CORRELATION OF CAROTID INTIMAL MEDIAL THICKNESS WITH eGFR AND CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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DECLARATION

I solemnly declare that this dissertation entitled " ***CORRELATION OF CAROTID INTIMAL MEDIAL THICKNESS WITH eGFR AND CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH CHRONIC KIDNEY DISEASE*** " was done by me at Madras Medical College and Government General Hospital, during 2007-2010 under the guidance and supervision of **Prof. P.CHITRAMBALAM, M.D.** This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree in General Medicine (Branch-I).

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CERTIFICATE

This is to certify that the dissertation entitled " ***CORRELATION OF CAROTID INTIMAL MEDIAL THICKNESS WITH eGFR AND CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH CHRONIC KIDNEY DISEASE***" is a bonafide work done by **Dr. J.DHANAPRIYA**, at Madras Medical College, Chennai in partial fulfillment of the university rules and regulations for award of M.D., Degree in General Medicine (Branch-I) under my guidance and supervision during the academic year 2007 -2010.

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CONTENTS

INTRODUCTION

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Chronic kidney disease is characterized by a decrease in glomerular filtration rate and histological evidence of reduction in nephron population[1]. The clinical course is typically one of a progressive and unrelenting loss of nephron function ultimately leading to end stage renal disease. Kidney failure is the most visible aspect of the spectrum, but it represents only a minority of the total population affected by kidney disease.

The time between initial onset of disease and development of terminal renal failure may vary considerably not only between different diseases but also in different patients with similar disease processes. The progressive nature of CKD and the ensuing ESRD is putting a substantial burden on global health resources since all modalities of treatment are expensive.

There are multiple causes of kidney injury that lead to the final common pathway of ESRD, and this syndrome is characterized by hypertension, anemia, renal bone disease, nutritional impairment, neuropathy, impaired quality of life, and reduced life expectancy. Increasing evidence acquired in the past decades indicates that the adverse outcomes of CKD such as renal failure, cardiovascular disease, and premature death can be prevented or delayed by early detection of CKD[3]. Earlier stages of CKD can be detected through laboratory testing only. Treatment of earlier stages of chronic kidney disease, as well as initiation of treatment of cardiovascular risk factors at early stages of CKD should be effective in reducing the rate of progression of CKD to ESRD.

In patients with CKD, the atherosclerotic cardiovascular disease is leading cause for morbidity and mortality[2]. Carotid intima-media thickness (cIMT) has been used as a marker for early atherosclerosis .The increased

incidence of CVD is the consequence of a high prevalence of both traditional risk factors, uremia-related,and "new factors," such as hyperhomocysteinemia, infections (herpes virus and Chlamydia pneumoniae) and oxidative stress, which increases atherosclerotic risk among these patients.

According to the 1999-2004 National Health and Nutrition Examination Survey (NHANES), the prevalence of CKD among the USA population is 15.3%. It becomes apparent that the severity of CKD along with CVD severity in any population makes a 'devastated' combination for both patients and healthcare systems. Approximately 50% of patients with ESRD die from a cardiovascular event , which indicates a cardiovascular mortality that is 30 times higher in dialysis patients and 500 times higher in 25- to 34-year-old ESRD patients than in individuals from the general population of the same age and race.

Previous studies have suggested that carotid intimal medical thickness can be used as a marker for atherosclerosis cardio vascular disease .Non invasive assessment of intima medial thickness of carotid arteries by high resolution B – mode ultrasonography is widely used in observational studies and trials as an intermediate or proxy measure of generalised atherosclerosis. Increased intima medial thickness of carotid arteries has been associated with unfavourable levels of established cardiovascular risk factors, prevalent cardiovascular disease and atherosclerosis elsewhere in the arterial system.

In this study we attempt to evaluate the association of increased intimal medial thickness with traditional and nontraditional cardiovascular risk factors in CKD patients.

AIMS AND OBJECTIVES

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To study

1. To study the prevalence of traditional and non traditional cardiovascular risk factors in patients with CKD.
2. Correlation of carotid intimal medial thickness to eGFR, traditional risk factors and non traditional risk factors for cardio vascular disease in patients with CKD.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

CHRONIC KIDNEY DISEASE

Chronic kidney disease represents the entire spectrum of disease that occurs following the initiation of kidney damage. The introduction of a formal definition for CKD has enabled standardize current medical communication, facilitate appropriate population based screening, and encourage timely prevention and treatment of kidney disease.

DEFINITION[4]

1. Kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased GFR, manifest by either
    - Pathological abnormalities; or
    - Markers of kidney damage, including abnormalities in the composition of the blood or urine, or abnormalities in imaging test.

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

The GFR is considered the best measure of overall kidney function. A GFR level below 60 mL / minute / 1.73 m^2 represents loss of one half or more of the adult level of normal kidney function. Normal GFR varies according to patient age, sex, and body size. The MDRD formula is a better estimate of GFR than those derived from 24-h urinary creatinine clearance or the Cockcroft-Gault formula. The abbreviated MDRD formula requires age, gender, race, and serum creatinine.

The Abbreviated MDRD Formula[5]

$eGFR = 186 \times ([SCR/88.4]^{-1.154)} \times (age)^{-0.203} \times (0.742$ if female) $\times (1.210$ if African-American)

where

eGFR = estimated glomerular filtration rate (ml/min/1.73m^2),

SCR = serum creatinine concentration (μmol/L), and age is expressed in years

AGE

In young adults, the normal GFR is approximately 120 to 130 ml /minute / 1.73 m^2 and declines with age.[6] A decreased GFR in an elderly patient appears to be an independent predictor of adverse outcomes such as mortality and cardiovascular disease[7,8]. Because of the age-related decline in GFR, the prevalence of chronic kidney disease increases with age; approximately 17 percent of persons older than 60 years have an estimated GFR of less than 60 mL / minute / 1.73 m^2.

GENDER

Male gender has been recognized as an important factor in the development of CKD[9]. Gender-based genetic variability has been linked to differences in BP in both black[10] and white

individuals[11]. Males may be more susceptible to CKD, which would explain the higher proportion in renal replacement therapy programmes. In contrast to testosterone, [12,13] estrogens may attenuate CKD progression by lowering the cardiovascular stress response to adrenergic stimuli[14].

Chronic kidney disease is a national public health problem beset by inequities in incidence, prevalence, and complications across race/ethnicity, and socioeconomic status.

SOCIOECONOMIC STATUS

In U.S, geographic analyses have revealed community-level poverty was strongly associated with higher ESRD incidence but was a more powerful predictor for black than for white individuals.[15] Racially divided communities may share low-income status but often differ in wealth, community assets, exposure to heavy metals or excess ambient air particulate matter, and other variables that may influence CKD-related outcomes.[16]

RACE

Racial factors also have a role in the susceptibility to CKD as shown by high prevalence of CKD related to hypertension, diabetes, or both, among Africans and native Americans in USA as well as Afro-Caribbean and Asian individuals in UK.[17] In U.S, ESRD rates in minorities ranged from 1.5 to 4 times those of age-adjusted counterparts, despite similar rates for the early stages of CKD.[1]

STAGING OF CHRONIC KIDNEY DISEASE

As patients pass through the continuum of progressive kidney damage, there are predictable complications, such as the development of anemia, and an elevated parathormone

levels and predictable management issues such as dialysis access preparation. The NKF/ KDOQI staging system[4] for CKD was developed to address this need.

Stage 1: Kidney damage (pathological abnormalities or markers of damage including abnormalities in blood or urine tests or in imaging studies) with normal or raised glomerular filtration rate (≥ 90 ml/min/1.73 m²)

Stage 2: Glomerular filtration rate 60 – 89 ml/min/1.73 m² with evidence of kidney damage

Stage 3: Glomerular filtration rate 30 – 59 ml/min/1.73 m²

Stage 4: Glomerular filtration rate 15 – 29 ml/min/1.73 m²

Stage 5: End-stage renal failure, glomerular filtration rate

< 15 ml/min/1.73m²

EARLY KIDNEY DISEASE – STAGES 1 AND 2

For stages 1 and 2, kidney damage is detected by a ratio of greater than 17 mg of albumin to 1 g of creatinine in men or greater than 25 mg of albumin to 1 g of creatinine in women on two untimed (spot) urine tests. The key issue in this group of patients becomes identification of whether renal function is likely to decline. The patients who at significant risk of progressing[19] include proteinuria >1 g/day[20], poorly controlled blood pressure, certain underlying diagnoses like diabetic nephropathy, should be promptly evaluated and managed to decrease the risk of progression to End Stage Renal Disease (ESRD).

STAGE 3 CKD

Patients with stage 3 CKD have significant renal impairment and are probably the very group in whom renal failure is poorly recognised.[21] In patients with progressive renal failure, it is desirable to institute treatment to delay the need for dialysis. There is good evidence to

support the efficacy of such measures in proteinuric patients.[22,23] The natural history of renal impairment in non-proteinuric patients, however, is not well-defined, and will depend at least in part on the underlying cause of renal damage. The large majority of these patients will not progress sufficiently to require dialysis.[24] However, patients with stage 3 CKD have substantially increased cardiovascular risk compared to patients with better renal function, with 43–100% increased risk of cardiovascular events[25] and most of them will die as a result of cardiovascular disease before ever needing dialysis.[26] Increased cardiovascular risk appears to start increasing as GFR declines below 75 l/min/1.73 m^2. [27] Management revolves around vigorous treatment of hypertension, particularly with blockade of the renin-angiotensin system, to a blood pressure <130/80 mmHg (<125/75 mmHg if proteinuria >1 g/day is present), and treatment of other cardiovascular risk factors.

STAGE 4 AND 5

These patients have marked disruption to normal physiology, causing complications such as renal anemia and renal osteodystrophy that require specialist management. These are also the stages at which preparations for dialysis and transplantation are required. Late referral of patients with advanced renal failure to nephrologists compromises the preparations for dialysis and subsequent survival of those patients[28] and is more costly than timely referral.[29] Even patients who are unsuitable for dialysis (or are unwilling to undergo it) will benefit from management of their anemia and bone disease, and potentially from palliative care.[30]

Kidney failure is defined as a GFR below 15 ml / minute / 1.73 m^2, usually accompanied by signs and symptoms of uremia, or as the need for initiation of kidney replacement therapy for management of the complications of a decreased GFR. In the United States, approximately 98 percent of patients begin dialysis when their GFR falls below 15 ml /minute / 1.73 m^2.[31]

The number of patients with end stage renal disease is growing worldwide. About 20-30 patients have some degree of renal dysfunction for each patient who needs renal replacement treatment.[32] Diabetes and hypertension are the two most common causes of end stage renal disease and are associated with a high risk of death from cardiovascular disease.[33] Early detection and treatment often can prevent or delay some of these adverse outcomes.[34] However, opportunities for prevention may be lost because chronic kidney disease is not diagnosed or is treated insufficiently[35,36] due to lack of uniform application of simple tests for the detection and evaluation of the disease.[37]

RISK FACTORS FOR CHRONIC KIDNEY DISEASE AND ITS OUTCOMES[4]

Type	Definition	Examples
Susceptibility factors	Factors that increase susceptibility to kidney damage	Older age, family history of chronic kidney disease, reduction in kidney mass, low birth weight, racial or ethnic minority status, low income or educational level
Initiation factors	Factors that directly initiate kidney damage	Diabetes mellitus, high blood pressure, autoimmune diseases, systemic infections, urinary tract infections, urinary stones, obstruction of lower urinary tract, drug toxicity

Progression factors	Factors that cause worsening kidney damage and faster decline in kidney function after kidney damage has started	Higher level of proteinuria, higher blood pressure level, poor glycemic control in diabetes, smoking
End-stage factors	Factors that increase morbidity and mortality in kidney failure	Infection, cardiovascular factors, anemia, low serum albumin level, late referral for dialysis

RISK FACTORS FOR CKD

DIABETES

In the United States, diabetic kidney disease is the most common cause of kidney failure. It accounts for nearly 45% of all new cases of ESRD starting renal replacement therapy between 1996 and 2006. Its earliest manifestation is microalbuminuria with a normal or elevated GFR. Effective control of blood glucose and blood pressure reduces the renal complications of diabetes. Meticulous control of blood glucose has been conclusively shown to reduce the development of microalbuminuria by 35% in type 1 diabetes (Diabetes Control and Complications Trial)[39] and in type 2 diabetes (United Kingdom Prospective Diabetes Study).[40] Other studies have indicated that glycemic control can reduce the progression of diabetic renal disease.[41]

Adequate control of blood pressure with a variety of antihypertensive agents, including angiotensin converting enzyme inhibitors, has been shown to delay the progression of albuminuria in both type 1 and type 2 diabetes[42,43] Recently, angiotensin receptor blockers have

been shown to have renoprotective effects in both early and late nephropathy due to type 2 diabetes.[44]

HYPERTENSION

Hypertension is the second most common cause of ESRD in the United States, accounting for 23% of incident ESRD patients between 1996 and 2000.[45] Hypertension is a well established cause, a common complication, and an important risk factor for progression of renal disease. Controlling hypertension is the most important intervention to slow the progression of renal disease. Angiotensin converting enzyme inhibitors are particularly effective in slowing progression of renal insufficiency in patients with and without diabetes.[46] Angiotensin receptor blockers have a renoprotective effect in diabetic nephropathy, independent of reduction in blood pressure.[50]

Non-dihydropyridine calcium channel blockers also have a role in retarding progression of renal insufficiency in patients with type 2 diabetes. Early detection and effective treatment of hypertension to target levels is essential. Hypertension is the most common complication of CKD. Hypertension is more difficult to control in patients with CKD. In one study, only 11% of CKD patients had BP levels lower than 130/85 mm Hg; 27% of these patients had a BP that was lower than 140/90 mm Hg; and 62% of them had a BP that was higher than 140/90 mm Hg.[48]

PROTEINURIA

Proteinuria, previously considered a marker of renal disease, is itself pathogenic and is

the single best predictor of disease progression. Reducing urinary protein excretion slows the progressive decline in renal function in both diabetic and non-diabetic kidney disease. Angiotensin blockade with angiotensin converting enzyme inhibitors or angiotensin receptor blockers is more effective at comparable levels of blood pressure control than conventional antihypertensive agents in reducing proteinuria, decline in glomerular filtration rate, and progression to end stage renal disease.[49]

DYSLIPIDEMIA

Lipid abnormalities may be evident with only mild renal impairment and contribute to progression of chronic renal disease and increased cardiovascular morbidity and mortality. Hydroxymethyl glutaryl coenzyme A reductase inhibitors (statins) decreased proteinuria and preserved glomerular filtration rate in patients with renal disease, an effect not entirely explained by reduction in blood cholesterol.[50]

HYPERURICEMIA

A link between hyperuricemia and the development of systemic hypertension, cardiovascular disease, and renal disease has also been postulated.[51]

OBESITY

Obesity has been associated with initiation and progression of glomerulonephritis.[52,53] Among NHANES III participants, the risk of either incident ESRD or kidney disease related death was independently a body mass index greater than or equal to 35 kg/m^2.[54] Obese people were more likely to have a decrease in estimated GFR.[55]

CIGARETTE SMOKING

Cigarette smoking has been implicated in initiation as well as progression of CKD.

The incidence of ESRD was increased by 5.9 times among heavy smokers (>15 pack years).[56] In another study, heavy smokers (> 20 pack years) had a risk of developing albuminuria three times that of non-smokers.[57] Smoking cessation alone may reduce the risk of disease progression by 30% in patients with type 2 diabetes.[58] Smoking increases the risk of cardiovascular events in men with kidney disease.[59]

ALCOHOL

Regular and heavy (> two drinks daily) consumption of alcohol might also increase the risk of ESRD.[60]

COMPLICATIONS OF CHRONIC KIDNEY DISEASE

ANEMIA

Anemia of chronic renal disease begins when the glomerular filtration rate falls below 30-35% of normal and is normochromic and normocytic. This is primarily caused by decreased production of erythropoietin by the failing kidney,[62] other factors contributing to anemia include inhibitors of erythropoiesis, shortened RBC life span, platelet dysfunction, decreased iron intake, and secondary hyperparathyroidism. Anemia is an independent predictor of mortality and has also been associated with increased morbidity in CKD. Correction of anemia improves the quality of life, cognitive and sexual function, reversal of ST-T changes on ECG, and reversal as well as prevention of left ventricular hypertrophy, reduces the frequency of heart failure and hospitalization among patients receiving dialysis.[63,].

The risk of coronary heart disease (CHD) increases when the anemia is not treated,

and recent studies have indicated that anemia in patients with chronic renal failure may predispose to ischemic heart disease, heart failure, and premature death Therefore, the risk of CHD may be distinctly higher in people with renal insufficiency and concomitant anemia, when compared with people with renal insufficiency but without anemia and with people with normal renal function[64]. A significant proportion of patients have established cardiovascular complications on initiation of dialysis, raising the possibility of early correction of anemia as a strategy for preventing cardiovascular co-morbidities among renal patients . It is thought that anaemia can increase the severity of heart failure and is associated with a rise in mortality, hospitalization and malnutrition. Anaemia can also further worsen renal function and cause a more rapid progression to dialysis than is found in patients without anaemia [65]. Partial correction of anemia with recombinant human erythropoietin likely reduces left ventricular mass and volume. Complete correction of anemia may prevent progressive left ventricular dilatation in patients with normal left ventricular volumes. In the present work we aimed to consider the adverse effects.Whether anemia accelerates the progression of renal disease is controversial. Treatment of anemia with recombinant human erythropoietin may slow progression of chronic renal disease.

Both National Kidney Foundation and European best practice guidelines recommend evaluation of anemia when hemoglobin is <11 g/dl and consideration of recombinant human erythropoietin to maintain a target hemoglobin of >11 g/dl.[66] But when The United States Normal Hematocrit study evaluated 1,233 hemodialysis patients with clinical evidence of congestive heart failure or ischemic heart disease, the risk ratio (for death and non-fatal myocardial infarction) was 1.3 for the normal hematocrit group as compared to the low hematocrit .

LIPOPROTEIN (a)

Elevated plasma Lpa level in chronic renal failure patients has been associated with a frequency distribution of apolipoprotein (a) (APOa) isoforms; similar to those found in the general population. This indicates that elevated LPa level in these patients is not due to genetic variation. Therefore, it has been suggested that kidneys have an important role in LPa metabolism, decrease LPa catabolism or increase liver production. Increased LPa levels could be a contributing factor in the increased incidence of atherosclerotic disease observed in CKD and hemodialysis patients. Subtle structural changes such as thickening of arterial intima-media complex thickness (IMT) occur early in the atherosclerotic disease process. B-mode ultrasonography is a safe and noninvasive tool for assessing early atherosclerosis and to study superficial vascular districts, such as the carotid or femoral artery. Indeed carotid arteries are an accessible area for studying the progression of atherosclerotic lesions from onset to fully developed plaque. Carotid IMT measurements are strongly related to the extent of athero-sclerosis in other vascular districts too. Consistent with their accepted role in atherogenesis, many known and conventional risk factors have been shown to be significantly associated with increased arterial wall thickness. However, much less is known about the effects of LPa on IMT of CKD and hemodialysis group[67]

HYPERPHOSPHATEMIA AND HYPERPARATHYROIDISM

Hyperparathyroidism is one of the earliest manifestations of impaired renal function,[68] found in patients with a glomerular filtration rate of 60 ml/min.[69] Parathormone is a major uremic toxin that causes bone disease, metastatic calcification, pruritus, encephalopathy, peripheral neuropathy, anemia, sexual dysfunction, and hyperlipidemia. Control of serum phosphate levels is a central goal in the management of chronic renal failure. Precipitation of calcium phosphate in renal tissue begins early, may influence the rate of progression of renal disease, and is closely related to hyperphosphatemia and calcium phosphate product. This plays a pivotal role in vascular calcification, CVD, calciphylaxis, and death. A calcium-phosphorus product greater than 72 mg^2/dL[70] is associated with a 34 percent increase in mortality as compared to a product of 45 to 52 mg^2/dL.[71]

Elevated serum phosphate is an independent risk factor for death due to cardiovascular events by enhancing vascular calcification of atherosclerotic plaques and increased myocardial calcification. Patients with serum phosphate levels greater than 6.5 mg/dl have a 41% greater risk of death resulting from coronary artery disease and a 20% greater risk of sudden death as compared with patients with serum phosphate levels between 2.4 and 6.5 mg/dl after adjusting for several known mortality risk factors.[68]

MALNUTRITION

The prevalence of hypoalbuminemia is high among patients beginning dialysis, is of multifactorial origin, and is associated with poor outcome. Hypoalbuminemia may be a reflection of chronic inflammation rather than of nutrition in itself. Spontaneous intake of protein begins to decrease when the glomerular filtration rate falls below 50 ml/min.

Progressive decline in renal function causes decreased appetite, thereby increasing the risk of malnutrition.

CARDIOVASCULAR DISEASE

The prevalence, incidence, and prognosis of clinical cardiovascular disease in renal failure is not known with precision, but it begins early and is independently associated with increased cardiovascular and all cause mortality.

RISK FACTORS ASSOCIATED WITH CARDIAC DISEASE[73]

Traditional

Age	Gender	Race
Smoking	Diabetes	Body mass index
Hypertension	Dyslipidemia	Left ventricular hypertrophy

CKD-related risk factors

Anemia	Calcium phosphate	Cytokines
Electrolyte imbalance	Malnutrition	Hypoalbuminemia
Inflammation	C-reactive protein	Endothelial activation
Prothrombotic factors	Increased oxidative stress	
Hyperhomocysteinemia	Advanced glycation end-products	

Therapy-related

Dialysis	Transplant– Acute rejection
	– Immunosuppressives

Cardiac disease, including left ventricular structural and functional disorders,atherosclerosis ,arteriosclerosis is an important preventable and potentially treatable comorbidity of early kidney disease.[74] Patients with chronic kidney disease should be considered in the "highest risk" group for cardiovascular events[75] and appropriately managed.

Atherosclerosis of coronary arteries is the primary cause of ischaemic heart disease in patients with CKD, with acute myocardial infarction accounting for 20% of all cardiac deaths. The coronary plaque in dialysis patients is a more advanced and complex lesion, characterised by greater degrees of medial thickening and calcification.However, a significant number (27 - 50%) of patients with ESRD who experience angina do not have large-vessel disease. Here, microvascular atherosclerosis, severe LVH and anaemia are thought to be the causative factors. Vascular remodelling is a pathological hallmark of CKD, affecting the large arteries as well as the coronary vessels. In part, this is due to medial calcification, which reduces compliance and manifests as an increase in pulse pressure with systolic hypertension.This process contributes to aortic stiffness, LVH and myocardial infarction, and parallels the increase in cardiovascular morbidity and mortality in the CKD patient.

In addition to the traditional risk factors, accelerated atherosclerosis peculiar to CKD involves the three related processes of vascular inflammation, oxidative stress and vascular calcification, all of which result in vascular remodelling. Oxidative stress has a central role in the pathogenesis of atherosclerosis and CKD is associated with an imbalance favouring pro-oxidant over antioxidant systems, contributing to the increased atherosclerotic burden. Serum C–reactive protein (CRP) is a reliable marker of atherosclerotic complications. Both CRP and

thrombogenic factors, such as fibrinogen, are also elevated in patients with ESRD, and are strong predictors of death and adverse cardiovasular events. Declining renal function itself is also associated with an inflammatory response, manifested by an increase in proinflammatory cytokines in both early and advanced CKD. Increased levels of the proatherogenic cytokine, IL-6, are independently associated with carotid atherosclerosis and predict mortality in dialysis patients.

Therefore, coronary angiography remains the gold standard for the detection of epicardial CAD, but complication rates tend to be higher among the CKD population. These include contrast nephropathy, atheroembolism,bleeding complications and contrast-induced pulmonary oedema. In the predialysis patient undergoing coronary angiography, the risk may be enough to precipitate ESRD as a result of the procedure.

TREATMENT PRINCIPLES

1. Hypertension is both a cause and a complication of chronic kidney disease and should be carefully controlled in all patients
2. Treatment of co morbid conditions, interventions to slow progression of kidney disease, and measures to reduce the risk for CVD should begin during stage 1 and stage 2.
3. Evaluation and treatment of other complications of decreased GFR, such as anemia, malnutrition, bone disease, neuropathy, and decreased quality of life, should be undertaken during stage 3, as prevalence of these complications begins to rise when GFR declines to less than 60 ml/min per 1.73 m^2.
4. Preparation for kidney replacement therapy should begin during stage 4, well before the

stage of kidney failure.

5. Initiation of dialysis and transplantation is triggered by the onset of uremic symptoms. Preparations for these treatments should begin when GFR declines to less than 15 ml/min per 1.73 m^2 (stage 5).

B MODE IMAGING

Ultrasound imaging is done "pulse echo techniques". An ultrasonic transducer is placed in contact with the skin. The transducer repeatedly emits brief pulses of sound at a fixed rate called the pulse repetition sequencing. After transmitting each pulse, the transducer waits for the echoes from the interfaces along the sound beam path. Echo signals picked up by the transducer are amplified and processed into a format suitable for display. The distance to a reflector is determined from the arrival time of its echo. Thus d=ct/2 where d is the depth of the interface. T is the echo arrival time and c is the speed of sound in tissue[76]. The factor 2 accounts for the round trip journey of the sound pulse and echo. The aforementioned equation is called the range equation in ultrasound imaging. The speed of sound 1540m/s is assumed in most scanners when calculating and displaying reflector depths from echo arrival times. The corresponding echo arrival time is 13mcs/cm of distance of the reflector to create images pulses of image are transmitted along various beam lines. Each followed by reception and processing of resultant echo signals.

Imaging is done with transduces arrays where echo signals are acquired by individual elements and are combined within a beam former into a single for each beam line. Following a beam former, echo signal processing for imaging consists of amplifying the signals; applying time gain compensation to offset the effects of beam attenuation; applying nonlinear

logarithmic amplification to compress the wide range of echo signal amplitudes into a range that can be displayed effectively into a monitor; demodulation which forms single spike like signal for each echo; and B mode processing. The B mode display is used in imaging[77].

Sclerotic and ageing changes in all cardiovascular stem of human is well reflected by the status and structure of *arteria carotis*[78]. This artery is well accessible by ultrasonic investigation is the main vessel supplying blood to the brain. Therefore, ultrasonic investigation of *arteria carotis* (AC) has been the target of numerous attempts. Findings in the structure of AC walls are very actual in anticipating of possible changes of coronary arteries, especially when there are no other symptoms of coronary ischemia[79]. AC wall structure and thickness are good indicators for estimation of risk for stroke and myocardial infarction. There are many additional relations established between AC state from one side and diabetes, high blood pressure, early sclerosis overweight and other pathologies from the other. The main changes in AC can be observed in the wall structure, which in its turn can be roughly divided into inner layer, contacting with blood (*intima*), middle layer of the wall (*media*) and outer layer (*adventitia*)[80].

Intima and media thickness (IMT) is recognized to be one of the most informative parameters for differential diagnosis. Changes in thickness are observed well in advance of sclerotic plaque appearance, thus enabling early diagnosis of sclerosis. Sclerotic damage of vascular system manifests itself by thickening of *intima* layer which is thin for young and healthy persons. *Media* of the AC wall consists mainly from spiral fibres of muscles and also is dependent on ability of arteries to support the blood flow and to react on stress factors. Ultrasonography of AC including measurement of *intima* and media thickness is a good mean for ischemic disease prediction, diagnosis and treatment control[81]. The main problem in

diagnostics of the state of AC is insufficient precision of *intima* and media thickness measurements, since this defines all diagnostic reliability. Two layers are to be clearly separated because high blood pressure causes thickening (hypertrophy) of *media,* while arteriosclerosis causes hypertrophy of *intima.* For differential diagnosis therefore is very important clear distinction of two layers as well as accurate measurement of absolute thickness.

Structure of carotid artery and acoustical model

Prior to ultrasonic investigation of structure of AC walls anatomical structure should be related to the acoustical model. Ultrasonic echoscopy is based on reflection and scattering of incident ultrasonic pulses by changes of acoustical impedance of the object under investigation. Relation between anatomic and acoustic layers (changes in acoustic impedance) was established and potential possibility to measure thickness was proven Since an ultrasonic transducer beam hits the artery from one side zones of *adventitia*, *media intima,* consequently causes reflections[82].

More convenient for thickness measurements are the AC wall on the far side from the transducer. Both walls can be measured simultaneously, or the high frequency transducer can be effectively used near wall of artery. The far wall has better reflections due to the interface blood-*intima-media-adventita* acoustics impedance sequence. Since an ultrasonic transducer beam hits the artery from one side zones of *adventitia*, *media,* consequently causes reflections. More convenient for thickness measurements are the AC wall on the far side from the transducer. Both walls can be measured simultaneously, or the high frequency transducer can be effectively used near wall of artery. Common Carotid artery (before it's bifurcation on its are usually used for carotid artery examinations. upper end) is accessible within about 10 cm along the artery.

Therefore, longitudinal variances of *intima-media* thickness can be measured or (with some assumptions) longitudinal information can be used for averaging of measurement results. Anyway, repeatable measurements raise the accuracy[83]. The general purpose echoscopy systems are usually used for the arteria carotis examinations. It is because the 7 – 8 MHz linear scanning transducers are suitable for such investigations.

Both A and B scanning methods can be used for ultrasonic investigations. B scan is used more frequently, since it gives overall view of the artery and general picture can be obtained for a quite long segment of the vessel.

Median population values of *intima-media* thickness range between 0.5 – 0.9 mm. IMT is thickening with age with 0.01 to 0.3 mm per year. The theoretical axial resolution of a 7 MHz transducer is about 0.3 mm. If IMT is thinner than 0.3 mm, the two echo interfaces cannot be clearly separated. If IMT is thicker than 0.3 mm, thickness can be measured directly.

Overall thickness of *intima* and *media* layers is the most important diagnostic parameter. However, thickness of separate layers would be useful for some kinds of pathological differentiation. Since boundary between *media* and *intima* isn't well demarcated in terms of acoustic parameters, in most cases *intima-media* layer thickness is taken into consideration.

B-mode ultrasound is a noninvasive method of examining the walls of peripheral arteries and provides measures of intima-media thickness (IMT presence of stenosis and presence of plaques. The IMT corresponds to the intima media complex, which comprises endothelial cells, connective tissue and smooth muscle and is the site of lipid deposition in plaque formation.

In healthy adults, IMT ranges from 0.25 to 1.5 mm and values above 1.0 mm are often regarded as abnormal. IMT has been proposed as a quantitative index of atherosclerosis of

value in monitoring disease progression and the effects of treatment and as a surrogate end point in clinical trials. The validity of IMT for these purposes has been assessed by making comparisons of mean IMT in people with and without clinical evidence of CVD and discriminatory ability has been demonstrated. Epidemiological studies, which are less prone to bias inherent in clinical case series, have reported associations between a range of cardiovascular risk factors (smoking, blood pressure, elevated blood cholesterol) and IMT. Age is one of the most powerful determinants of IMT, with increases of from 0.01 to 0.02 mm per year and consequently may confound comparisons of IMT made between groups if appropriate age adjustment is not made[84].

Reported findings have demonstrated inconsistent associations between IMT, risk factors and clinical disease and have also highlighted the importance of the presence and severity of arterial wall plaque as determinants of clinical events. Some of this variation in findings is likely to be due to the method of measuring IMT: mean bifurcation, mean bulb origin, mean common carotid, mean internal carotid, and combinations of these. Correlations between these different approaches are reported to be high. It has been suggested that measurement of IMT at the "common carotid artery alone, particularly for studies of association of risk factors with carotid arterial disease, cohort studies or clinical trials, in that it, too, is associated with the status of coronary atherosclerosis" is a reasonable alternative to more detailed and technically difficulty measurement at other sites. However, plaque formation is not common in the common carotid artery. Since thicker IMT bifurcation and bulb origin values tend to occur in people who also have plaques, it is possible that presence or absence of plaque, and not IMT at either the common carotid or bifurcation sites, is the more relevant indictor of early atherosclerosis

MATERIALS AND METHODS

MATERIALS AND METHODS

SETTING

Patients attending the department of Internal medicine and department of Nephrology, Madras Medical College and Government General Hospital, Chennai

COLLABORATION DEPARTMENTS

Institute of Internal Medicine

Department of Nephrology

ETHICAL APPROVAL

Institute Ethical Committee approved the study

STUDY DESIGN

Single Center

Non randomized cross sectional study

DURATION OF STUDY

February 2009 to December 2009

SELECTION OF PATIENTS

Inclusion Criteria

CKD patients getting treated at Nephrology department and Department of Internal Medicine, Government General Hospital with stage 2, 3, and 4.

Exclusion Criteria

1. CKD stage 1 & 5
2. Patients with nephrotic syndrome
3. Patients on statins

SAMPLE SIZE

In the study period of 11 months among the patients seen under the Department of Internal medicine and nephrology, after applying inclusion criteria, 60 patients were included in this study.

SELECTION OF STUDY SUBJECTS

The patients who were diagnosed as chronic kidney disease based on the National Kidney Foundation definition.

CONSENT

All participates gave informed consent.

METHODOLOGY

Patients who were included in the study were asked for the history of diabetes mellitus, hypertension,smoking,intake of alcohol and hyperlipidemia. pulse rate and blood pressure were taken. Height and weight were measured for body mass index calculation. The information was entered based on the proforma prepared. Patients are subjected to carotid Doppler for measuring carotid intimal medial thickness. Urine sample for urine protein and blood samples for hemoglobin, hematocrit, urea, creatinine, fasting blood sugar, calcium, phosphorus, albumin, fibrinogen, lipid profile are collected and subjected to biochemical tests.

STATISTICAL ANALYSIS

Excel and SPSS 12 were used for data analysis

CONFLICT OF INTEREST

None

RESULTS

RESULTS AND OBSERVATIONS

POPULATION CHARACTERISTICS

Among the 60 patients included in the study, 45 (75%) were males and 15 (25%) were females.

Among 60 patients, 25(41.7%) were in 25 -45yrs, 30(50%) were in 45 -65 yrs, 5 (9.3 %) were in >65 yrs age groups.

TABLE1. AGE AND SEX DISTRIBUTION OF THE STUDY POPULATION

AGE GROUP in Years	TOTAL	PERCENTAGE	MALE	FEMALE
25-45	25	41.7	20	5
45-65	30	50	22	8
>65	5	9.3	3	2

TABLE 2
CORRELATION OF CIMT WITH AGE

AGE In years	C I M T		Total
	<=0.89 mm	>0.89 mm	
25 – 45	11	14	25
45 – 65	9	21	30
>65	2	3	5
Total	22	38	60

P=0.55.

Correlation of CIMT with age is not statistically significant

TABLE -3

CORRELATION OF CIMT WITH SEX

SEX	C I M T		Total
	<=0.89 mm	>0.89 mm	
MALE	17	28	45
FEMALE	5	10	14
Total	22	38	60

P=0.75

Correlation of CIMT with sex is not statistically significant**.**

TABLE 4
CORRELATION OF CIMT WITH SEX WITH eGFR

eGFR	C I M T		Total
	<=0.89 mm	>0.89 mm	
60-90	6	18	24
30 – 60	6	18	24
15 – 30	10	2	12
Total	22	38	60

P=<.001

Correlation of CIMT with eGFR is statistically significant.

EDUCATIONAL STATUS

In our study, 38 (63.33%) patients were illiterates, 4(6.66%) had primary education, 16 (26.66%) had secondary education, while the rest, 2 (3.3%) were graduate.

DIABETES MELLITUS IN THE STUDY POPULATION

Out of 60 patients in our study, 30 (50%) had diabetes mellitus, of which were 22 (73%)were males and 8(26.6 %) were females.

TABLE 5
COMPARISON OF CAROTID INTIMAL MEDIAL THICKNESS IN DIABETIC AND NON DIABETIC

P=.59

	C I M T		Total
	<=0.89 mm	>0.89 mm	
DIABETIC	12	18	30
NON-DIABETIC	10	20	30
Total	22	38	60

Correlation of CIMT with diabetes is not statistically significant.

HYPERTENSION IN THE STUDY POPULATION

In our study 32 (53.33%) patients had hypertension, of which, 26(86.66%) were males and 6(13.33%) were females.

TABLE 6
COMPARISON OF CAROTID INTIMAL MEDIAL THICKNESS IN HYPERTENSIVE AND NON HYPERTENSIVE

	C I M T		Total
	<=0.89 mm	>0.89 mm	
HYPERTENSIVE	13	18	31
NON-HYPERTENSIVE	9	20	29
Total	22	38	60

P=.38

Correlation of c IMT with hypertension is not statistically significant.

FAMILY HISTORY OF CVD:

Of the 60, 16 (26.66%) patients were with family history of CVD, Of which 14 (87.5%) were males and 2(12.5%) were females .

ALCOHOLISM IN THE STUDY POPULATION

Among 60 patients,19(31.67%) were alcoholics.All were males.

TABLE 7

COMPARISON OF CAROTID INTIMAL MEDIAL THICKNESS AMONG ALCOHOLIC AND NON-ALCOHOLIC

-
-

P=.55

Correlation of CIMT with Alcoholism is not statistically significant.

	C I M T		Total
	<=0.89	>0.89	
	C I M T mm	mm	Total
ALCOHOLIC	<0.89 8	>0.89 11	19
	mm	mm	
NON-ALCOHOLIC	14	27	41
SMOKERS	10	12	22
Total	22	38	60
NON-SMOKERS	12	26	3
Total	22	38	60

SMOKING IN THE STUDY POPULATION:

Among 60 patients 26(43.33%) were smokers All were males.

TABLE- 8
COMPARISON OF CAROTID INTIMAL MEDIAL THICKNESS AMONG SMOKERS AND NON-SMOKERS

P=.55

Correlation of CIMT with Smoking is not statistically significant.

LDL mg/dl	eGFR			Total
	60 – 90	30 – 60	15 – 30	
<130	7	10	12	29
>=130	5	14	12	31
Total	12	24	24	60

DYSLIPIDEMIA AMONG STUDY POPULATION:

PREVALENCE OF HYPERLIPIDEMIA IN CHRONIC KIDNEY DISEASE

TABLE 9

HDL mg/dl	eGFR			Total
	60 – 90	30 – 60	15 – 30	
<=40	7	11	13	33
>40	5	13	11	27
Total	12	24	22	60

P=.60

Correlation of eGFR with serum LDL is not statistically significant.

TABLE 10

P=.74

TOTAL CHOLESTEROL TGL LEVEL mg/dl	CIMT <=0.89 mm	CIMT >0.89 mm	Total
mg/dl			
<=150	5	8	13
<=240	15	23	38
>150	17	30	47
>240	7	15	22
Total	22	38	60
Total	22	38	60

Correlation of eGFR with serum HDL is not statistically significant.

TABLE 11
COMPARISON OF CIMT WITH CHOLESTEROL LEVEL

P=.55

Correlation of CIMT with serum cholesterol is not statistically significant.

LDL mg/dl	CIMT <=0.89 mm	CIMT >0.89 mm	Total
<130	12	17	29
>=130	10	21	31
Total	22	38	60

TABLE 12
COMPARISON OF CIMT WITH LDL LEVEL

P=.46

Correlation of CIMT with serum LDL is not statistically significant.

TABLE 13
COMPARISON OF CIMT WITH TRIGLYCERIDES

P=.87

Correlation of CIMT with serum TGL is not statistically significant

TABLE 14
COMPARISON OF CIMTWITH HDL

P=.204

Correlation of CIMT with serum HDL is not statistically significant.

HEMOGLOBIN IN THE STUDY POPULATION

The mean hemoglobin in the study population was 8.97±1.44 g/dl. Anemia (hemoglobin less than 10g/dl) was present in 47 (78%) while 13 (21.67%) had hemoglobin more than 10g/dl.

Hb Mg/dl	eGFR			Total
	60 – 90	30 – 60	15 – 30	
<=10	4	21	22	47
>10	8	3	2	13
Total	12	24	24	60

HDL mg/dl	CIMT <=0.89 mm	CIMT >0.89 mm	Total
<=40	9	22	31
>40	13	16	29
Total	22	38	60

TABLE 15
PREVALENCE OF ANEMIA

Hb mg/dl	CI M T		Total
	<=0.89 mm	>0.89 mm	
<=10	12	35	47
>10	10	3	13
Total	22	38	60

P<.001

Correlation of Hemoglobin with eGFR is statistically significant.

TABLE 16
CORRELATION OF CAROTID INTIMAL MEDIAL THICKNESS WITH ANEMIA

P<.001

Correlation of CIMT with Hemoglobin is statistically significant.

S. PHOSPHATE IN THE STUDY POPULATION

Mean S.Phosphate of the study population is 4.33±.78, varying within a range of 3.1 -6.9. S.Phosphate was less than 4.3mg/dl in 37(61.67 %.) and more than 4.3mg/dl in 23 (38.33%) patients

Phosphate mg/dl	eGFR			Total
	60 – 90	30 – 60	15 – 30	
<4.3	11	16	10	37
>=4.3	1	8	14	23
Total	12	24	24	60

TABLE 17
PREVALENCE OF HYPERPHOSPHATEMIA

P=.01

Correlation of serum Phosphate with eGFR is statistically significant.

TABLE 18
COMPARISON OF CIMT WITH SERUM PHOSPHATE

BMI	CI M T		Total
	<=0.89 mm	>0.89 mm	
<25	8	16	24
25 – 30	12	16	28
>30	2	6	8
Total	22	38	60

P=.014

Correlation of CIMT With serum phosphate levels is statistically significant.

TABLE 19

COMPARISON OF CIMT WITH B.M.I.

Phosphate mg/dl	CI M T		Total
	<=0.89 mm	>0.89 mm	
<4.3	18	19	37
>=4.3	4	19	23
Total	22	38	60

P=.59

Correlation of CIMT With BMI Levels is not statistically significant.

TABLE 20

CORRELATION OF CIMT WITH SERUM ALBUMIN

P=.01

Correlation ofC IMT With Albumin Levels is statistically significant.

TABLE 21
CORRELATION OF CAROTID INTIMAL MEDIAL THICKNESS WITH SERUM LIPOPROTEIN (a) LEVELS

Sr.ALBUMIN	C I M T		Total
	<=0.89	>0.89	
<3	1	1	2
3 – 4	19	35	54
>4	2	2	4
Total	22	38	60

Sr.LIPOPROTEIN (a) mg/dl	C I M T		Total
	<=0.89 mm	>0.89 mm	
<30	13	2	15
30 – 60	8	31	39
>60	1	5	6
Total	22	38	60

P<.001

Correlation of CIMT With serum lipoprotein levels is statistically significant.

DISCUSSION

AGE AND GENDER

In our study of 60 patients with CKD, 75% were males, which are consistent with the CKD Registry of India Report where males constituted 68% of the total CKD patients and CMC Vellore Study where 62% were males, probably reflect the faster decline in GFR in males as compared to females due to hormonal influence. Majority of the patients were in the group 45-65years, with a mean age of 50±12.06 years. The mean age in CKD Registry of India Report is 48.3±16.6 years and CMC, Vellore study [38.2]±14.5 years.

EDUCATIONAL STATUS

In our study, out of the 60 patients, 71% of the patients were illiterate or just had primary education. Though relation of low socioeconomic and educational status with CKD has already been found in previous related studies, it cannot be inferred from our study because we cater to patients with low socioeconomic status.

FAMILY HISTORY OF CVD

Family history of CVD was present 26.6% patients.

HABITS AND CKD

Cigarette smoking was prevalent in 43.33%, alcohol consumption in 31.67%, which might have contributed to the faster progression of the disease in these patients whereas the CKD Registry of India Report, shows cigarette smoking was prevalent in 32%, alcohol

consumption in 6.4%

DYSLIPEMIA:

Mean total cholesterol is 223.09 ± 51.14 mg/dl. Mean LDL is 141±44mg/dl. Mean TGL is 190±45 mg/dl. Mean HDL is 40±5 mg/dl 38 (63.33%) patients have total cholesterol levels <240 mg/dl and 22(36.6%)have >240mg/dl

29(48.33%) patients have LDL levels < 130 mg/dl and 31(51.67%) have >130 mg/dl. 13(21%) patients have TGL levels <150 mg/dl and 47 (79.33%) have >150mg/dl. 31 (51.67%) patients have HDL levels <40 mg/dl and 29(49.33%) have >40 levels

There is no significant correlation observed between altered lipid levels and e GFR

BODY MASS INDEX:

Mean BMI is 25.9 ±3.6.

24 (40%) patients have BMI < 25, 28 (46.67%) have between 25 and 30, 8 (13.33%) have > 30.I n our study there is no significant correlation between BMI and IMT.

SERUM LIPOPROTEIN a :

Mean serum lipoprotein a level is 39.6±13. mg/dl. Normal is < 30 mg/dl

15 (25 %) have levels < 30 mg /dl, 39 (65 %) have levels 30 – 60 mg/ dl and 6 (10 %) have > 60 mg /dl.

There is highly significant correlation between lipoprotein a levels with IMT and e GFR. Studies concerning the effect of LPa on IMT of normal persons showed various results. Sramek et al found no increased IMT in the carotid or femoral artery at high levels of LPa in asymptomatic men and concluded that LPa level was not associated with early atherosclerotic

vessel wall changes in the carotid or femoral arteries. Dentil et al, in a study on elderly subjects (mean age 78 years), showed no association between carotid IMT and LPa and concluded that the LPa was unrelated to the severity of atherosclerosis in the extra cranial vessels, while Baldassarre et al found increased IMT of carotid in hypercholesterolemic patients with plasma LPa levels > 30 mg/dl than in those with moderate hypercholesterolemia or normocholesterolemic subjects. Finally, Raitakari suggested no association between IMT and LPa in healthy subjects but found significant positive correlation with total cholesterol, LDL-C, LDL/HDL ratio, age, and triglycerides

SERUM ALBUMIN LEVELS:

4 (6.67%) have albumin levels > 4gm/dl, 54 (90%) have levels between 3-4 gm/dl and 2 (3.33%) have < 3gm /dl.

In our study there significant correlation between serum albumin levels and **IMT.**

Beddu et al showed association between Sr. albumin levels and cardio vascular diseases. Owen et al showed hypoalbuminemia as a strong predictor of mortality in CKD patients.Stenvinkel et al showed increased IMT with hypoalbuminemia.

CAROTID INTIMAL MEDIAL THICKNESS;

Mean c IMT is 0.917±0.11mm.

22 (36.66%) patients have IMT <.89 mm and 38 (63.33%) have > .89 mm

There is significant correlation between IMT and e GFR.Zhang et al showed IMT .83±23 in stage 2 ,.94±.38 in stage 3 and .11±.21 in stage 4 CKD patients.

There is no significant correlation of IMT with age,sex of the patients.

Though we found diabetics, hypertensives,smokers and alcoholics have an increased IMT more frequently a significant correlation could not be found.Pascasio et al. observed a large number of vascular plaques in uremia patients and concluded that the process of advance atherosclerosis might be started with the commencement of renal failure; he suggested that there are other factors than HD treatment to accelerate arthrosclerosis. Damjanovic et al. evaluated IMT of 45 CKD patients found higher mean carotid IMT in HD than in control group; also showed positive correlation of IMT with certain risk factors for atherosclerosis (age, duration of dialysis and lipid parameters). Shoji and Hojs et al shows only significant determinant of number of plaques and concluded that CKD patients had advanced atherosclerosis in the carotid arteries compared with normal subjects.

Savage et al noted more prevalence of plaque in carotid and femoral artery in HD and correlation between femoral artery plaque score and age of the subjects as well as correlation of age with IMT of carotid artery. Recently, Kato et al showed a significant correlation of IMT with age in HD patients. Moreover, Papagianni et al showed a positive correlation of plaque score with age of the subjects.

Although there is altered lipid levels in CKD patients, no correlation were found with IMT in our study. Patricia et al shows significant increase in IMT with elevated levels. Maria et al showed increase in IMT with elevated total cholesterol levels.Zancetti et al found no correlation with any of the lipid parameter

HEMOGLOBIN

The mean hemoglobin level in the study population was 8.97±1.44g/dl. 47 (78.33%) had anemia (cutoff taken as 10g/dl) , while 21.67% had a value more than 10g/dl. Prevalence of anemia increased from Stage 2 to stage 4 and the correlation was statistically significant. This is consistent with the CKD Registry of India Report[77] where anemia was present in 32.6% of Stage 3, 57.5% of Stage 4 and 83.2% of Stage 5 patients.

There is positive correlation between hemoglobin levels and IMT.

SERUM.PHOSPHATE

The mean S.Phosphate level in the study was 4.33±0.78mg/dl. 37 (61.67%) had S.Phosphate below value of 4.3mg/dl. while 23 (38%) had a value more than 4.3mg/dl. Mean S.Phosphate level increases from stage 2 to stage 4 and there is statistically significant correlation between S.Phosphate levels and eGFR which is consistent with the observations in CKD Registry of India Report[77] where mean S.Phosphate levels were 4.54mg/dl in Stage 3, 4.93mg/dl in Stage 4 and 5.91mg/dl in Stage 5.The percentage of patients with S.Phosphate more than or equal to 4.3mg/dl increased from 55.5% in stage 3 to 66.67% in stage 4 to 93.55% in stage 5.

There is a significant correlation between serum phosphate levels and IMT. Ishimura et al show that in addition to advanced age, greater serum phosphate level is a significant and independent factor associated with advanced arteriosclerosis in CKD patients with and without diabetes, suggesting that phosphate levels should be controlled appropriately to prevent an increase in arterial wall thickness in such patients.

The key focus should be the early detection and prevention of progression of CKD at stages 1 and 2 using established and emerging therapies. Cardiovascular risk factor

identification and management may depend on CKD staging. Special focus on non-traditional risk factors in CKD stages 3-5 may be appropriate in addition to traditional risk factor modification initiated in CKD stages 1 and 2. Lastly, there is a need to disseminate information to primary care providers who may be key players in initiating and maintaining the most appropriate management strategies. For those with established CVD and CKD that require intervention, the increased risks must be considered and addressed

To execute a change in the management of patients with CKD, medical students, healthcare professionals, and established physicians, need to be educated about the prevalence and consequences of CKD. The concept that CKD is a risk factor for cardiovascular disease, and needs to be managed should be emphasized. Screening of the high risk individuals (those with hypertension, diabetes mellitus, cardiovascular disease and first degree relatives of patients with hypertension, diabetes mellitus or renal disease) will maximize the detection of CKD and benefit a large population of patients.

LIMITATIONS

1. Most of the patients attending the centre of the study belong to the low socioeconomic and educational status and hence are not an accurate representation of the general population.
2. Etiological diagnosis was not taken into account
3. B mode ultrasonography method liable to inter observer variation.
4. Presence of atherosclerosis was not confirmed by angiogram.
5. Hypoalbuminemia is a non specific marker of micro inflammation and is elevated in systemic lupus erythematosus, rheumatoid arthritis and liver diseases.
6. This is a cross sectional study where follow up of the patients is not possible.

CONCLUSION

CONCLUSION

High prevalence of traditional risk factors like diabetes,hypertension,smoking ,increased BMI ,dyslipidemia and non traditional risk factors like anemia, elevated phosphate levels,hypoalbuminemia and lipoprotein (a) in Chronic kidney disease patients in the study population.

1. More than half of the patients were illiterates and one fourth patients give family history of CVD.
2. Complications like anemia and hyperphosphatemia increased with progression of stage of chronic kidney disease.
3. Significant correlation between IMT with serum phosphate levels, anemia, hypoalbuminemia, e GFR, serum lipoprotein (a) levels were noted.
4. Lipoprotein (a) as a non traditional risk factor in progression of atherosclerosis could play an important role in accelerating progressive atherosclerosis observed in CKD patients which needs more attention.
5. Carotid IMT is a strong predictor of cardiovascular disease in CKD patients and may be usefully applied for risk stratification in this group of patients.

7. Correlation between IMT and dyslipidemia could not be established in the study.

8. Association of IMT with DM, HT, smoking, alcoholism and obesity could not be correlated significantly in this study.

9 Identifying modifiable risk factors for the progression of cardiovascular disease may lead to targeted medical interventions in high-risk groups.

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APPENDIX

- **ABBREVIATIONS**
- **PROFORMA**
- **MASTER CHART**
- **ETHICAL COMMITTEE APROVAL ORDER**

ABBREVIATIONS

CKD	-	Chronic Kidney Disease
ESRD	-	End Stage Renal Disease
eGFR	-	estimated Glomerular Filtration Rate
MDRD	-	Modified Diet in Renal Diseases
NKF/KDOQI	-	National Kidney Foundation/ Kidney Disease Outcome Quality Initiative
NHANES	-	National Health And Nutritional Examination Survey
C IMT	-	carotid intimal medial thickness
CVD	-	Cardiovascular Disease
LVH	-	Left Ventricular Hypertrophy
DM	-	Diabetes mellitus
AC	-	Arteria Carotis
LPa	-	Lipoprotein (a)

PROFORMA

Name : Age : Sex :

Occupation : Education:

Duration of Disease:

History of Angina / MI / Stroke / PVD :

Past H/O : DM / HT :

Smoking : Yes / No Pack years:

Alcohol : Yes / No

Family H/o CVD : Yes / No

Hyperlipidemia : Yes / No

Diagnosis :

PR : BP : Ht : Wt : BMI :

INV

Hb Hematocrit

Urea

Creatinine

FBS

Calcium Phosphorus

Sr.Albumin Sr.Fibrogen Sr.Lipoprotein

Lipid Profile

Urine Protein

ECG ECHO

Carotid Intimal medial thickness

S.No	Name	Age	Sex	Education	H/O				Family H/O CVD	Lipid Profile			
					DM	HT	Alcoholic	Smoker		TC	LDL	TGL	
1	SRINIVASAN	70	M	ILLITERATE	✓	✓	-	-	-	160	97	138	
2	SELVAM	41	M	ILLITERATE	-	✓	✓	✓	-	242	162	180	
3	NAGULAN	50	M	5th STD	-	✓	✓	✓	-	217	127	197	
4	ANANDAN	40	M	XII STD	✓	-	-	✓	-	320	220	292	
5	NAYAGAN	61	M	ILLITERATE	✓	✓	-	-	-	272	192	181	
6	KUMAR	38	M	B.Sc.,	-	✓	✓	✓	✓	182	96	156	
7	MARIMUTHU	60	M	ILLITERATE	-	-	✓	✓	✓	221	145	180	
8	ELLAMMAL	52	F	ILLITERATE	✓	✓	-	-	-	206	106	172	
9	PADMA	40	F	ILLITERATE	-	✓	-	-	✓	242	162	160	
10	VATHANAI	34	F	ILLITERATE	✓	-	-	-	-	211	152	182	
11	MUNIRATNAM	62	M	ILLITERATE	✓	✓	✓	✓	✓	215	139	190	
12	ARJUNAN	32	M	X STD	-	✓	-	-	-	180	128	182	
13	AJAY	45	M	XII STD	✓	✓	✓	✓	✓	277	209	188	
14	THOMAS	55	M	ILLITERATE	✓	-	-	-	-	160	83	132	
15	SAMYNATHAN	50	M	ILLITERATE	✓	✓	-	-	✓	217	163	197	
16	SARAVANAN	51	M	X STD	-	-	-	-	-	320	230	268	
17	RAMANI	43	F	ILLITERATE	✓	-	-	-	-	244	159	172	
18	NARAYANASAMY	61	M	ILLITERATE	✓	✓	✓	✓	✓	206	141	161	
19	PONNURANGAM	80	M	X STD	-	-	-	-	-	292	208	260	
20	SELVAM	40	M	ILLITERATE	-	-	✓	✓	✓	242	130	163	
21	RAMALINGAM	55	M	ILLITERATE	✓	✓	✓	✓	✓	150	92	227	
22	PAPPATHY	61	F	ILLITERATE	-	-	-	-	-	250	141	200	
23	BABU	50	M	X STD	-	-	-	-	-	210	136	141	
24	MAHENDRAN	45	M	ILLITERATE	✓	-	-	✓	✓	192	106	132	

25	ESAKKIMUTHU	55	M	XII STD	✓	✓	-	-	-	252	192	152
26	ARUNACHALAM	40	M	ILLITERATE	-	-	-	-	-	162	92	152
27	SELVARAJ	55	M	X STD	-	-	✓	✓	✓	250	120	163
28	RAJAVEL	45	M	ILLITERATE	✓	-	-	-	-	211	120	171
29	PAPPAMMAL	75	F	ILLITERATE	✓	✓	-	-	-	176	107	89
30	PASUPATHY	56	M	ILLITERATE	✓	✓	-	-	-	196	105	124
31	KAREEM	70	M	VIII STD	-	-	-	✓	-	241	165	180
32	MAHALAKSHMI	45	F	ILLITERATE	-	✓	-	-	-	192	107	198
33	SAMPTH KUMAR	45	M	ILLITERATE	✓	✓	-	✓	✓	240	170	151
34	RAJALAKSHMI	46	F	X STD	-	-	-	-	✓	191	121	158
35	DHANALAKSHMI	65	F	ILLITERATE	✓	✓	-	-	-	310	220	250
36	RAJAN	33	M	IX STD	-	✓	-	✓	-	142	96	121
37	PAPPV	57	M	ILLITERATE	-	-	-	-	-	148	82	120
38	JAGAN	33	M	ILLITERATE	-	-	✓	✓	✓	212	92	181
39	AYYAPPAN	60	M	ILLITERATE	-	✓	-	-	-	340	216	210
40	SANGEETHA	33	F	ILLITERATE	-	-	-	-	-	191	110	154
41	PALAYAM	55	F	ILLITERATE	-	-	-	-	-	138	82	114
42	SARASWATHI	56	F	VIII STD	✓	-	-	-	-	212	96	191
43	ESAKKIMUTHU	59	M	X STD	✓	-	✓	✓	✓	314	220	280
44	SRIDHAR	26	M	B.Com.,	-	-	-	✓	-	291	190	202
45	XAVIER	33	M	ILLITERATE	-	✓	✓	✓	-	310	222	210
46	RAJENDRAN	55	M	ILLITERATE	✓	-	-	-	-	240	140	180
47	BALAKRISHNAN	54	M	X STD	✓	✓	✓	✓	-	190	121	140
48	BALAN	55	M	ILLITERATE	-	✓	-	-	-	230	192	160
49	SRINIVASAN	45	M	ILLITERATE	✓	✓	✓	✓	✓	250	208	152
50	CHELLIAH	56	M	ILLITERATE	-	✓	-	-	-	226	192	164
51	DURAIKANNU	45	M	ILLITERATE	-	-	✓	✓	-	240	163	186
52	SUBBULAKSHMI	65	F	ILLITERATE	✓	-	-	-	-	190	119	142

53	LAKSHMI	56	F	ILLITERATE	✓	✓	-	-	-	250	177	189	
54	BALAN	66	M	ILLITERATE	-	✓	✓	✓	-	126	80	137	
55	SEKAR	42	M	X STD	-	✓	✓	✓	-	165	73	329	
56	ZAHEER BASHA	60	M	ILLITERATE	✓	-	✓	✓	-	240	110	190	
57	ETHIRAJ	57	M	ILLITERATE	✓	✓	-	✓	-	280	110	245	
58	RAMANI	38	M	XII STD	✓	-	-	-	-	125	152	229	
59	DHANALAKSHMI	35	F	V STD	✓	-	-	-	-	246	110	202	
60	KALLAPPAN	25	M	X STD	-	✓	-	-	-	240	109	140	