yes | no | yes |
| 41347 | no | yes | no | no | no | no | no | no | no |
| 41346 | yes | no | no | no | yes | no | no | no | yes |
| 41357 | no | no | no | no | yes | no | no | no | no |
| 41366 | no | no | yes | no | no | no | yes | no | no |
| 41386 | no | no | no | yes | no | no | no | no | yes |
| 42010 | no | no | no | no | no | no | no | no | no |
| 41394 | yes | yes | yes | no | no | no | yes | no | no |
| 42023 | no | no | no | no | no | no | no | no | yes |
| 41456 | no | no | no | yes | no | no | no | no | no |
| 41412 | yes | no | no | no | no | no | no | no | yes |
| 42035 | no | no | no | no | no | no | no | no | no |
| 41403 | no | no | no | no | yes | no | no | no | no |
| 42047 | no | no | yes | no | no | no | no | no | no |
| 41427 | no | no | no | no | no | no | no | no | no |
| 42060 | no | no | no | no | no | no | no | no | yes |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 41438 | no | no | yes | no | no | no | yes | no | no |
| 42072 | no | no | no | no | yes | no | no | no | no |
| 41447 | yes | no | no | no | no | no | no | no | yes |
| 42083 | no | no | no | no | no | no | no | no | yes |
| 41461 | no | no | yes | no | no | no | yes | no | no |
| 42095 | yes | no | yes | no | no | no | yes | no | yes |
| 41475 | no | no | no | no | yes | no | no | no | no |
| 42177 | no | no | no | yes | no | no | no | no | no |
| 41483 | no | no | no | no | no | no | no | no | no |
| 42163 | no | no | no | no | yes | no | no | no | yes |
| 41492 | no | no | no | no | no | yes | no | yes | no |
| 42175 | yes | no | no | no | no | no | no | no | yes |
| 41506 | no | no | no | no | no | no | no | no | no |
| 42157 | no | no | yes | no | no | no | yes | no | no |
| 41520 | no | yes | no | no | no | no | no | no | yes |
| 42148 | no | no | no | no | no | no | no | no | no |
| 41536 | yes | no | no | yes | no | no | no | no | yes |
| 42137 | no | no | no | no | no | no | no | no | yes |
| 41549 | no | no | yes | no | no | no | yes | no | no |
| 42123 | yes | no | no | no | no | no | no | no | yes |
| 41560 | no | yes | no | no | no | no | no | no | no |
| 42112 | no | no | no | no | no | no | no | no | no |
| 41573 | yes | no | yes | no | no | no | yes | no | yes |
| 41892 | no | no | no | no | yes | no | no | no | yes |
| 41582 | no | No | no | no | no | no | no | no | no |
| 41883 | no | No | yes | no | no | no | yes | no | no |
| 41592 | no | No | no | no | no | no | no | no | no |
| 41871 | yes | No | no | no | no | no | no | no | yes |
| 41599 | no | No | no | no | no | no | no | no | no |
| 41848 | yes | No | no | no | no | no | no | no | yes |
| 41624 | yes | No | no | no | no | no | no | no | yes |
| 41823 | no | No | no | no | no | no | no | no | no |
| 41617 | no | Yes | no | no | no | no | no | no | no |
| 41812 | no | No | no | yes | no | no | no | no | no |
| 41636 | no | No | yes | no | no | no | yes | no | yes |
| 41809 | no | No | no | no | yes | no | no | no | yes |
| 41642 | no | No | no | no | no | no | no | no | no |

# Abbreviations

UREA- Blood urea levels in mg/dl

Create- serum creatinine levels in mg/dl

Na+- serum levels of sodium in meq/l

K+- serum levels of potassium in meq/l

T.C.- total cholesterol

LVH- Left ventricular hypertrophy in ECG

LAE- Left atrial enlargement in ECG

ISCHEMIA- Ischemic changes in ECG

Arrythmia- arrhythmia in ECG

Conduction abn – conduction disturbances in ecg

PE- Pericardial effusion

# ANNEXURE IV-ABBREVIATIONS

## ABBREVIATIONS

CKD - Chronic Kidney Disease

CVD - Cardiovascular Disease

CAD- Coronary artery disease

ESRD- End stage renal disease

ECG - Electrocardiography

NKF - National Kidney Foundation

ECHO - Echocardiography

GBM- glomerular basement membrane

JGA- the juxtaglomerular apparatus

BP- Blood pressure.

MDRD- Modification of Diet in Renal Disease

GFR - Glomerular Filtration Rate

eGFR - Estimated Glomerular Filtration Rate

NHANES - National Health and Nutrition Examination Survey

LVEF - Left Ventricular Ejection Fraction

LVH - Left Ventricular hypertrophy

Ca2+- calcium

Na+- sodium

H20 – water

[Lp(a)]- Lipoprotein-a

ECF- Extra cellular fluid

RBC- Red blood cells

CRP- C reactive protein

Zn- Zinc

Se- Selenium

EBCT- Electron-beam ultrafast computed tomography

MRI- Magnetic resonance imaging

LAE- Left atrial enlargement

HDL - High Density Lipoprotein

TGL- triglycerides

VLDL- very low density lipoprotein

EF - Ejection Fraction

LDL - Low Density Lipoprotein

ESRD - End Stage Renal Disease

RBBB - Right Bundle Branch Block

LBBB - Left Bundle Branch Block

MI - Myocardial Infarction

PTH - Paratharmone

# ANNEXURE V- CONSENT FORM

# CONSENT FORM

I _____ hereby give consent to participate in the study conducted by **DR. A. VIMAL RAJ,** post graduate in department of General medicine, thanjavur medical college & hospital, thanjavur – 613004 and to use my personal clinical data and result of investigation for the purpose of analysis and to study the nature of disease. I also give consent for further investigations

Place :

Date : Signature of participant

# INFORMATION SHEET

- We are conducting a prospective study titled "**A Study of Electrocardiographic Changes in Patient With Chronic Kidney Disease"** in the department of General medicine, thanjavur medical college & hospital, thanjavur – 613004.

- At the time of announcing the results and suggestions, name and identity of the patients will be confidential.

- Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

- The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

**Signature of investigator** **Signature of participant**

**Date:**