A STUDY OF LIPID PROFILE IN CHRONIC KIDNEY DISEASE PATIENTS

DISSERTATION

Submitted in partial fulfilment of requirements for

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BONAFIDE CERTIFICATE

Certified that this dissertation is the bonafide work of ***Dr.K.GANESAN*** *on* "**A STUDY OF LIPID PROFILE IN CHRONIC KIDNEY DISEASE PATIENTS**" *during his M.D. (General Medicine) course from May 2009 to April 2012 at the K.A.P.Viswanatham Govt Medical College attached to Annal Gandhi Memorial Govt Hospital, Trichy.*

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DECLARATION

I solemnly declare that the dissertation titled ***"A STUDY OF LIPID PROFILE IN CHRONIC KIDNEY DISEASE PATIENTS"*** *is done by me at K.A.P.Viswanatham Govt Medical College attached to Annal Gandhi Memorial Govt Hospital, Trichy during 2010-2011 under the guidance and supervision of* ***Prof. Dr. G. Anitha, M.D.,***

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University towards the partial fulfilment of requirements for the award of M.D. Degree (Branch I) in General Medicine.

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CONTENTS

Proforma

A Study on Lipid profile in CKD

Name of the patient :

Age / Sex :

IP/OP No :

Address :

Height (cms) : Weight (kgs) : BMI :

Diagnosis :

Chief Complaints :

Past History of

1. DM : Yes/No
2. Coronary heart disease : Yes/No
3. Hypertension : Yes/No
4. Thyroid Disease : Yes/No
5. Drug intake (Steriods, Anti thyroid drugs, Estrogen/OCP, B-blockers) : Yes/No
6. PD : Yes/No
7. HD : Yes/No

Personal History of

1. Smoking :
2. Alcoholism :

General Examination

PR (per min) :

BP (mm Hg) :

Xanthomas/Xanthelesma :

Arcus senilis :

Systemic Examination

CVS :

RS :

Abdomen :

CNS :

Investigations

Blood sugar(mg/dL) : FBS- PPBS-

HbA1c- sr.albumin-

Urea (mg/dL) :

Creatinine (mg/dL) :

Sodium(mEql/L) : Potassium (mEql/L) :

24 hrs urine protein: Urine P/Cr:

Creatinine clearance :

(ml/min)

Lipid profile(mg/dL)

TC : TGL : HDL

LDL

TSH

Urine

ECG:

USG abdomen :

INTRODUCTION

Cardiovascular disease (CVD) is a major cause of mortality in patients with mild to moderate chronic kidney disease (CKD) and end-stage renal disease (ESRD) [1, 2]

Cardiovascular mortality 500 times higher in 25- to 34-year-old ESRD patients than in individuals from the general population of the same age and race. [2, 3]

Primary care physicians (PCP) often manage patients with CKD in the early stages of the disease and have a pivotal role in affecting long-term outcomes in CKD patients related to cardiovascular and all-cause mortality. [7]

In a retrospective cohort study only a tiny minority of patients (0.5–1%) with mild to moderate CKD developed ESRD over a 5-year follow-up,while as many as 19 and 24% of these patients with mild and moderate renal insufficiency, respectively, died mostly of cardiovascular complications in the same period[4] .

Hyperlipidemia, one of the important risk factor of atherosclerosis, is an abnormality commonly encountered in patients with chronic kidney disease.

Other risk factor includes hypertension, diabetes mellitus, smoking, and obesity.

Indian studies on lipid profile abnormalities in chronic renal failure (CRF) have varied from no abnormalities at all to significant abnormality (Hypertriglyceridemia and reduced HDL) as described in the Western literature.

The study by B Shah, S Nair, demonstrates that CRF is commonly accompanied by lipid abnormality in the form of Hypertriglyceridemia. [5]

The study by Sumathi M.E, Manjunath M Tempad showed serum TGL, TC, HDL-C, have significantly increased in conservatively managed patients than in Haemodialysis patients. [6]

The present study is undertaken to explore the altered lipid, lipoprotein abnormalities in CKD from stage III to stage V classified as per National Kidney Foundation Kidney Disease Outcomes Quality Initiative

(NKFK/DOQI) guidelines, which plays a vital role in development of atherosclerotic cardiovascular disease.

There is also associated thyroid dysfunction seen in CKD patients.

A few reports have appeared from India, where various parameters of thyroid function were measured in patients with CRF. In order to gain further insight, this study included measuring the Thyroid Stimulating Hormone (TSH) levels.

AIMS and OBJECTIVES OF THE STUDY

1. To identify lipid pattern in chronic kidney disease patients.

2. To analyze lipid alterations that can occur in Chronic Kidney Disease patients.

3. To study the correlation between renal function and lipid abnormalities in Chronic Kidney Disease.

REVIEW OF LITERATURE

Definition of Chronic Kidney disease

The Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) defines chronic kidney disease as either kidney damage or a decreased glomerular filtration rate (GFR) of less than 60 ml/min/1.73 m^2 for 3 or more months.[8]

1. Kidney damage for ≥3 months is defined by structural or functional abnormalities of the kidney with or without reduction in GFR manifest either by
   A. pathological abnormalities or
   B. Markers of kidney damage including abnormalities of composition of blood or urine or abnormalities in imaging tests.

2. GFR <60ml/min/1.73m2 for ≥3 months with or without kidney damage.

Epidemiology of CKD in India

The epidemiology of CKD in India is very different from the West. Patients are roughly two decades younger, and a substantial proportion

present with small kidneys. In the absence of nationwide reporting systems or registries, the true incidence and prevalence is difficult to determine.

The socioeconomic implications of a young population afflicted with a potentially terminal illness are devastating and in the face of growing epidemics of diabetes and hypertension, the burden of CKD is not likely to ease.[9]

Combining all the available literature, both published and unpublished, from various sources, it will not be unwise to comment that the yearly incidence of ESRD in India is approximately 150–200 pmp and diabetes is also an important cause of CKD in approximately 30–40% of the patients. [10]

ETIOLOGY

Diabetes has emerged as the most frequent cause (30–40%) followed by hypertension (14–22%), CGN (16–20%), CIN (5.4–12.7%),heredofamilial disease (8.4%) and obstruction including calculus (2.9%).[11]

Other causes include Primary glomerular diseases like Membranous nephropathy, IgA nephropathy, Focal and segmental glomerulosclerosis (FSGS) and Membranoproliferative glomerulonephritis.

Vascular causes are renal artery stenosis, vasculitis, atheroemboli and Hypertensive nephrosclerosis.

The Causes for tubulointerstitial disease includes Drugs (e.g., sulfa, allopurinol), Infection (viral, bacterial, parasitic), Heavy metals and Radiation nephritis.

Pathophysiology of Chronic Kidney Disease [12]

This is categorized by two broad sets of mechanisms of damage

1. Initiating mechanisms specific to the underlying aetiology (genetically determined abnormalities in kidney development or integrity, immune complex deposition and inflammation in certain types of glomerulonephritis).
2. A set of progressive mechanisms, involving hyper filtration and hypertrophy of the remaining viable nephrons.

The responses to reduction in nephron number are mediated by vasoactive hormones, cytokines, and growth factors. Increased intra renal

activity of the renin-angiotensin axis appears to contribute both to the initial adaptive hyper filtration and to the subsequent maladaptive hypertrophy and sclerosis, the latter, in part, owing to the stimulation of transforming growth factor (TGF).

Pathophysiology and Biochemistry of Uremia

Accumulation serum urea and creatinine do not account for the many symptoms and signs but hundreds of toxins that accumulate in renal failure have been implicated in the uremic syndrome. These include water-soluble, hydrophobic, protein-bound, charged, and uncharged compounds. Additional categories of nitrogenous excretory products include guanidino compounds, urates and hippurates, products of nucleic acid metabolism, polyamines, myoinositol, phenols, benzoates, and indoles.

A host of metabolic and endocrine functions normally performed by the kidneys is also impaired or suppressed, and this results in anaemia, malnutrition, and abnormal metabolism of carbohydrates, fats, and proteins.

Plasma levels of many hormones, including PTH, FGF-23, insulin, glucagon, steroid hormones including vitamin D and sex hormones, and prolactin, change with renal failure. The inflammation associated with

renal impairment is important in the malnutrition-inflammation-atherosclerosis/calcification syndrome, which contributes in turn to the acceleration of vascular disease.

STAGES of GFR

Stage	GFR, mL/min per 1.73 m^2
0	>90[a]
1	90[b]
2	60–89
3	30–59
4	15–29
5	<15

[a]With risk factors for CKD [b]with demonstrated kidney damage (e.g., persistent proteinuria, abnormal urine sediment, abnormal blood and urine chemistry, abnormal imaging studies)

In stage 1 and stage 2 chronic kidney diseases, GFR alone does not clinch the diagnosis. Other markers of kidney damage, including abnormalities in the composition of blood or urine or abnormalities on imaging studies, should also be present in establishing a diagnosis of stage 1 and stage 2 chronic kidney disease.

The plasma creatinine value will approximately double with a 50% reduction in GFR. A rise in plasma creatinine from a baseline value of 0.6

mg/dl to 1.2 mg/dl in a patient, although still within the reference range, actually represents a loss of 50% of functioning nephron mass. [12]

CLINICAL FEATURESAND LABORATORY ABNORMALITES

Fluid and electrolyte disturbances

- Volume expansion,
- Hyponatremia,
- Hyperkalemia,
- Hyperphosphatemia.

Endocrine - Metabolic disturbances

- Secondary hyperparathyroidism,
- Adynamic bone disease,
- Vit. D deficient osteomalacia,
- Carbohydrate resistance,
- Hyperuricemia,
- Hypertriglyceridemia, Increased Lp (a) levels,
- Decreased HDL level Malnutrition,
- Amenorrhea, infertility,
- Sexual dysfunction,
- β2 micro globulin associated amyloidosis.

Neuromuscular Disturbances

- Fatigue,
- Sleep disorders,
- Headache,
- Impaired mentation,
- Lethargy,
- Asterixis,
- Muscular rigidity,
- Peripheral neuropathy,
- Restless leg syndrome,
- Myoclonus, Seizures, Coma,
- Muscle cramps, Myopathy,
- Dialysis disequilibrium syndrome.

Cardiovascular and pulmonary complication

- Arterial hypertension,
- Congestive heart failure or pulmonary edema,
- Pericarditis,
- Hypertrophic or dilated cardiomyopathy,
- Accelerated atherosclerosis,
- Hypotension and arrhythmias, vascular calcification.

Dermatologic Disturbances

- Pallor,
- Hyper pigmentation,
- Pruritus,
- Ecchymoses,
- Fibrosing dermopathy and Uremic frost.

Gastro Intestinal disturbances

- Anorexia, Nausea and vomiting,
- Gastroenteritis,
- Peptic ulcer,
- Gastrointestinal bleeding,
- Idiopathic ascites,
- Peritonitis.

Hematologic and Immunologic disturbances

- Anaemia,
- Lymphocytopenia,
- Bleeding diathesis,
- Increased susceptibility to infection,
- Leukopenia, Thrombocytopenia.

INVESTIGATIONS

Complete blood count (CBC), blood urea, serum creatinine, urinalysis, with calculation of renal function, urine PCR ratio, and 24hrs urine protein.

Serum albumin levels may also be measured, as patients may have hypoalbuminemia due to urinary protein loss or malnutrition.

A lipid profile should be performed in all patients with chronic kidney disease because of their increased risk of cardiovascular disease.

Serum phosphate, 25 hydroxy vitamin D, alkaline phosphatase, and intact parathyroid hormone (PTH) level.

Renal ultrasound and other imaging studies.

Measurement of GFR

1. Equation from the Modification Diet in Renal Disease study

MDRD Study equation provides a clinically useful estimate of GFR up to approximately 90 mL/min/1.73 m^2

Estimated GFR (mL/min per 1.73 m^2) = 1.86 x $(P_{Cr})^{-1.154}$ x $(age)^{-0.203}$

Multiply by 0.742 for women Multiply by 1.21 for African Americans

2. Cockcroft-Gault equation

Estimated creatinine clearance (mL/min)

$$= \frac{(140 - \text{age}) \times \text{body weight (kg)}}{72 \times P_{Cr}\ (\text{mg/dL})}$$

Multiply by 0.85 for women

The CKD-EPI Creatinine Equation

The CKD-EPI creatinine equation is based on the same four variables as the MDRD Study equation, but uses a 2-slope "spline" to model the relationship between estimated GFR and serum creatinine, and a different relationship for age, sex and race. The equation was reported to perform better and with less bias than the MDRD Study equation, especially in patients with higher GFR.

$$GFR = 141 \times \min(scr/\kappa, 1)^{\alpha} \times \max(scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018\ (\text{if female}) \times 1.159\ (\text{if black})$$

(The National Kidney Foundation K/DOQI Clinical Practice Guidelines for Estimation of Glomerular Filtration Rate)[13]

TREATMENT

Fluid, Electrolyte, Acid-Base Disorders

Adjustments in the dietary intake of salt and use of loop diuretics, with metolazone.

Water restriction is indicated only if there is a problem with hyponatremia.Intractable ECF Volume expansion, despite dietary salt restriction and diuretic therapy, may be an indication to start renal replacement therapy.

Hyperkalemia needs dietary restriction of potassium, avoidance of potassium supplements and ACE inhibitors or ARB. While potassium-binding resins, can promote potassium loss through the GI tract and may reduce the incidence of hyperkalemia in CKD patients.

Intractable hyperkalemia is an indication to consider institution of dialysis in a CKD patient. The renal tubular acidosis and subsequent anion-gap metabolic acidosis in progressive CKD will respond to alkali supplementation, typically with sodium bicarbonate will respond to sodium bicarbonate.

Management of Hypertension

In CKD patients with diabetes or proteinuria >1 g per 24 h, blood pressure should be reduced to 125/75

- Salt restriction
- ACE inhibitors and ARBs, side effect of these are hyperkalemia.

Metolazone can improve potassium excretion in addition to improving blood pressure control.

Management of Cardiovascular Disease

Lifestyle changes, including regular exercise and Hyperlipidemia in patients with CKD should be managed according to national guidelines. If dietary measures are not sufficient, preferred lipid-lowering medications, such as statins, should be used.

Proteinuria –To reduce to <1g/24hr use an Angiotensin converting enzyme inhibitor or angiotensin receptor antagonist.

Glycemic control in DM - Hb AIC < 7%

Smoking – cessation

Severe ↓ GFR -Preparation for kidney replacement therapy.

DYSLIPIDEMIAS

Dyslipidemia has been established as a well-known traditional risk factor for CVD in the general population and large-scale observational studies have shown that total and low-density lipoprotein (LDL)-cholesterol values are two of the most important independent predictors of cardiovascular morbidity and mortality [14]. Recent meta-analyses of prospective studies indicate that elevated triglycerides are also an independent risk factor for CAD. Factors contributing to elevated triglycerides in the general population include: obesity, physical inactivity, cigarette smoking, excess alcohol intake, high carbohydrate diet, type 2 diabetes, chronic renal failure, certain drugs like corticosteroids and estrogens.

ATP III Classification of LDL, Total, and HDL Cholesterol(mg/dL)[15]

LDL Cholesterol

<100mg/dL	Optimal
100-129mg/dL	above optimal
130-159mg/dL	Borderline high
160-189mg/dL	High
>190mg/dL	Very high

Total Cholesterol

<200mg/dL	Desirable
200-239mg/dL	Borderline high
>240mg/dL	High

HDL Cholesterol

<40mg/dL	Low
>60mg/dL	High

Triglycerides

<150 mg/dL	Normal triglycerides
150-199 mg/dL	Borderline-high
200-499mg/dl	High
>500 mg/dL	very high

The Pathways of Lipid Transport

These pathways include the exogenous pathway, the endogenous pathway, and the pathway of reverse cholesterol transport.

Exogenous Pathway

Dietary triglycerides are hydrolyzed by lipases within the intestinal lumen and emulsified with bile acids to form micelles. Cholesterol is esterified in the enterocyte to form cholesteryl esters Longer-chain fatty acids (>12 carbons) are incorporated into triglycerides and packaged with apoB-48, cholesteryl esters, retinyl esters, phospholipids, and cholesterol to form chylomicrons. Nascent chylomicrons are secreted into the intestinal lymph and delivered via the thoracic duct directly to the systemic circulation. The particles encounter lipoprotein lipase (LPL), in the endothelial surfaces of capillaries in adipose tissue, heart, and skeletal muscle The triglycerides of chylomicrons are hydrolyzed by LPL, and free fatty acids are released. The released free fatty acids are taken up by adjacent myocytes or adipocytes and either oxidized to generate energy or reesterified and stored as triglyceride. The chylomicron particle progressively shrinks in size creating chylomicron remnants.which are rapidly removed from the circulation by the liver through a process that requires apoE as a ligand for receptors in the liver.

Endogenous Pathway

The triglycerides of VLDL are derived predominantly from the esterification of long-chain fatty acids in the liver. The packaging of hepatic triglycerides with the other major components of the nascent VLDL particle (apoB-100, cholesteryl esters, phospholipids, and vitamin E) requires the action of the enzyme microsomal triglyceride transfer protein (MTP). After secretion into the plasma, VLDL acquires multiple copies of apoE and apolipoproteins of the C series by transfer from HDL. As with chylomicrons, the triglycerides of VLDL are hydrolyzed by LPL, especially in muscle, heart, and adipose tissue. After the VLDL remnants dissociate from LPL, they are referred to as IDLs, which contain roughly similar amounts of cholesterol and triglyceride. The liver removes approximately 40–60% of IDL by LDL receptor–mediated endocytosis via binding to apoE .*Lipoprotein(a)* [Lp(a)] is a lipoprotein similar to LDL in Lipid and protein composition, but it contains an additional protein called *apolipoprotein(a)* [apo(a)]. Apo(a) is synthesized in the liver and attached to apoB-100 by a disulfide linkage. The major site of clearance of Lp(a) is the liver, but the uptake pathway is not known.

HDL Metabolism and Reverse Cholesterol Transport

Cholesterol in peripheral cells is transported from the plasma membranes of peripheral cells to the liver and intestine by a process termed "reverse cholesterol transport" that is facilitated by HDL.

HDL cholesterol is transported to hepatocytes by both an indirect and a direct pathway. HDL cholesteryl esters can be transferred to apoB-containing lipoproteins in exchange for triglyceride by the cholesteryl ester transfer protein (CETP). The cholesteryl esters are then removed from the circulation by LDL receptor–mediated endocytosis. HDL cholesterol can also be taken up directly by hepatocytes via the scavenger receptor class B1 (SR-B1), a cell surface receptor that mediates the selective transfer of Lipids to cells.

HDL particles undergo extensive remodelling within the plasma compartment by a variety of Lipid transfer proteins and lipases.

Dyslipidemia in CKD

It Varies according to renal function and degree of proteinuria. As GFR falls TGL increase and HDL falls and as proteinuria increases TC,TGL,LDL increases. Low HDL is an independent risk factor for CV events. [16]

According to ARIC(Atherosclerosis risk in communities) Study High TGL and low HDL increases the risk of declining kidney function.[17]

Dyslipidemia, regardless of underlying cause (DM, HT), has a role in development of cardio vascular events and progression of CKD.[18]

According to ATP (Adult Treatment program) III for CAD in the management of CKD focuses on LDL as primary target.[19]

Sharma, *et al* [38] and Kunde et al [39] observed no hyperlipidemia in patients of CRF. On the other hand, Gupta [40] and Das *et al* [41] observed lipid abnormalities similar to those reported in Western studies i.e. Hypertriglyceridemia and reduced High density lipoprotein (HDL).

Triglyceride abnormalities

Hypertriglyceridemia is partially due to a down regulation of lipoprotein lipase (LPL), hepatic lipase, very low-density lipoprotein (VLDL) and low-density lipoprotein receptor (LDL-r) expression [54] and as well as increased plasma apoC-III (a potent inhibitor of lipoprotein lipase) apoC-II (activator of lipoprotein lipase) ratio.[20]

The down regulation of the expression of several genes [21–23] along with the changes in the composition of lipoprotein particles [24] and the direct inhibitory effect of various uremic 'toxins' on the enzymes involved in lipid metabolism[25], represent the most important pathophysiological mechanisms underlying the development of Hypertriglyceridemia in renal failure. [21]

CKD-induced hyperparathyroidism to the pathogenesis of lipoprotein lipase deficiency impaired HDL maturation, insulin resistance, reduced physical activity and diminished thyroxin to triiodothyronine conversion, which are common features of ESRD, contribute to diminished production and impaired activity of lipoprotein lipase. Recurrent heparinization in the course of haemodialysis procedure is thought to further contribute to lipoprotein lipase depletion in ESRD patients by promoting release and degradation of the tissue-bound stores of this molecule.[26]

HDL Abnormalities in CKD

The overall reduction in plasma HDL in the ESRD population which appears to be due to its diminished production [27]. The primary reason for impaired maturation of Cholesterol ester poor pre-HDL to mature cholesterol ester-rich HDL in advanced CKD is LCAT deficiency. Serum

LCAT activity and concentration are markedly reduced in ESRD patients [28] which is due to its diminished production by the liver in CKD.[29,30]

In addition, hypoalbuminemia commonly seen in advanced CKD may, in part, contribute to reduced HDL cholesterol level.

Reduction in HDL cholesterol in advanced CKD is coupled with elevated HDL triglyceride contents. This is primarily due to deficiency in hepatic triglyceride lipase. The reduction in HDL antioxidant and anti-inflammatory properties in ESRD is most likely due to the prevailing Oxidative stress and inflammation as shown in other conditions.

LDL cholesterol

Elevated plasma LDL cholesterol concentration is common in nephrotic syndrome but is not a typical feature of patients with advanced CKD, especially those who are on HD. There are, however, qualitative changes in LDL in patients with CKD and dialysis patients. The proportions of sdLDL and IDL, which are considered to be highly atherogenic, are increased. sdLDL is a subtype of LDL that has high propensity to penetrate the vessel wall, becomes oxidized, and triggers the atherosclerotic process. LDL removed from the circulation, mainly by macrophages, through scavenger receptors. This leads to formation of

cholesterol-engorged foam cells, a crucial early step in atheromatous plaque formation Expression of both major scavenger receptors, SR-A and CD36, is increased in uremic patient. Furthermore, uptake of unmodified LDL by LDL receptors is enhanced in inflammation, a state that often accompanies CKD. This also leads to foam cell formation and is believed to constitute a risk factor for accelerated atherogenesis.

Total cholesterol

Plasma total cholesterol is usually normal or reduced and only occasionally elevated in patients with ESRD.

It should be noted that heavy proteinuria leads to up regulation of HMG-CoA reductase Therefore, heavy proteinuria, when present, can modify HMG-CoA reductase expression and activity in humans causing hypercholesterolemia in ESRD patients maintained on peritoneal dialysis in whom CRF is compounded by substantial obligatory losses of proteins through the peritoneum.

However, heavy proteinuria alone or in combination with chronic renal insufficiency results in acquired LDL receptor deficiency, which plays a central role in the genesis of the associated hypercholesterolemia.[31, 32.]

Lipoprotein [Lp(a)]

Lipoprotein [Lp(a)] is an LDL-like particle whose protein moiety contains apolipoprotein (a) [apo(a)] that is covalently bound to an LDL particle. Lp(a) concentrations are strongly genetically determined by the apo(a) gene. Individuals with high molecular weight or large apo(a) isoforms have on average low plasma Lp(a) concentrations, whereas those with low molecular weight or small isoforms usually exhibit high plasma Lp(a) concentrations.

In kidney disease, plasma Lp(a) levels are also influenced by GFR. In patients with large apo(a) isoforms but not those with small apo(a) isoforms, plasma Lp(a) levels begin to increase in stage1 CKD before GFR starts to decrease [37] This isoform-specific increase in plasma Lp(a) levels was observed in several studies in non-nephrotic patients with CKD and HD patients [37] In contrast, in patients with nephrotic syndrome and PD patients, increases in plasma Lp(a) levels occur in all apo(a) isoform groups, probably as a consequence of the pronounced protein loss and a subsequently increased production in the liver. The elevation of Lp(a) in CKD is an acquired abnormality, mostly influenced by the degree of proteinuria and less by the cause of kidney disease.[33]

Thus it has been shown that Lp(a) is an independent risk factor for CVD in both the general and the CKD population. Its levels are increased in CKD and especially in patients undergoing PD as a result of significant protein losses and subsequent apolipoprotein overproduction.

Common features of serum lipid/lipoprotein profile in predialysis CKD patients with treated with chronic haemodialysis or peritoneal dialysis[35] follows.

Serum Lipid	CKD Patients		Hemodialysis Patients	Peritoneal Dialysis Patients	
	Heavy proteinuria	Minimal proteinuria			
Triglycerides	↑	↑	↑	↑	
Total cholesterol	↑	↔, ↓	↔, ↓ Rarely ↑	Frequently ↑	
LDL cholesterol	↑	↔, ↓ or ↑	↔, ↓ Rarely ↑	Frequently ↑	
Small dense LDL	↑	↑	↑	↑	
IDL cholesterol	↑	↑	↑	↑	
HDL cholesterol	↓	↓	↓	↓	
apoA-I, apoA-II	↓	↓	↓	↓	
apoC-III	↑	↑	↑	↑	

CONSEQUENCES OF DYSLIPIDEMIA

Hyperlipidemia can potentially accelerate progression of renal disease by several mechanisms. First, reabsorption of fatty acids, phospholipids, and cholesterol contained in the filtered proteins (albumin and lipoproteins) by tubular epithelial cells can stimulate tubulointerstitial inflammation, foam cell formation, and tissue injury[36] Second, accumulation of lipoproteins in glomerular mesangium can promote matrix production and glomerulosclerosis[37,38]. In addition, impaired HDL-mediated reverse cholesterol transport can further contribute to tissue injury by limiting the unloading of the excess cellular cholesterol and phospholipid burden.

The risk of cardiovascular morbidity and mortality is profoundly increased in patients with CKD. For instance, the majority of patients with CKD die of cardiovascular events before reaching ESRD.

Accumulation of oxidation-prone atherogenic lipoprotein remnants and impaired HDL-mediated reverse cholesterol transport, which are the defining features of uremic dyslipidemia, may play a major part in the pathogenesis of atherosclerosis in this population.

Thyroid abnormality in CKD [16]

There is ↓ T3, normal r T3, low or normal T4,and the TSH may be normal or rises in hypothyroidism.

Iodide excretion decreases in advanced kidney failure. The increase in iodide blocks thyroid hormone (Wolf -chaikoff effect) which leads to Hypothyroidism (Kidney International).

Decreased level T3 is due to decreased conversion of T4-T3, this is not associated with increased T4-rT3; this differentiates from other patients of chronic illness.

MATERIALS AND METHODS

This study was conducted in 50 patients with chronic kidney disease and 50 normal people taken as controls.

All the patients in this study group were selected from those who were admitted to department of Internal Medicine, Govt. Annal Gandhi Memorial Govt Hospital, attached to K.A.P.Viswanatham Govt Medical college, Trichy.

Inclusion Criteria:

1. Patients between age group of 40 to 80 years with established chronic Kidney disease.
2. Patients who were on conservative treatment.
3. Established renal failure was ensured by radiological evidence.

EXCLUSION CRITERIA

1. Patients with Acute renal failure, nephrotic syndrome.
2. Who are on drugs β blockers, statins and oral contraceptive pills.
3. Pregnant female patients.

STUDY DESIGN: Descriptive observational study

Written consent is obtained from all the patients and controls

History regarding symptoms and duration of the kidney disease, hypertension, diabetes, smoking, alcoholism, drug intake and treatment were elicited. A detailed clinical examination was performed in all patients including Height and Weight, Blood Pressure, renal function tests, abdominal ultra sonogram and Electrocardiogram were done for all patients.

After 12 hours of overnight fasting blood sample was taken for lipid profile from patients and controls and for TSH levels from patients.

The following tests are also performed:

Fasting blood glucose and post prandial (mg/dL)

Haemoglobin A1C, Serum albumin

24 Hrs urine proteins, urine P/Cr ratio and creatinine clearance

Estimated Glomerular filtration rate (eGFR), as assessed by CKD-EPI

LABORATORY METHODS FOR ESTIMATING LIPIDS

HDL-C Estimation: (Erba Mannheim - XL System packs)

Methodology:

The assay is based on a modified polyvinyl sulfonic acid (PVS) and polyethylene-glycol-methylether (PEGME) coupled classic precipitation method with the improvements in using optimized quantities of PVS/PEGME and selected detergents. LDL, VLDL and chylomicron (CM) react with PVS and PEGME and the reaction results in inaccessibility of LDL, VLDL and CM by cholesterol oxidase (CHOD) and cholesterol esterase (CHER).The enzymes selectively react with HDL to produce H2O2 which is detected through a Trinder reaction. Reagent1 (R1) contains PVS and PEGME and Reagent2 (R2) contains cholesterol esterase and cholesterol oxidase.

$$\text{HDL+LDL+VLDL+CM} \xrightarrow[\text{PEGME}]{\text{PVS}}$$

HDL + (DLD+VLDL+CM).PVS/PEGME

$$\text{HDL+CHOD+ CHER} \xrightarrow[\text{Peroxidase}]{} \text{Fatty acid} + H_2O_2$$

$$2H_2O_2\text{+4-AA+ TODB} \longrightarrow \text{Quenone}+5H_2O$$

EXPECTED VALUES:

Adults male: 35.3 -79.5mg/dl

Adults female: 42.0 -88.0 mg/dl

Cholesterol estimation (Erba Mannheim - XL System packs)

METHODOLOGY:

This method is based on the Trinders methodology.

PRINCIPLE:

1. Cholesterol ester + H_2O $\xrightarrow{CHE}$ Cholesterol +Fattyacids
2. Cholesterol + O_2 $\xrightarrow{CHO}$ Cholest-4-en-3-one+H_2O_2
3. $2H_2O_2$+4AAP+Phenol $\xrightarrow{POD}$ Quinoneimine dye + $4H_2O$

CHE : Cholesterol esterase

CHO : Cholesterol Oxidase

4AAP : 4-Aminoantipyrine

POD : Peroxide

Absorbance of Quinoneimine so formed is directly proportional to cholesterol concentration.

CALCULATION:

Cholesterol (mg/dl) = (Abs of Test/Abs of standard) *

Concentration of std (mg/dl)

Expected values:

Adults < 200 mg/dl.

TRIGLYCERIDE ESTIMATION *(Erba Mannheim - XL*

METHODOLGY

The series of reactions involved in the assay system is as follows:

$$\text{Triglycerides} + H_2O \xrightarrow{\text{LPL}} \text{Glycerol} + \text{Free Fatty acids}$$

$$\text{Glycerol} + \text{ATP} \xrightarrow{\text{GK}} \text{Glycerol-3-Phosphate} + \text{ADP}$$

$$\text{Glycerol-3-Phosphate} + O_2 \xrightarrow{\text{GPO}} \text{DAP} + \text{H2O2}$$

$$H_2O_2 + \text{4AAP} + \text{ADPS} \xrightarrow{\text{POD}} \text{Quinoneimine dye} + H_2O$$

1. Triglycerides are enzymatically hydrolyzed by lipase to free acids and glycerol.
2. The glycerol is phosphorylated by adenosine triphosphate (ATP) with glycerol kinase (GK) to produce glycerol-3-phosphate and adenosine diphosphate (ATP).

3. Glycerol-3-Phosphate is oxidized to dihydroxy-acetone phosphate (DAP) by glycerol phosphate oxidase producing hydrogen peroxide (H_2O_2).

4. In a Trinder type colour reaction catalyzed by peroxidase, the H_2O_2 reacts with 4-aminoantipyrine (4AAP) and 4-Chlorophenol (3, 5 ADPS) to produce a red coloured dye .The absorbance of this dye is proportional to the concentration of triglycerides present in the sample.

EXPECTED VALUES:

Recommended Triglycerides levels for adults:

Male : 40-160 mg/dl

Female: 35-135 mg/dl

LDL was estimated by using **Friedwald** formula

LDL = Total cholesterol - (HDL-C + TGL/5)

LABORATORY METHODS FOR ESTIMATING TSH

This method is generally regarded as the most sensitive indicator available for the diagnosis of primary and secondary hypothyroidism Increase in serum concentrations of TSH is an early & sensitive indicator of thyroid reserve.

PRINCIPLE OF THE TEST:

The ERBA THYROKIT TSH kit is a solid phase enzyme-linked immunosorbent assay (ELISA) based on the sandwich principle.

The microtiter wells are coated with a monoclonal (mouse) antibody directed towards a unique antigenic site of the TSH molecule. An aliquot of patient sample containing endogenous TSH is incubated in the coated well with enzyme conjugate, which is an unbound conjugate, is washed off.

The amount of bound peroxidase is proportional to the concentration of TSH in the sample.

Having added the substrate solution, the intensity of colour developed is proportional to the concentration of TSH in the patient sample.

Normal range is from **0.3 to 4.0 mlU/L**

Sensitivity: 70.8%

Specificity: 100%

Radiological imaging studies

Ultra sonogram showing reduced kidney size (<9cm) with altered cortico medullary differentiation was taken as radiological evidence of chronic kidney disease.

Electrocardiogram of all patients was studied in detail.

In this study

LDL > 130 mg/dl

HDL < 40 mg/dl

TGL > 160 mg/dl

TC > 200 mg/dl were considered abnormal

STATISTICAL METHODS

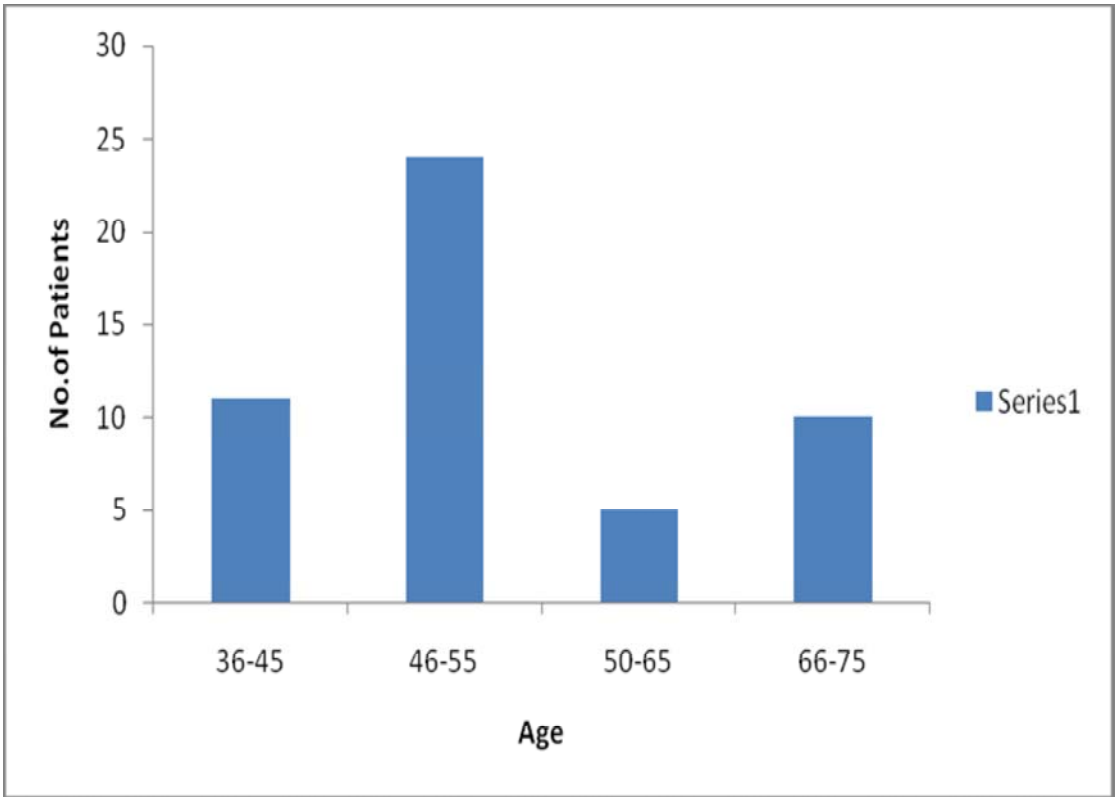
Mean values were obtained for LDL, HDL, TGL & Total cholesterol separately. Then standard deviations were calculated for each category of observations for both study and control group. Students T test was performed & T value was obtained. P value from t value was calculated. P value of <0.05 was considered significant.

RESULTS AND OBSERVATIONS

AGE DISTRIBUTION

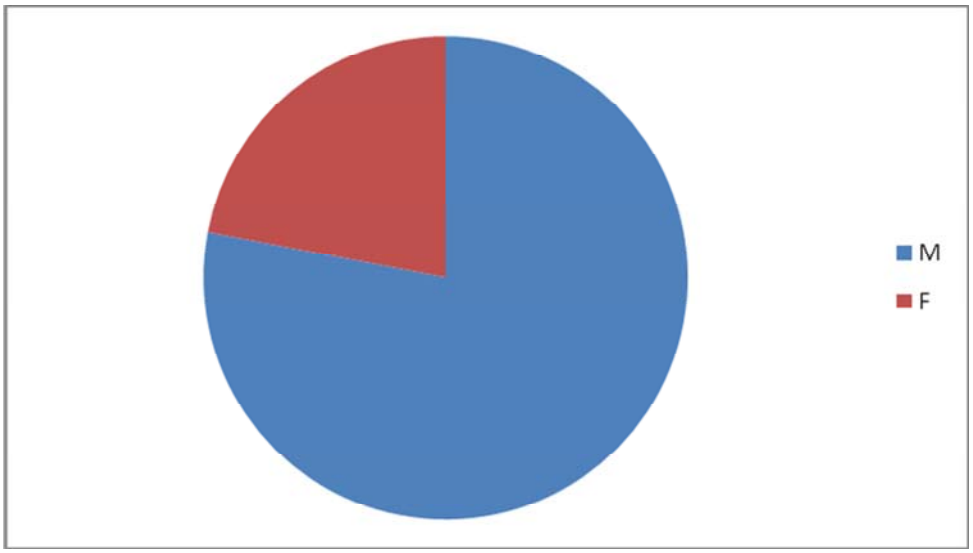
Age of the patients varied from 40 yrs to 75 yrs. Majority of patients fall in the age group between 46-55 years.

AGE DISTRIBUTION IN PATIENTS



SEX DISTRIBUTION

Males constitute 39(78%) and females constitute 11(22%) in this study



PERSONAL HABITS

In this study10 patients of the patients were smokers And 6 patients were alcoholics

RENAL PARAMETERS

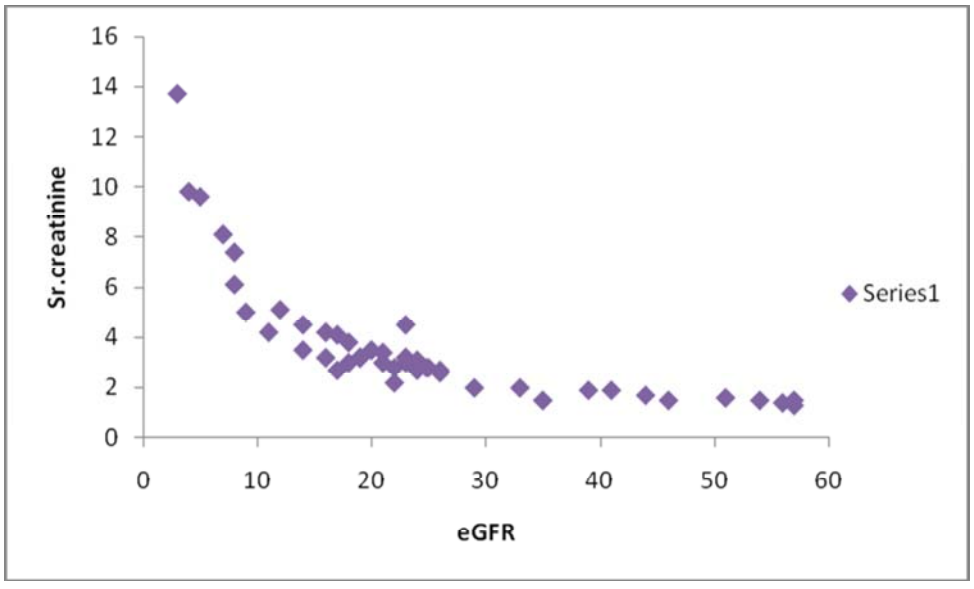
Lowest urea value found in these patients was 38 and the highest was 157mg/dl

Creatinine values ranged between 1.3 mg/dl to 13.7 mg/dl.

GFR-EPI Values

GFR	No. of patients
<15ml	11
15-29ml	28
30-59ml	11

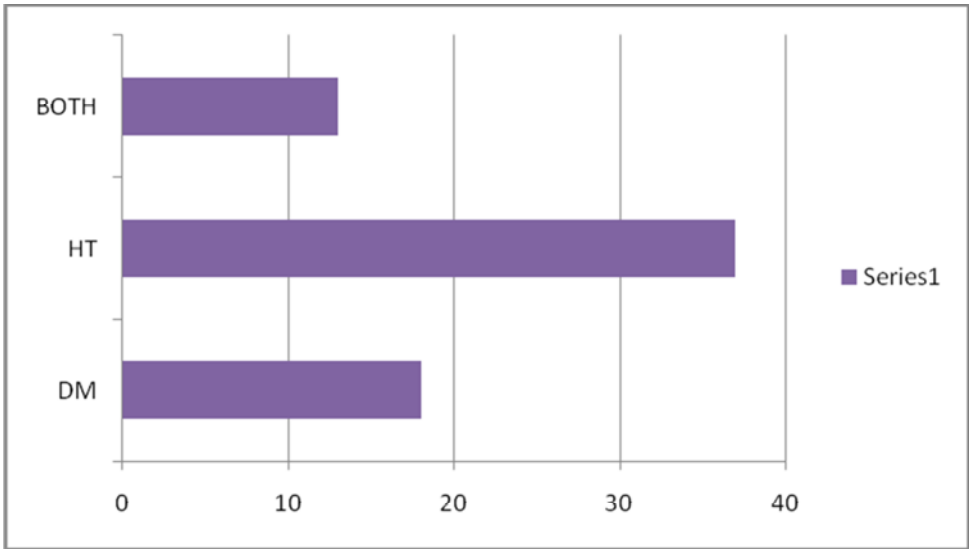
Correlation between GFR and sr.creatinine.



BLOOD PRESSURE READINGS

Patients with blood pressure of more than 140/90 were considered hypertensives. Most patients (36 patients) were hypertensives at the time of presentation. Only 14 patients had blood pressure less than 140/90mmHg.

DIABETIC STATUS It was found that 18patients were diabetic



RADIOLOGICAL EXAMINATION

Radiological examination was done by abdominal ultra sonogram. In 39 patients the kidney size was less than 9cm in one or both kidneys.

ECG RESULTS

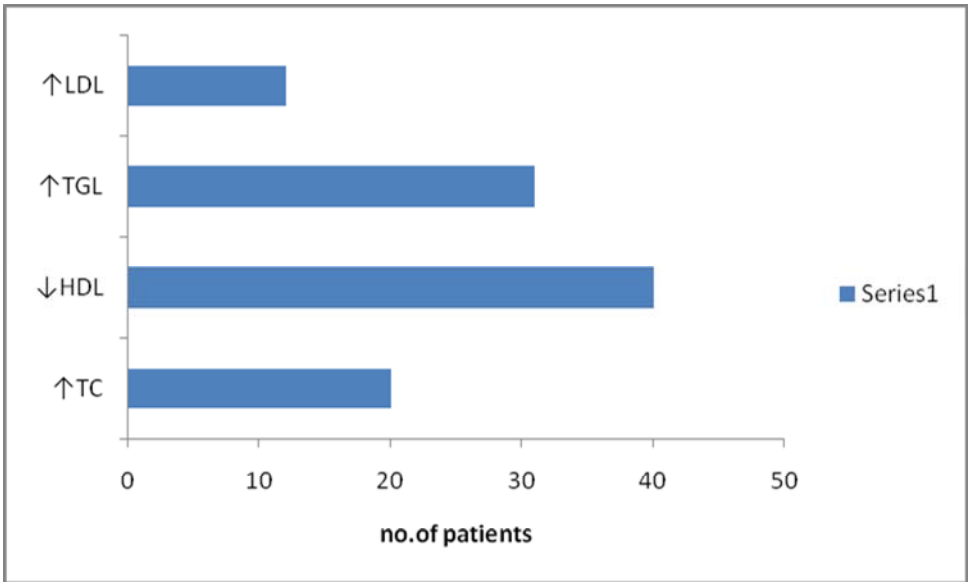
Patient's electrocardiograms were analysed. It was found that 17 patients showed left ventricular hypertrophy. 16 patients showed ischemic changes. One patient had tall peaked T waves.

ECG CHANGES IN CKD PATIENTS (STUDY GROUP)

Type of ECG changes	Males	Females	Total
LVH	15	2	17 (34 %)
Ischemic changes	12	4	16 (32%)

CKD PATIENTS SHOWED THE FOLLOWING LIPID DISORDER

Type of lipid Disorders	Number of Patients
Elevated Cholesterol	20
Decreased HDL	40
Elevated Triglycerides	31
Increased LDL Cholesterol	12



LIPID PATTERN IN OUR STUDY

HDL PATTERN

Serum HDL values ranged between 23mg/dl to 46mg/dl.Patients showed abnormal HDL levels (<40 mg/dl) were 40.Its mean value was 35.08 and standard deviation was 4.84. The P value is <0.01 Among the control groups, the lowest value of HDL was 36 mg/dl and the highest was 58 mg/dl. Their mean was 46.96 and standard deviation was 5.59 .P value, <0.01

It showed that there was a significant reduction in HDL-C levels in patients with CKD than that of controls.

LDL PATTERN

Lowest value of LDL 52mg/dl and the highest value were189mg/dl. Abnormally high LDL levels (>130mg/dl) were found in 12 patients. Their mean value was 188.78 mg/dl and standard deviation was 5.680 and P value was < 0.01 significant.

For controls lower value is 76mg/dl, highest value is126mg/dl their mean was 105.58 and standard deviation is 12.59 and P value was <0.01 which is significant

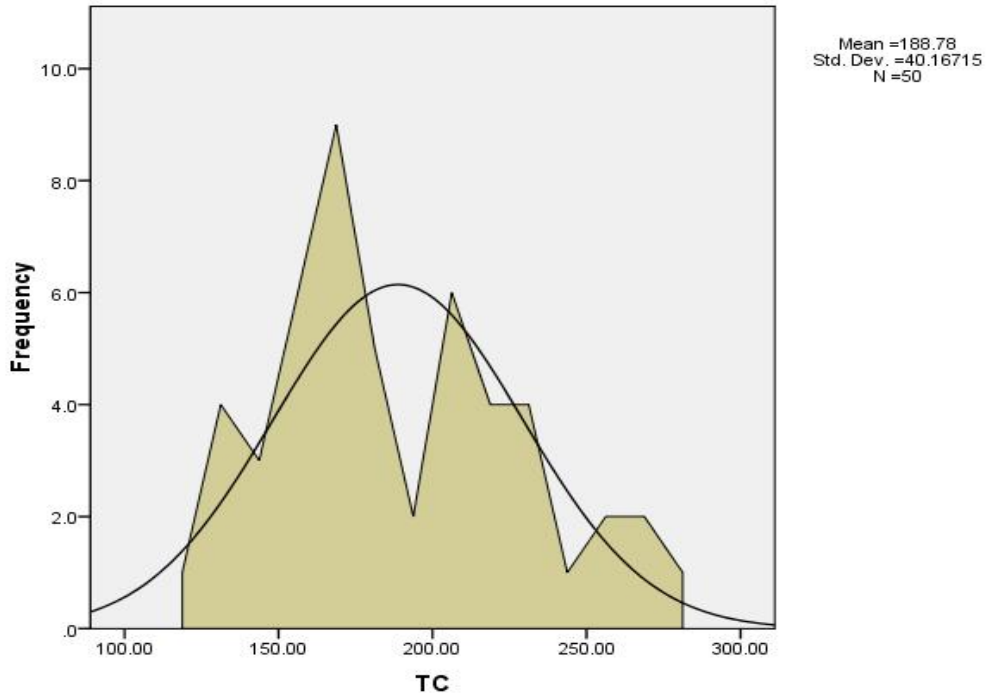
TGL PATTERN

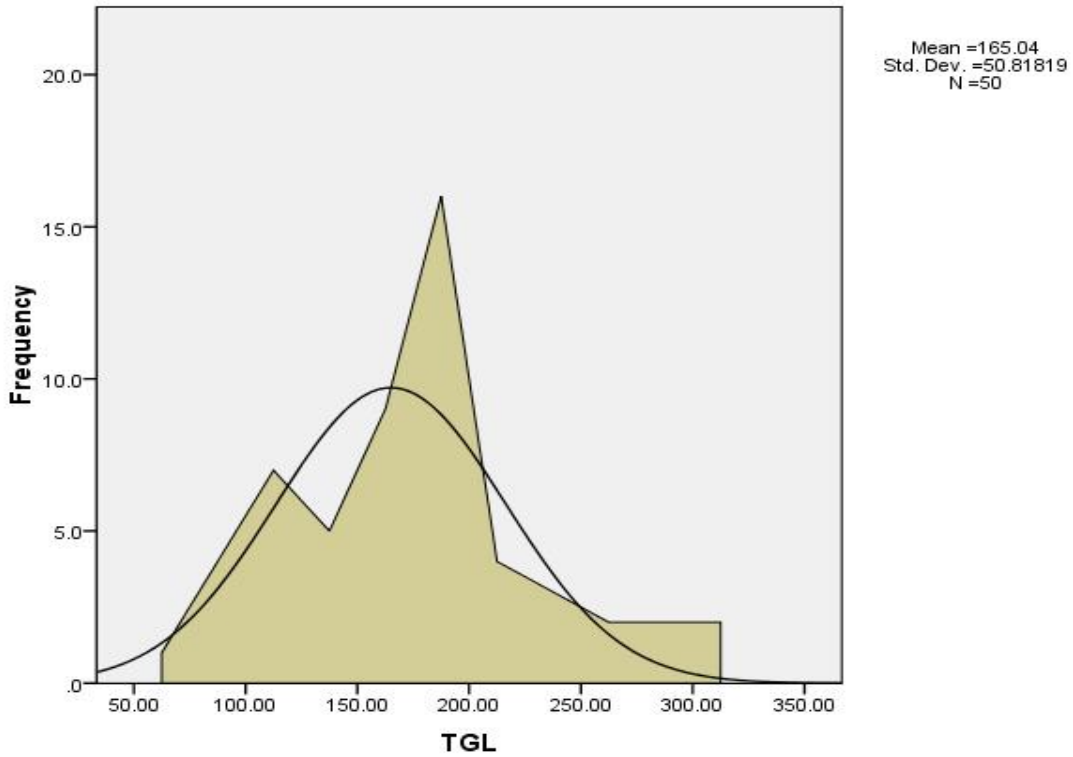
TGL value in our study group ranged between the minimum of 73mg/dl and the maximum of 313mg/dl. TGL levels were abnormal in 31 patients >160mg/dl).Mean and standard deviation of study group were 165.04and 50.8 In controls, the lowest value is 70 and the highest is 170mg/dl. The mean and standard deviation were 117.68 and 17.43. P value was significant ($P < 0.01$) in both the groups.

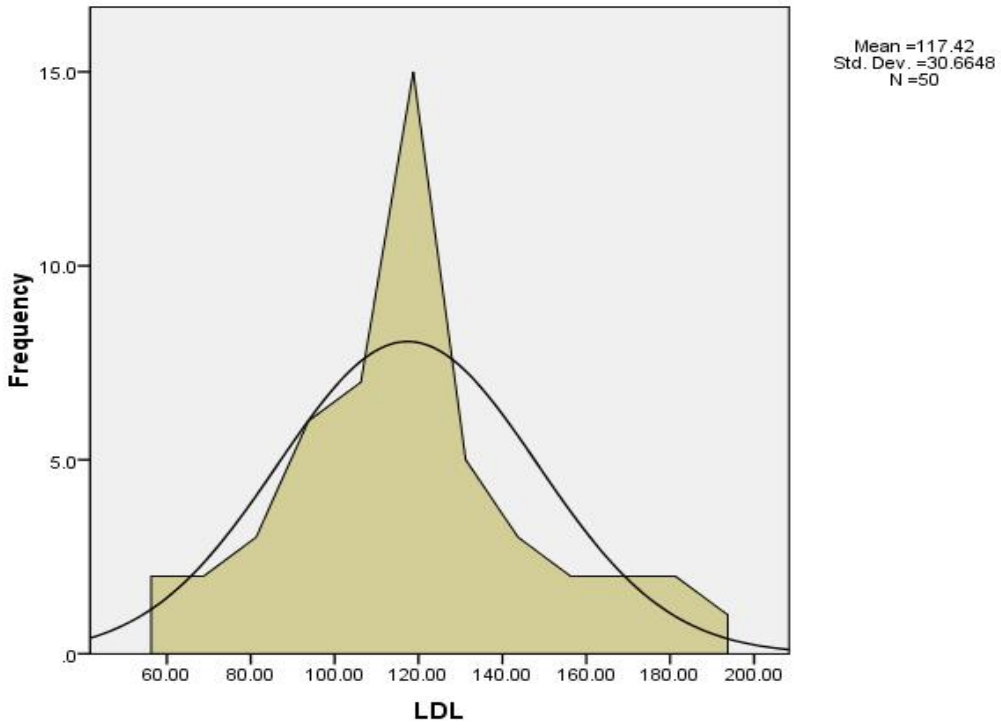
TOTAL CHOLESTEROL

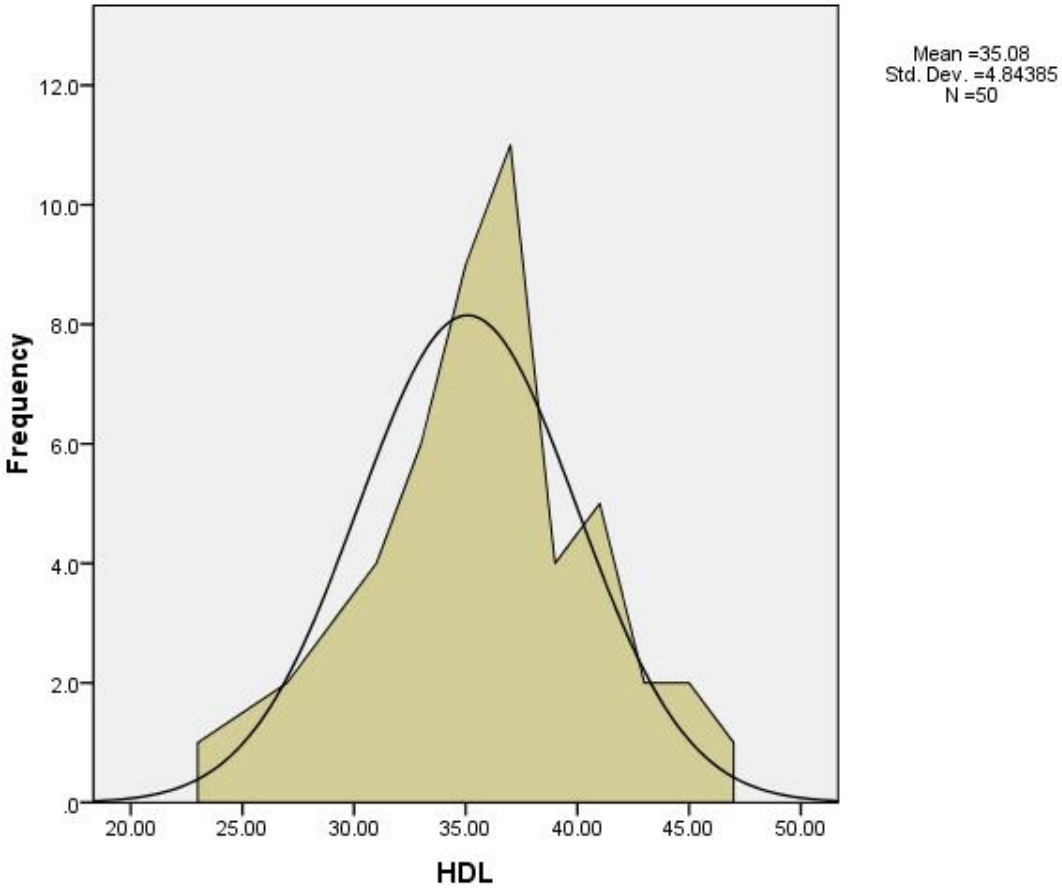
Range of TC levels in study group was 120mg/dl to 280 mg/dl. Lowest value in control group was 143 and the highest value was 220mg/dl. Total cholesterol was more than 200mg/dl in 20 patients. The mean values and standard deviations of study group were 188.78 and 40.16. In the control group. The mean values and standard deviations of were 117.68 and 17.43 P value was ($P<0.01$) significant in both the groups.

GRAPHS (STUDY GROUP)






Mean =117.42
Std. Dev. =30.6648
N =50
Frequency
15.0
10.0
5.0
.0
60.00
80.00
100.00
120.00
140.00
160.00
180.00
200.00
LDL


Mean =35.08
Std. Dev. =4.84385
N =50
Frequency
12.0
10.0
8.0
6.0
4.0
2.0
.0
20.00
25.00
30.00
35.00
40.00
45.00
50.00
HDL

CORRELATION BETWEEN LIPID FRACTIONS AND GFR IN PATIENTS

LIPIDS	eGFR<15ml	15-29ml	30-59ml
TC ↑	5	12	3
TGL ↑	5	19	7
HDL ↓	8	23	9
LDL ↑	3	6	2

TSH Level

TSH level increased in 16 patients in this study.

DISCUSSION

In our study, most common lipid abnormalities found were Low HDL levels and Hypertriglyceridemia.

DECREASED HIGH DENSITY LIPOPROTEIN LEVELS

The low HDL levels in patients with chronic kidney disease in our study were consistent with Diana M Lee LG et al [43] who studied the lipid profile in CRF patients.

This low HDL cholesterol levels was also an independent risk factor for the development of CKD in the Framingham off spring study. Several mechanisms may underlie these reductions in HDL cholesterol levels, which is usually an indication of impaired reverse cholesterol transport. Apo AI, which is the activator of lecithin cholesterol acyltransferase (LACT), is reduced in CKD due to down regulation of hepatic Apo AI genes leads to decline in the activity of LACT, which causes reduced cholesterol esterification and impairment of HDL maturation. The activity of LACT is consistently diminished in CKD, so there is decrease in HDL levels. [44]

In MDRD study [55] low HDL levels in CKD patients were one of the independent risk factor for progression of kidney disease. In our study the mean value was significantly less than the age matched healthy controls.

ELEVATED TRIGLYCERIDES

Triglyceride levels were significantly elevated in our study than control group. Abnormal triglyceride values were found in 31 of patients in our study. The present study demonstrates that CRF is commonly accompanied by lipid abnormality in the form of hypertriglyceridemia. This is similar to the observations made in Western studies and recent Indian studies[45,46,47,48] by Gupta DK,Das BS and Bagdae J. Elevated triglyceride levels are due to impaired activity lipoprotein lipase (LPL)[49] and direct inhibitory effect of various uremic 'toxins' on the enzymes involved in lipid metabolism[50] represent the most important pathophysiological mechanisms underlying the development of hypertriglyceridemia in renal failure.

Chan MK et al [48] also found hypertriglyceridemia was the major abnormality in their studies. Hypertriglyceridemia represents an early feature of renal failure.

ELEVATED LOW DENSITY LIPOPROTEIN

LDL was significantly elevated than that of controls in our study. We found that 12 of patients showed elevated LDL levels. Most studies find that Uremic Patients usually have normal or slightly reduced concentrations of LDL-C levels and they exhibit important disturbance in the density distribution of LDL sub fraction that is characterized by a predominance of small dense LDL particles.[51]

In the present study we find significantly high levels of LDL cholesterol in the group with GFR15-29ml.

TOTAL CHOLESTEROL

Total cholesterol levels were elevated in 20 patients in our study group heavy proteinuria alone or in combination with chronic renal insufficiency results in acquired LDL receptor deficiency, which plays a central role in the genesis of the associated hypercholesterolemia. [53]

Correlation Studies:

It was found that abnormal serum triglycerides, TC, HDL, were found to be increased significantly in the group of eGFR between15-29ml

ECG changes:

Out of 50 patients, 17 (34%)of patients showed changes suggestive of LVH and 16 (32 %) of patients showed ischemic changes.

The risk of dying of cardiac complications is 65 times higher in dialysis patients between 45-54 years and 500 times higher than the general population. The risk factors which are responsible for increased morbidity and mortality were hypertension, DM, high LDL, low HDL and smoking.

CONCLUSION

1. HDL-C levels were lower and triglycerides, total cholesterol and TGL levels were higher in the study group compared to controls.
2. There is a statistically significant increase in serum triglycerides level in patients with CKD stage 3,4 and 5.
4. Predominant lipid abnormalities were reduced HDL-C levels and elevated TGL.
5. There was a negative correlation exists between serum HDL-C level and GFR levels which was statistically significant.
6.. Significant number of patients showing ECG changes of left ventricular hypertrophy 34 %and ischemic changes 32%.

LIMITATIONS OF THE STUDY

1. Smoking, alcoholism and diabetics may alter the lipid pattern in the body. Their influences in the study group also have to be considered.

2. Since we had not analysed the echocardiogram of the patients, the real scenario of ischemia in CKD patients was not known.

3 . We had not estimated the lipid abnormalities in patients who underwent dialytic treatment or renal transplantation.

ACRONYMS

Apo - Apolipoprotein

BP - Blood Pressure

CGN-chronic glomerulonephritis

CIN-chronic interstitial nephritis

CKD - Chronic Kidney Disease

CVD - Cardio Vascular Disease

DM - Diabetes Mellitus

ECG - Electro Cardiogram

ESRD - End Stage Renal Disease

GFR - Glomerular Filteration Rate

HDL-C - High Density Lipoprotein Cholesterol

HTN - Hypertension

ID No - Patient identification Number

K+ - Potassium

K/DOQI - Kidney Disease Outcome Quality Initiative

LCAT - Lecithin Cholesterol Acyl Transferase

LDL-C - Low Density Lipoprotein Cholesterol

LK - Left Kidney

LPL - Lipoprotein Lipase

LVH - Left Ventricular Hypertrophy

MDRD study - Modification of Diet in Renal Disease study

Na+ - Sodium

PD-peritoneal dialysis

PMP - Per Million Population

PTH-parathyroid hormone

RK - Right Kidney

Sd LDL - Small Dense Low Density Lipoprotein

TC - Total Cholesterol

TGL/TG - Triglycerides

USG - Ultra Sonogram

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Sl Number	Name	Age	Sex	ID No	Height cm	Weight kg	Smoking	Alcoholism	BP	DM	HT	FBSmg%	PPBSmg%	HbA1c%	Sr.alb g/dl	Ureamg%	Sr.creatininemg%	Na meq/l	K meq/l	24hrs U.pro mg	urine p/cr ratio	cr.clea ml/mt	Urine- alb	TC	TGL	LDL	HDL	TSH	eGFR	ECG	USG RK size	USG Lk size
1	Arumugam	50	M	512038	170	65	N	N	150/90	N	Y	94	124	3.4	3.4	64	3	137	4	450	1.2	30	nil	220	170	124	46	2.3	23	LVH	7.4	7.4
2	Abdul Nazeer	47	M	86118	145	50	N	N	140/80	N	Y	76	120	3.1	4.1	47	1.9	141	4	397	0.9	35	nil	280	301	189	31	10	41	N	8	9.2
3	Antony	68	M	35122	160	55	N	Y	150/90	N	Y	106	126	3.7	3.2	144	13.7	136	4	300	1.2	20	nil	130	120	70	36	3.4	3	N	3.3	4.3
4	Ammasi	67	M	32165	150	50	N	Y	180/100	N	Y	117	263	2.9	3.5	68	3.2	131	5	350	1.1	14.6	+	215	161	127	41	11.4	19	N	8.3	8
5	Andi	65	M	34752	154	51	N	N	140/90	N	Y	96	127	3.6	3.3	60	3	137	4	340	1.4	18	+	204	200	120	36	2.5	21	N	8.3	8
6	Bala Sundaram	51	M	36625	160	60	N	N	140/80	Y	Y	126	240	4.5	3.4	65	2.7	142	45	250	0.9	23	nil	207	180	120	36	2.5	26	LVH	10.4	9.6
7	Kandasamy	55	M	267109	160	60	N	N	160/80	Y	Y	150	263	4.8	3.2	48	1.4	136	4	240	0.8	48	nil	160	165	109	30	1.6	56	LVH	10.2	11.1
8	kadhar moideen	50	M	15740	160	65	N	N	170/100	N	Y	91	114	3.2	3.5	52	1.5	132	4	103	0.13	35	nil	175	103	119	46	1.8	54	N	8.2	9.8
9	Kamaraj	48	M	42747	150	45	Y	N	140/90	N	Y	80	117	3.2	3.4	58	2.8	135	4	290	1.1	21	nil	174	181	107	33	10.4	24.8	N	7.5	7.5
10	Karuppiah	49	M	34760	153	50	N	N	160/90	Y	Y	165	260	3.5	3.8	72	4.2	135	4	249	1.6	13	+	130	95	89	46	5.2	16	T↓L2,aVL,V5-V6	8	7.5
11	Kunju Pillai	65	M	39478	165	60	N	N	160/80	N	Y	94	194	3.8	3.4	76	3.2	138	3	500	2	15	+	147	179	82	30	0.9	19	T↓V5-V6	7.2	7.8
12	Krishnan	47	M	345671	160	50	Y	N	160/90	Y	Y	160	274	6.5	3	67	3.5	139	4	400	1.3	20	+	165	194	140	34	2.1	20	LVH	8.7	8.1
13	Marutha muthu	40	M	31754	150	55	N	N	160/90	N	Y	92	124	3.4	3.4	104	8.1	135	42	300	0.8	10	nil	204	93	103	23	3.3	7	LVH	6.4	6.2
14	Murugan	70	M	23011	160	58	N	N	170/100	N	Y	83	142	3.2	4	64	3.2	139	5	280	0.7	17	nil	256	258	170	35	0.8	19	T↓V1-V6	8.2	8.3
15	Muthusamy	70	M	37654	150	50	N	N	140/80	N	Y	95	116	3.1	3.4	157	9.6	130	3	400	1.2	4	+	168	73	121	32	4.8	5	T↓L1,aVL,V5-V6	5.6	4.8
16	Natesan	70	M	33226	165	55	N	Y	100/60	Y	Y	94	120	2.1	2.7	84	2.8	125	5	192	0.9	7	nil	143	169	72	38	5.5	22	LVH	7.2	7
17	palanisamy	46	M	235107	160	57	N	N	110/80	N	N	81	117	3.3	3.2	60	3	136	4	374	0.7	25	nil	231	189	120	36	5.1	24	N	8.3	8.2
18	Paramasivam	52	M	1107	163	60	N	N	130/80	N	N	96	130	3.4	3.3	58	2.6	138	4	126	0.35	20	nil	187	173	117	32	3.2	26	T↓L2,L3,aVL,V2-V3	8	7.8
19	Raju	64	M	14411	165	60	N	N	160/100	N	Y	102	127	3.1	4.2	59	2.7	140	4	149	0.3	24	nil	168	128	107	36	0.6	24	T↓V5-V6	8.2	8.8
20	Ramraj	42	M	245178	160	58	Y	N	150/90	N	Y	86	112	3	3.9	82	3.8	132	4	725	2.5	24	++	135	163	76	27	2.8	18	N	8.2	8
21	Rayappan	70	M	38451	154	50	N	N	180/80	N	Y	60	110	3.2	3.4	42	1.5	140	4	200	0.7	40	nil	170	189	95	38	9	46	LVH	9	8.8
22	Rajalingam	65	M	34768	152	60	N	N	170/80	N	N	84	120	3.6	3.7	38	1.3	140	4	300	0.9	45	+	196	180	120	36	2	57	N	8.7	8.4
23	Rengasamy	55	M	47247	156	57	Y	Y	150/90	N	N	162	264	4.3	3.9	54	1.9	138	4	252	0.9	38	nil	162	176	92	35	1.7	39	T↓V1-V3	7.1	7.4
24	Rengasamy	55	M	50061	154	58	N	N	160/80	N	N	113	147	4.2	4.1	60	1.7	135	4	260	1.2	42	nil	155	85	106	32	5.1	44	N	8.2	8
25	Rengasamy	51	M	34765	154	56	N	N	140/90	N	N	104	148	2.7	4.8	67	5.1	137	4	720	2.9	30	++	164	97	117	28	2.1	12	N	7.6	7.3
26	Sakthivel	40	M	17094	155	56	Y	N	150/100	N	N	130	262	2.8	3.6	60	3.2	140	5	222	0.8	40	+	180	135	117	36	1.8	23	N	9.4	10
27	Sakthivel	42	M	1006	158	58	N	N	150/90	N	N	126	262	2.8	3.6	60	3.2	136	4	222	0.8	40	nil	180	135	117	36	2.2	23	N	8.4	8.1
28	Sasikumar	44	M	38807	154	54	N	N	180/100	N	Y	150	190	4.6	3.1	125	4.5	131	4	261	0.86	23	nil	191	118	135	33	7.7	15	LVH	9	8
29	Savariayar	50	M	69238	158	56	N	N	100/80	N	Y	102	126	3.1	3.8	40	1.5	137	5	391	0.5	42	+	147	129	88	34	1.3	57	T↓V1-V6	9	8
30	Selvaraj	42	M	29750	156	60	N	N	160/90	N	Y	92	0.5	2.7	3.6	95	4.1	129	5	270	0.9	18	nil	155	110	106	27	0.5	17	N	7.6	7.8
31	Sivaanandham	58	M	36025	160	50	N	N	150/90	Y	Y	143	231	4.8	3.2	60	2.8	134	4	600	1.2	20	nil	231	209	178	45	3.5	24	ST dep.L2,L3,aVF,T↓aVL	9	8.5
32	Syed Jaffer	45	M	44410	162	60	Y	Y	160/100	N	Y	86	127	3.2	3.4	58	3	138	4	400	1.1	22.5	+	240	200	168	38	3.7	24	LVH with strain	7.8	9.1
33	Thangarajan	40	M	36721	168	61	N	N	150/100	N	Y	90	124	3.1	3.4	62	3.1	136	4	270	0.8	25	nil	168	174	108	34	5.1	24	LVH,T↓L1,,aVL,V5-V6	8.1	8.4
34	Vellayan	50	M	38742	152	50	Y	N	120/70	N	Y	87	140	3.4	3.3	52	2.8	135	4	180	0.4	24	nil	180	194	117	34	3	25	T↓,LVH,V1-V6	8.8	8.5
35	Yusuf	71	M	37942	160	60	N	N	150/100	N	Y	96	130	4.2	3.4	55	2	141	5	300	0.9	34	nil	220	258	127	42	1	33	SVT,LVH,RAE	9	8.6
36	Vadivel	45	M	32907	158	54	Y	N	160/100	N	Y	120	140	2.7	2.6	48	1.6	129	5	152	0.4	26	nil	158	138	97	34	2.1	51	LVH	7.6	7
37	Sakthivel	40	M	345678	164	58	N	N	180/100	N	Y	96	126	3.8	3.6	60	3.4	136	4	240	0.7	25	nil	216	190	124	36	5	21	LVH	7.8	7.6
38	Arockiamary	45	F	35507	150	45	N	N	150/90	N	Y	96	130	3.8	3.6	101	6.1	140	4	197	0.32	8.5	+	205	179	147	28	8.8	8	T↓L1,L2,aVL,V4-V6	8.3	8
39	Krishnammal	54	F	32230	145	45	N	N	130/80	Y	Y	126	263	6.6	2.9	126	4.2	136	4	335	1.2	3.5	+	128	103	52	45	3.1	11	N	10	10.1
40	Maria pusham	47	F	29212	150	50	N	N	160/100	N	Y	81	114	3.7	3.3	54	3.2	134	4	354	0.6	18	nil	264	103	119	30	1	16	T↓V1-V3	8	7.8
41	Muthulakshmi	48	F	38583	154	56	N	N	140/90	Y	Y	137	337	6.7	3	69	3	140	4	250	0.6	20	nil	152	150	80	44	3.8	18	N	9.6	9.8
42	Periammal	69	F	345832	145	65	N	N	150/90	N	N	92	119	3.1	3.5	82	2.7	128	5	198	9	12.8	++	267	313	161	38	3.2	17	LVH	8.3	9.1
43	Ponnammal	47	F	6764	158	67	N	N	130/80	N	N	82	124	3.5	3.4	65	2	134	4	315	1.4	17	+	210	179	127	34	3.3	29	LVH	8	8
44	Ranjitha mary	70	F	38984	150	45	N	N	160/80	N	N	103	278	3.2	3.6	62	2.2	135	5	128	4.1	35	nil	173	113	123	28	1.4	22	N	7.8	8
45	Sarabee	47	F	385399	150	45	N	N	120/80	N	N	185	270	5.6	3.3	158	9.8	128	4	200	0.8	13	nil	120	151	56	34	2	4	N	8.7	10.4
46	Sarojini ammal	55	F	38502	145	50	N	N	140/80	N	Yes	117	132	3.2	3.3	81	3.5	140	4	450	1.6	10	+	212	182	153	33	3.3	14	N	7.8	8
47	Thangammal	55	F	39299	150	48	N	N	170/90	N	Yes	178	290	5.8	3.2	90	5	140	4	128	5.1	13	nil	172	192	98	36	7.5	9	T↓L2,aVF,V4-V6	8	8.2
48	Chellammal	70	F	18518	145	46	N	N	150/90	N	Yes	109	127	3.2	3.2	45	1.5	136	3	587	1.3	25.3	+	260	178	184	41	1.5	35	St dep.V1-V3,T↓V1-V6	7.6	7.7
49	ananda gopal	55	M	55116	150	50	Y	N	120/80	N	yes	87	117	3.1	3.3	88	4.5	135	4	350	1.2	16	+	235	187	135	35	5.1	14	LVH	8.4	7.9
50	marimuthu	50	M	37284	160	55	Y	Y	140/100	Y	N	146	265	6.2	3.4	123	7.4	118	5	400	1.5	6	+	229	200	147	42	7	8	tall T waves	11.4	11.3