"STUDY OF RELATIONSHIP BETWEEN FEMORAL ARTERY INTIMA-MEDIA THICKNESS AND ATHEROSCLEROSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE- A ONE YEAR HOSPITAL-BASED CROSS-SECTIONAL STUDY"

BY

REG. NO. BS0119011

Dissertation

Submitted to the

KLE Academy of Higher Education and Research

Belagavi, Karnataka

In partial fulfillment of the requirements for the degree of

M.D.

IN

RADIO-DIAGNOSIS

DEPARTMENT OF RADIO-DIAGNOSIS

J. N. MEDICAL COLLEGE
BELAGAVI -590010. KARNATAKA

APRIL 2022

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH,

BELAGAVI, KARNATAKA

Endorsement by the HOD/Principal/ Head of the Institution

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LIST OF ABBREVIATIONS

USG	Ultrasonography
MRI	Magnetic resonance imaging
CT	Computed tomography
CKD	Chronic kidney disease
FiMT	Femoral Intima media thickness
PVD	Peripheral vascular disease
eGFR	Estimated glomerular filtration rate
DM	Diabetes mellitus
CFA	Common femoral artery
SFA	Superficial femoral artery
DFA	Deep femoral artery

ABSTRACT

BACKGROUND

Atherosclerosis is a gradually progressing disease over several decades before signs and symptoms. It would be too late by the time complications arise as it's a silent disease and would have already caused irreversible histological alterations.Chronic kidney disease is one of the major risk factors for developing cardiovascular diseases. There is limited data about the co-relation between USG measures of the femoral artery of peripheral vascular disease & renal functional status. This research hence will help us in the establishment of a relationship between femoral IMT with CKD. Also, IMT assessment might help in earlier detection of atherosclerotic plaques & hence PVD.Cost-effectiveness, patient ease, reduced radiation risk has made femoral Doppler ultrasonography a preliminary investigation in assessing peripheral vessels.This study was done to study the relationship between femoral artery intima-media thickness and atherosclerosis in patients with chronic kidney disease using femoral Doppler ultrasonography with an aim to identify the pathology early, which will reduce the morbidity and mortality in the patients.

MATERIALS AND METHODS

This is a cross-sectional study carried out on 99 patients who were known cases of chronic kidney disease who satisfied the inclusion criteria.After obtaining informed written consent, baseline data was collected on a predesigned proforma and then all the patients underwent femoral artery ultrasonography on GE VOLUSON 8 machine (GE Healthcare, USA) fitted with a linear array transducer of 7.5-12 MHz high frequency.The findings of the Doppler ultrasound were assessed and analyzed.

RESULTS

- 99 CKD cases were included in this study, who underwent femoral Doppler ultrasonography,of which 46 had a symptom of edema, and 22 had symptom of decreased urine output. It was found that males were affected more as compared to females.Maximum numbers of cases with raised IMT were in the age group of 61-70 years,however all the subjects of age group of 71 to 80 years had raised IMT,making it the vulnerable age group.Out of 99 subjects, 69 patients had raised IMT and 30 patients had normal IMT. The overall prevalence of atherosclerosis in the given study group was found to be 69.70 %. CKD Stages 4 & 5 had the highest prevalence of thickened IMTs.Higher prevalence of raised IMT among diabetics (75.0%). None of the CKD Stages had any significant co-relation with PVD.A significant association between lower eGFR values and higher triglyceride levels was found in the study. Very high prevalence of anemia among CKD patients of our study.

CONCLUSION

Colour Doppler ultrasonography is the safest and first-line investigation for evaluation of peripheral vessels since its non-invasive, economic, and devoid of any radiation. This study establishes evidence of the atherosclerotic prevalence in the form of raised IMT in patients suffering from CKD. This underlines the importance for early detection of raised IMT in CKD and its management to prevent progression to complications.

KEYWORDS: Doppler ultrasonography of femoral artery, atherosclerosis in CKD, Prevalence.

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INTRODUCTION

Chronic renal disorder refers to the gradual loss of renal function over a long period, maybe months to years.

It arises when one or both of the following conditions are seen:

-When there is renal damage for more than 3 months, that is by renal anatomical or physiological dysfunction in addition to reduced or a normal eGFR or, as seen either by pathological/biochemical disturbances / by renal damage markers, with urine /blood abnormalities or imaging abnormalities.[1]

-When the GFR is less than 60 ml per min per 1.73 m^2 for more than 90 days having renal damage or without it.

Chronic kidney disease is divided according to GFR value and the presence or absence of proteinuria.[1]

Stage 1: No decrease in GFR but with renal abnormalities.

Stage 2: Mild CKD with an estimated GFR of 60 to 89 ml per min per 1.73 m^2 and renal abnormalities.

Stage 3: GFR = 30 to 59 ml per min per 1.73 m^2.

Stage 4: GFR = 15 to 29 ml per min per 1.73 m^2.

Stage 5 is renal failure: GFR of less than 15 ml per min per 1.73 m^2.

Diseases with a longer prevalence are one of the leading causes of deaths and diseases worldwide. Exact prevalence of chronic renal disorder is not known in Indian subcontinent since not many longitudinal studies have been done. As per a few studies, however, it is estimated approximately to be 800 /million population. Most frequent cause is diabetic nephropathy as found by community-based studies.[2]

Atherosclerosis is defined as a disease of occlusion of the vessels that results from an accumulation of lipid-laden plaques. The people at risk are elderly, one with long-term high blood pressure, uncontrolled sugars, hyperlipidemia, tobacco consumption, etc.

Atherosclerosis is a major mortality factor in India, commonly noticed with chronic kidney disease (CKD) patients. CKD-related metabolic abnormalities, endocrine abnormalities, and inflammatory conditions have also been known to play a role in atherosclerosis in cardiac disorder patients.[3]

Such abnormalities occur way prior in the pathway of chronic renal disorder along with usual inciting factors that further add to formation of plaques /arteriosclerosis.

Previously capability of vascular ultrasound of carotid arteries predicting cardiovascular disease has been subject to research. As of now, thickness of intima-media measured by USG is thought to represent the substitute indicator of vascular disease.

There is limited data about co-relation between USG measures of femoral artery of peripheral vascular disease & renal functional status. This research hence will help us in establishment of a relationship between femoral IMT with CKD. Also, IMT assessment might help in earlier detection of atherosclerotic plaques & hence PVD.

AIM:

To study the association between femoral IMT of chronic kidney disease patients with or without dialysis.

OBJECTIVES:

- To assess the femoral vessel IMT in CKD subjects.
- To calculate the estimated eGFR in CKD patients & analyze the relationship of femoral IMT in subjects with low eGFR.

REVIEW OF LITERATURE

The external iliac artery gives rise to common femoral artery (CFA) at the level of the inguinal region. In the inguinal crease, CFA passes below inguinal ligament. There seem to be variation in diameter and its linear measure of it as per demography of the person.[4]

DIVISION:

The CFA divides itself into superficial and profunda femoris artery. The superficial branch becomes popliteal artery after passing through adductor hiatus. In the thigh region, the deeper branch gives off many penetrating end arteries.

Before CFA divides into (Superficial femoral artery) SFA & (Deep femoral artery) DFA, it gives off superficial epigastric & superficial circumflex artery, external pudendal artery.

SUPPLY:

The SFA has important task of supplying blood to the entire lower leg. Descending genicular artery arises from it in the knee region which vascularizes part of the knee. As it descends it gives minor branches to the thigh musculature. Once present in the adductor hiatus, it now forms popliteal artery. Lateral & medial circumflex arteries arise from DFA. The Medial branch supplies femur head region, trauma to which leads to avascular necrosis. Lateral branch gives supply to hip joint. DFA ends as perforating branches distally.[5]

CLINICAL IMPORTANCE:

Femoral artery is important because it is a common cause of vascular disorders that can cause claudicating symptoms in the leg region and is the initial access site for a lot of interventional procedures.

Clinical features of (Peripheral arterial disease) PAD of CFA or SFA include claudicating pain of thigh or calf region, loss of warmth, discolored feet, poor wound healing of the lower extremity, loss of touch sensitivity, and in progressed stage digital necrosis /gangrene might happen.[6]

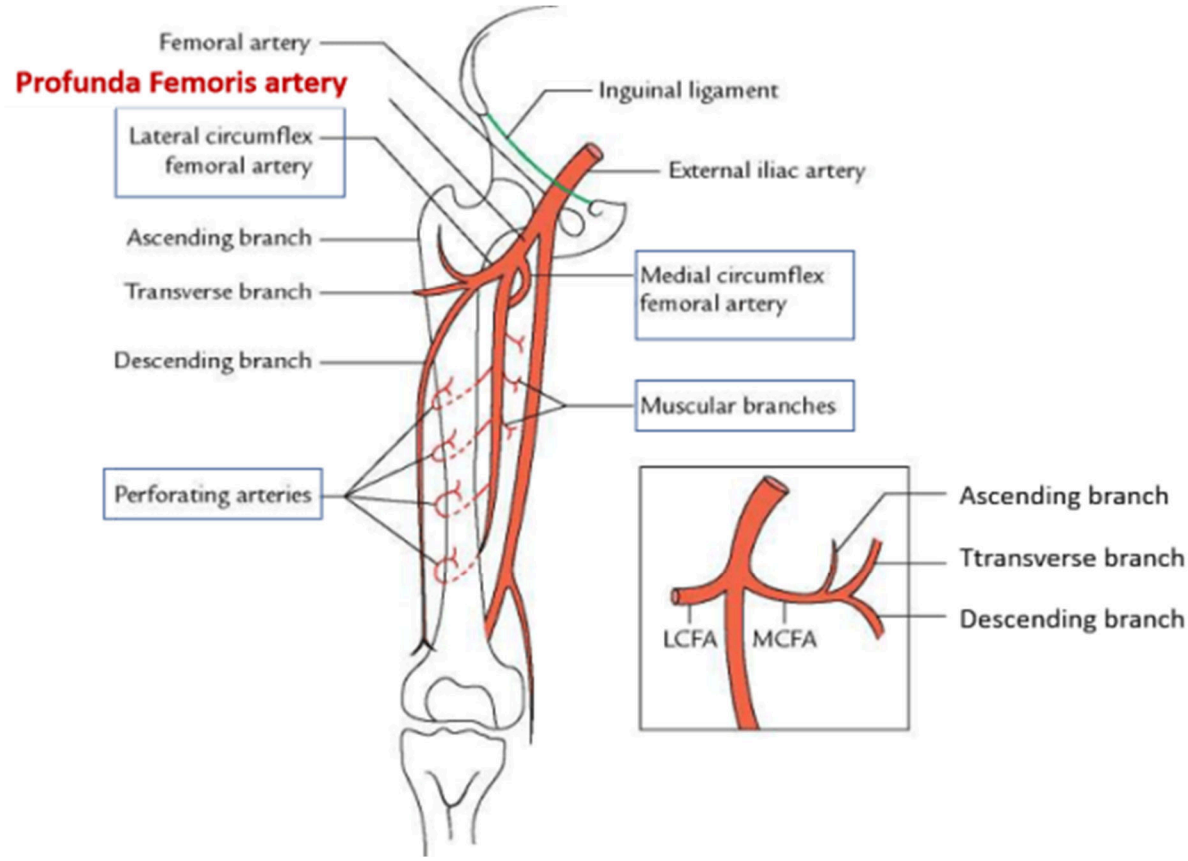
Comorbidities that increase the risk of a PAD patient include old age, increased BMI, uncontrolled sugars, high blood pressure, hypercholesterolemia, coronary disease, sedentary habits, and tobacco consumption.

VASCULAR ANOMALIES AND VARIATIONS:

Most variants are benign; however, few are considered life-threatening:

- Variability of origins of distal-most branches of femoral artery
- Doubled or non-visualization of DFA, medial & lateral circumflex branches, arising off CFA, SFA instead of the DFA.
- Variation in the level of CFA bifurcation
- Persistent sciatic artery- in this case, it acts as dominant vessels of lower limb and can have increased rates of life-threatening complications like aneurysm or thromboembolism
- Duplicated SFA[7]

Fig.1: Diagrammatic illustration of Femoral artery anatomy



Microscopic anatomy of the carotid artery wall:

Arteries are categorized as follows according to their size and function:

(i) Arteries that are large and has high elasticity

(ii) Moderate sized muscular arteries

(iii) Small-sized arteries and blood vessels

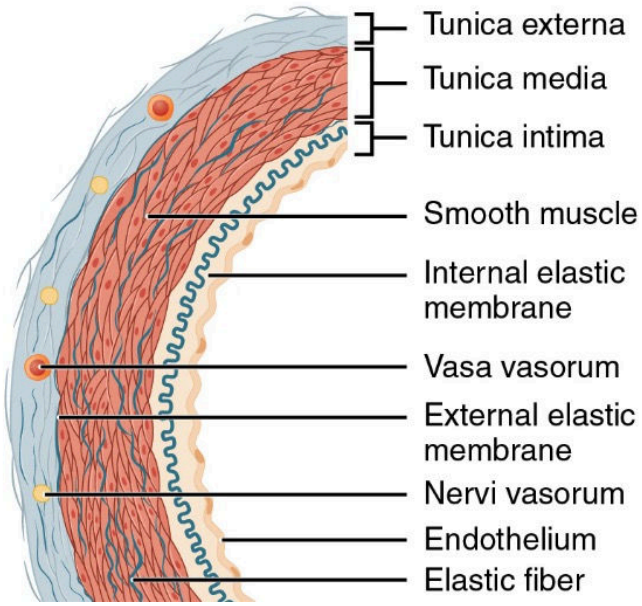
The artery wall consists of three strata as follows:

(i) Tunica intima: This is the artery's innermost stratum lined by flat endothelial cells.

(ii) Tunica media: This is the mid-layer of the artery which is composed of smooth muscles, elastic fibers that are accountable for the stretch-ability of a vessel during systole and diastole recoil.

(iii) Tunica adventitia: It is made of collagen and elastin which anchors arteries to the adjacent structures.[8]

Fig 2: Diagrammatic illustration of strata of walls of an artery.



Atherosclerosis is a gradually progressive disease characterized by the accumulation of lipids and fibrous elements in the arteries.[9]

Usual vascular structures which show signs of atherosclerosis are three, they are

1) Carotid arteries 2) Coronary arteries and 3) peripheral arteries.

EPIDEMIOLOGY:

In the last 10 years, with the increase in longevity and prevalence of lifestyle diseases, an increase in prevalence of CKD by 30% is noted among US citizens. However, no such longitudinal study has been done in India and there's no much information about CKD prevalence .[10]

However, according to SEEK research (2013) done in Indian continent, the prevalence of different stages of CKD was as follows:

CKD stage 1 - 7%

CKD stage 2 - 4.3%

CKD stage 3 - 4.3%

CKD stage 4 -0.8%

CKD stage 5 - 0.8%, accordingly. [11]

But the numbers did not accurately represent Indian population. In another study done in rural India, the CKD stage 3 prevalence was 6.3 % which was the maximum found so far from any epidemiologist of India .[11]

The longevity of the Indian population raised from 41.38 years (1960) to 66 years (2013), hence also hypertension or diabetes prevalence. Hence as in developed countries, the CKD prevalence might increase constantly in coming days.[12]

In a study done by Ana planca et al, increased prevalence of sub-clinical atherosclerosis was seen in CKD patients, also it accelerates fast in patients with diabetes mellitus (DM)[13]. It was also found that DM surpasses the other risk factors of CKD[14]

Pathophysiology:

Classical & Emerging risk factors:

Classical	Emerging
Age	Mineral bone metabolism
Male	Vascular calcification
High blood pressure	Uremic toxins
Smoking	Abnormal lipid modifications
High cholestrolemia	Inflammation
Diabetes mellitus	Oxidative stress
Sedentary lifestyle	Endothelial dysfunction

CKD patients didn't have the same predictive value for usual risk factors as that responsible for cardiovascular morbidity, especially in advanced stages of CKD, as in general population. This points out that additional pathological processes may have a role in emerging risk factors. However, the molecular pathways that initiate risk factors of CKD are poorly specified. Despite this, a small number of genes were differently expressed in non-pathological arteries of advanced CKD patients than the individuals with normal kidney function.[15]

Of the genes that undergo a process of modulation process, 23 genes underwent down-regulation and 8 genes underwent up-regulation, and the gene expression was not always reflected with corresponding changes in cellular protein.[16]

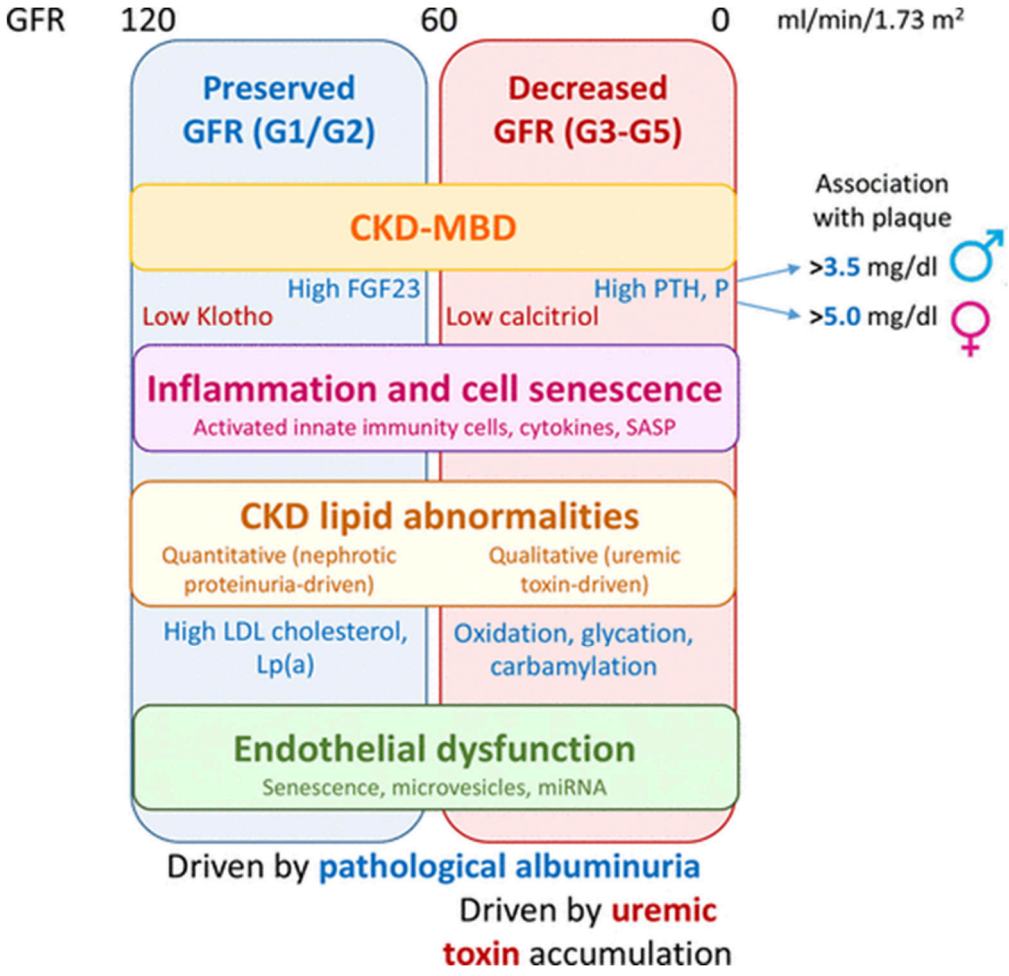


Fig 3. Diagrammatic illustration of factors affecting atherosclerosis in CKD.

MBD- mineral and bone disorder; and PTH- parathyroid hormone.

The above figure also shows relationship of albuminuria with GFR. GFR was graded as G1-G2 representing the preserved GFR, i.e. Glomerular filtration rate more than 60 mL/min/1.73 m2 and G3-G5 representing the advanced GFR, i.e., Glomerular filtration rate less than 60 mL/min/1.73 m^2. The amount of protein excretion increases with

decreased glomerular filtration rate. In divisions G1-G2 the albuminuria was more, i.e. nephrotic syndrome, and independent in divisions in G3-G5.[17]

Mineral bone metabolism derangements:

Many studies have analyzed the relationship between mineral bone metabolism and CKD-related vascular injury and favor the hypothesis of calcium deposition in the vessels.[18,19,20] But still there is a dilemma if wall calcification is seen in patients with CKD to be assumed as an atherosclerotic process like that of as in community or as an entirely separate entity that is CKD specific.[21]

In large-sized arteries, the atheromatous plaques are associated with vascular calcifications, and in small-sized arteries which have plenty of vascular smooth muscle cells have wall (intima-media) calcification without atheromatous plaques.[21,] The process of wall calcification starts in an early stage of CKD(CKD category G1) there is decreased production of phosphaturic factor Klotho by kidney starts even when the GFR is still normal but albuminuria is present.[21] Inflammation process and albuminuria themselves are Klotho suppressors. Decreased production of Klotho factor results in increase production of FGF23, which is already increased in vascular calcification and CKD G2.[21]

Coming to vessel wall calcification, occurs due to instability of Ca^{2+} and PO^{4-} ions in the circulation along with altered differentiation of VSMC to osteo or chondroblast cells.[21] The Ca^{2+} & phosphatic ionic changes occur due to the inability of the kidney to contribute to calcium and phosphate homeostasis and lack of calcium supplementation with vitamin D drugs.[17] The altered derivation of VSMC happens because of multiple external stimuli like bio-active metabolites, uremic toxins, and paracrine signals from macrophages or autocrine signals from stimulation of native cells.[22-25]

Also, it's been found that phosphate and calcitriol directly change the phenotype of vascular smooth cells which contributes to the pathophysiology.[26-29]

According to the NEPHRONA study which is a multi-center observational study, it was found that increased phosphate levels were linked with atherosclerosis prevalence in advanced chronic renal disease stages, i.e. G3, G4 & G5, whereas increased hs-CRP was found in CKD category G4, G5, and decreased vitamin D in CKD category 5D[30]. But the evaluation of peripheral arterial disease by indirect methods like by Ankle-brachial index (ABI) gave similar results but not conjoining results altogether.[30,31] Hence here we highlight the importance of evaluating peripheral arterial disease by direct plaque measurement rather than indirect method.

Hyperlipidemia and atherosclerosis in CKD:

Hyperlipidemia is one of the main causes of atherosclerosis but not the whole reason for atherosclerosis in the community. The molecules at blame are the altered or oxidized lipoproteins that have interaction with vascular cell receptors resulting in vessel damage.[32,33]

In CKD, an increase in quantity of usual lipids was not prone to atherogenesis[34,35]. Also, it was found that there was a relationship between increased triglyceride levels and sub-clinical atherosclerosis in CKD category G3, but the total cholesterol level had a poor association with the presence of atheromatous plaque in CKD category [36].

On the other hand, there was an association between qualitative changes in lipid spectrum and atherogenesis. Hence, in CKD there was a link with deposition of VLDL (very low-density lipoprotein), decrease in LDL particle size, variation in triglyceride and cholesterol components of HDL & LDL.[37] Other pathological processes that

contributed to the qualitative changes in lipid spectrum were carbamylation, glycation, and oxidation of LDL & HDL which are involved in activation of pro-inflammatory pathways and receptors.[38-42]

Inflammation and vascular insult:

Inflammation has now been considered as the main process for atherosclerosis and for obvious reasons systemic inflammation is been characterized in CKD.[43-46] In advanced CKD the pro-inflammatory changes were increased blood levels of CRP and cytokines, activated macrophages, native vessel cells, and increased ROS(reactive oxygen species).[44,47-51]

Cellular aging has been linked to the process of vessel wall insult due to uremia which presents as decreased ability to regenerate, cessation of physiological functions, concentration of oxidative damage & nuclear molecules.[37, 52, 53]

The crucial role of the endothelium in vessel damage in CKD:

The endothelium has a very important role in maintaining homeostasis of the cardiovascular system with involvement of balance between cell death and aging.[54,55] Uremic toxins and inorganic phosphates seem to cause disturbance in endothelial dysfunction.[56-58]

When endothelial damage occurs in CKD, there seems to be a release of micro-vesicles and miRNA92a (a kind of miRNA) which in turn cause further vessel damage. [59,60] Additionally there is seen increasing levels of vascular endothelial growth factor (VEGF) in later stages of CKD.

Prevalence of atherosclerosis in CKD:

Atherosclerotic prevalence in CKD has been studied using various methods.[17] Lot of researches proved that subjects with chronic renal disorder have high degree coronary artery disease along with an increased number of calcified plaques, increased intima medial wall thickness, and wall calcification as compared to non-CKD patients.[61-63]

Kato et al proved CKD subjects were having raised lipid indices, increased calcium, disruption of plaque, and crystals of cholesterol.[64]

Ankle-brachial index:

The most frequent cause of amputation of advanced CKD is peripheral artery disease.[17] The index used for assessing this is an ankle-brachial index, and an index value of < 0.9 is considered for diagnosis.[65] The value of more than 1.4 suggests that there is increased stiffness of vessels[66] and calcification[67]. For more than 40 years this index has been used for peripheral arterial disease[68], however, this index is considered less sensitive in the early stage of PAD, where there is earlier development of atherosclerosis and vessel dysfunction than a lower ABI since it needs a plaque that's sufficiently occlusive enough to decrease blood pressure distally. Also using ABI in CKD patients is troublesome as there is a higher chance of them having stiff arteries, leading to a lower sensitivity of ABI.[69-72]

Carotid and femoral atherosclerosis:

Many studies have shown that there is an association between increased carotid IMT (cIMT)[73,74] and decreased kidney function, in fact, it has been proved many times that there is a faster increase in cIMT.[75]

However, in contrast to carotid atherosclerosis, femoral atherosclerosis has been less studied. CKD was quantifiably having association in relation to plaque prevalence of femoral artery, even in subjects with normal ABI.[76]

Observational studies on atherosclerosis progression in CKD:

The chronic renal disease seems to affect two or one of the processes:

1)A gradual asymptomatic process of setting up of atheromatous plaques, and

2)Symptomatic process of thrombus formation that results in occlusion which is triggered by endothelial injury[77]

Few studies outside the NEPHRONA cohort, have mentioned plaque progression and significance of sub-clinical atherosclerosis.[78,79] In a study done in Canada, showed that plaque progression rate was slower in CKD category G4 as compared to CKD category 2-3a.[80] Thus even with the conclusion about the association of CKD with increased cardiovascular risk, there is limited data about atherosclerosis progression and its prevalence in chronic renal disease, also there was no definite conclusion on whether the end-stage renal disorder was having an association of raised or decreased atherosclerosis progression.[80,81,82]

Though in advanced CKD patients, atheromatous progression is well associated with cardiovascular risk than a number of plaques, it was seen that the progression in CKD patients was mostly in those who already had atherosclerosis.[83]

The NEPHRONA cohort, also showed that in 69% of CKD patients there was atheromatous progression who had a baseline plaque, and in 40% of CKD patients without baseline plaque[83]

Diagnostic modalities:

Diagnostic modalities used in the evaluation of femoral vasculature:

1. Intra-arterial contrast study of vessels or Conventional angiogram
2. CT angiogram
3. MRI angiogram
4. Duplex USG

Conventional angiogram: There is a still need for Angiography in PAD evaluation and is mainly used if an intervention is planned. It gives complete details regarding vessel details and is regarded as the benchmark diagnostic test for peripheral arterial diseases.

The vessel with atherosclerosis in angiography appears irregular, tortuous with atheromatous plaque and stenosis of the lumen.

Advantages:

i. It allows the study of the entire lower peripheral vascular system

ii. Plaque shape and size with collateral formation if any can also be assessed correctly.

Disadvantages:

i. Invasive

ii. Costlier

iii. Neurological complications can be a risk sometimes

Computed tomographic angiography (CTA):

Its gives considered as an excellent aid for the assessment of femoral or other peripheral arterial occlusion and in the grading of a degree of stenosis, However it does have some disadvantages like the need for more contrast material, need for syncing between contrast administration and image acquisition & need of an advanced CT machine with post-processing methods for better image reconstruction.

MR angiography (MRA):

Various techniques are used for MRI angiography:

- Time of flight MRA (TOF-MRA),
- Black blood MR angiography (BBMRA)
- MR angiography for phase-contrast (PC MRA)

Among these Time of flight, MRA is preferred.

It helps in the diagnosis of the disease and interventional planning if required.

Bosma et al. did a comparison of Magnetic Resonance angiography with classic vessel study in terms of economic benefit & life quality. The study found that though MRA was nearly 20% cheaper, the study didn't find much difference in the quality of life[84].

Advantages:

- Assessment of both large and small vessels can be done.

Disadvantages:

- Expensive, time-consuming
- Not universally available.
- Difficult in severely morbid patients or one with a pacemaker and underwent implant surgery recently.

Doppler ultrasonography:

It's a safer, non-invasive, cheaper technique and doesn't use a contrast agent.
Duplex ultrasound uses both B-mode and pulsed Doppler mode. B-mode stands for "brightness mode", it provides real-time images in greyscale. Pulsed Doppler mode measures flow dynamics in vessels. To check the presence or to analyze the severity of PAD in lower limb arteries, a high-frequency probe is used since it has a good spatial resolution for superficial structures.

Doppler physics:

Doppler effect was first described by Australian physicist Johann Christian Doppler in 1842.

Principle:

The Doppler effect can be described as a frequency difference in the detected sound while the source or the indicator is moving. Clinically, a Doppler shift happens when reflectors move relatively with the transducer. The difference between receiving and transmitting frequencies is known as Doppler shift frequency.

The analysis uses this theory, that is, the velocity increases when a vessel is narrowed

Duplex ultrasound of lower limb arteries allows their direct visualization. The vessels are classified into four groups[85]. The first group has 1-19 % stenosis, which is considered normal, next is 20-49%, followed by 50-99% stenosis, and lastly full occlusion. The knowledge about the location and severity of stenosis helps the clinician to decide the therapy needed as, either no treatment needed medical treatment or invasive treatment like in that of bypass surgery[86]. A study done by Whelan et al. showed it was 95%

sensitive and 99 % specific for patency versus occlusive disease, 92% sensitive, and 97 % specific for hemodynamically important lesions[87].

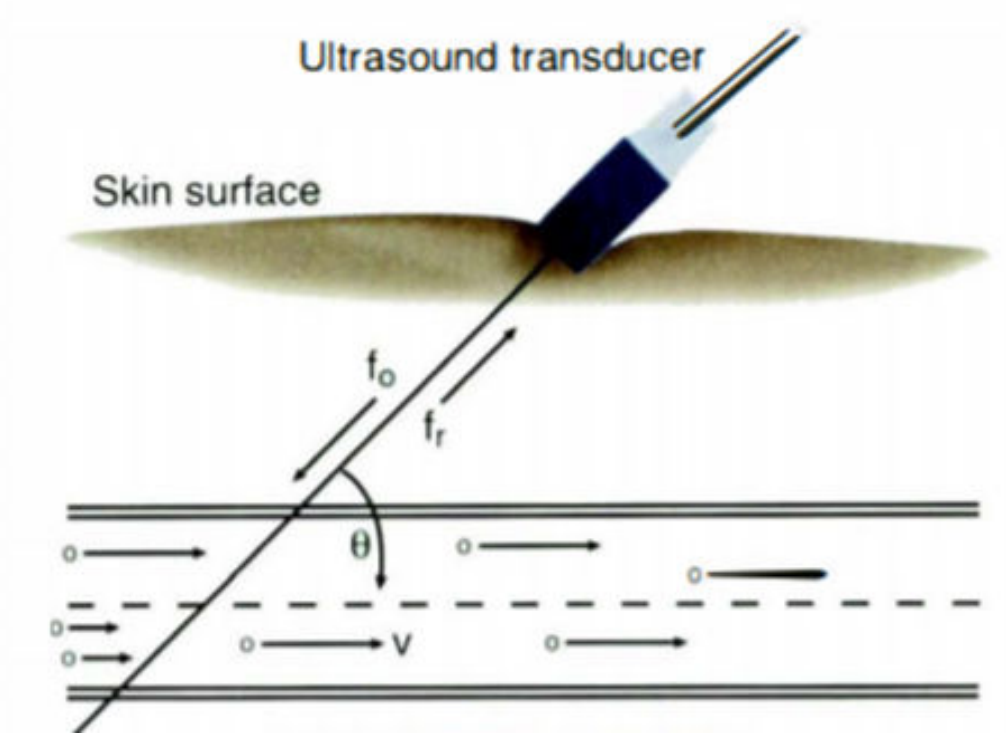


Fig 4: Diagrammatic illustration of the equation of Doppler study

The doppler shift frequency is given by:

$$\Delta F = (F_R - F_T) \frac{2F_T.V.Cos\Phi}{C} \quad \text{or} \quad V = \frac{\Delta F.C}{2F_T Cos\Phi}$$

θ is an angle formed between the flow direction and the ultrasound beam's axis.

F_T-F_R is a difference in frequency that is sent and received

V is the speed of fluid

C -speed of sound in tissue

DIFFERENT DOPPLER MODES USED:

The most commonly utilized imaging modality for detecting atherosclerosis in PVD is duplex or dual ultrasound. Other modes are continuous doppler & pulsed doppler.

DUAL ULTRASOUND MODE:

It uses a regular mode scanner combining integrated Doppler mode. Anatomical structures are best delineated by a high-resolution B-mode scanner whereas the Doppler analysis gives information about the blood flow and movement patterns.

Barber et al, first described duplex sonography in 1974, which displays the real-time image simultaneously with pulsed wave Doppler wave-forms.

INTERPRETATION:

A complete and detailed vascular study plays a vital role in determining the disease diagnosis and progression.

A linear array high frequency (7.5-12 MHz) transducer is used for the evaluation of peripheral vessels.

Sonographic anatomy of the femoral artery walls:

- High-resolution ultrasonography is used to visualize various strata of arterial walls. In the long axis, the two walls appear as hyperechoic lines with a dark region in between.

- The initial echoic line on the farther wall originates from close opposition between vascular lumen, while later nearer echoic line originates from apposition between

medial & adventitial layer. The inside margin of an echoic adventitial layer is sharpened by a less bright medial layer. Combined intima-media thickness is the length between the distance from the first bright line along the far wall to the second bright line.

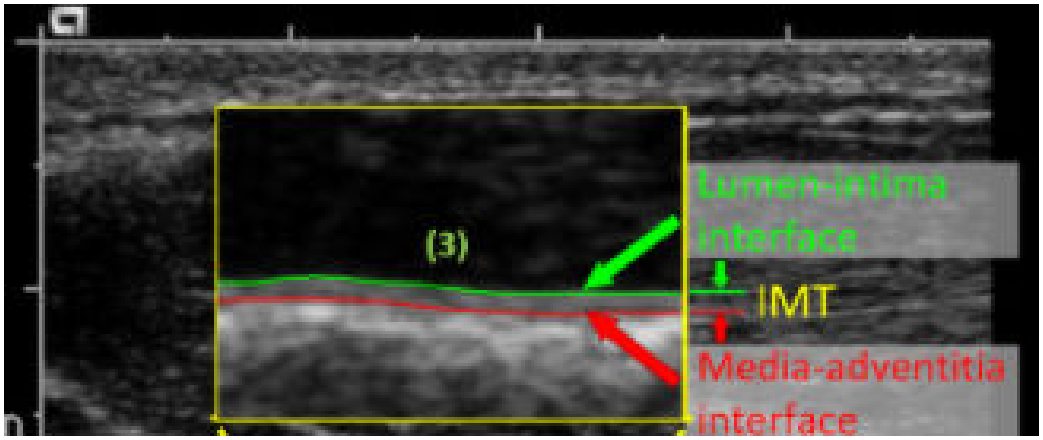


Fig 5: Figure showing different layers of a normal femoral artery wall.

Intima-Media Thickness (IMT):

It is checked in the superficial or common femoral artery. The study done by Ayoola et al found normal fIMT as 0.6mm.[88]

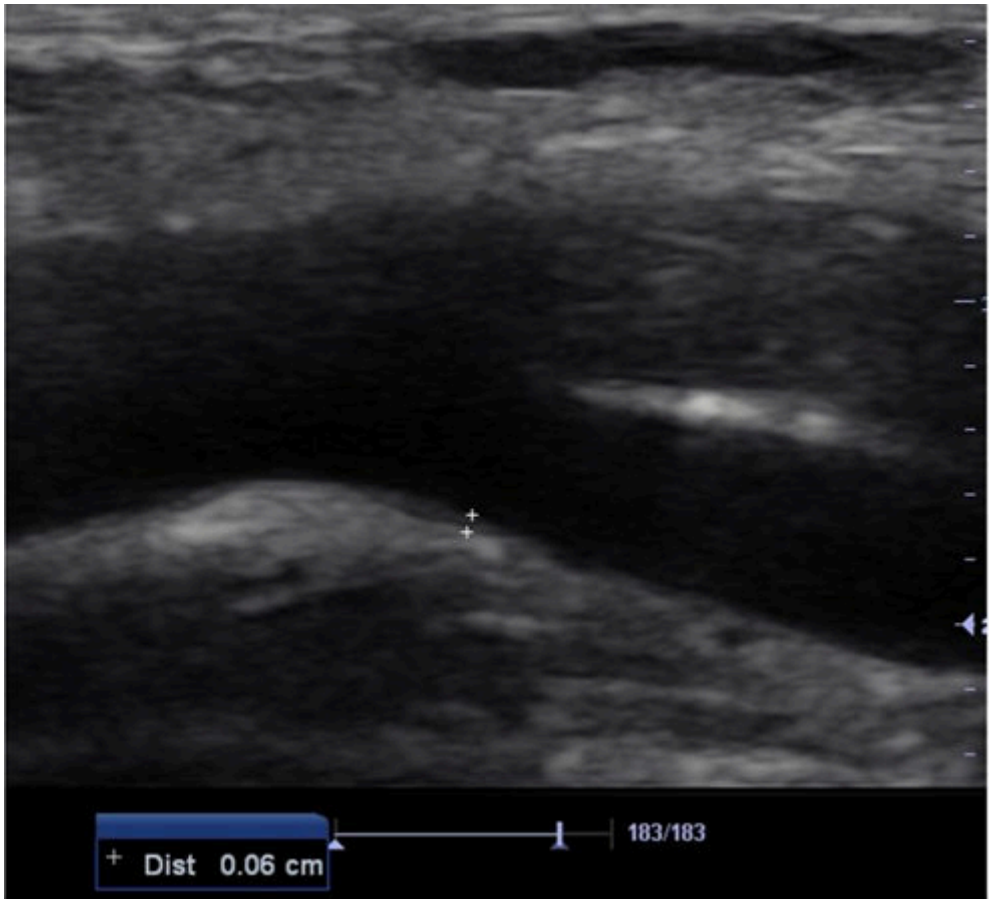


Fig 6: Figure shows normal IMT of a femoral artery wall.

The main arterial pathology detected by B mode USG is atherosclerosis.

"Atherosclerotic plaque is denoted by echogenic material encroaching on the arterial lumen and which produces signal void on B mode USG."[89]

Plaques are detected by B-mode ultrasonography, value ≥1.2 mm (lumen to adventitia) indicates the presence of plaque.

REVIEW OF STUDIES

Over the decade the burden of morbidity of non-communicable diseases is rising and the global CKD burden is also adding to it. Many studies have been done globally like in Asia, Australia, Africa, Norway, and a few in India to estimate the prevalence of CKD.

According to a study done on the global burden of CKD disease from 1990-2017, it stated that almost the worlds' two-thirds of CKD patients were from China and India, with the Indian number being 115.1 million.[90] As stated in a journal authored by P.P.Varma, CKD stage 3 prevalence in the rural belt of Karnataka was 6.3 %.[91] The rough estimate of CKD prevalence in the Indian subcontinent is calculated to be 800pmp. [92]

There are many observational, cohort, prospective studies done in relation to the relationship between CKD and fIMT, also few of them have found a significant correlation between the two, and a lesser of them have found no correlation between the two parameters. One of the first large-scaled multi-centered cohort studies to describe sub-clinical atherosclerosis in various stages of CKD was the NEPHRONA study. This study found that there was a higher rate of atherosclerosis in femoral artery (12.6 % vs. 10 % in control).

A study was done in USA from June 2008 to 2010, by Naiman nezami et al., with a sample size of 89, which was categorized into three divisions, one division of chronic renal disorder patients, a negative control group of kidney donors, and a positive control group of coronary artery disease patients. The atherosclerosis was assessed histopathologically. It was seen that the case group i.e. CKD group had higher femoral intima-media thickness than the negative control group ($p = 0.004$). The grade of atherosclerotic degree in CKD was correlated with femoral intima-media thickness and

fIMT measure more than 0.57 mm indicated the presence of atherosclerosis (sensitivity 92%).

A study done by Simon et al, at San Diego from 2007 to 2011 with 1029 subjects, concluded that atherosclerosis in femoral vessels as having a significant association with prevalence of chronic renal disorder in the community and also found that its USG might help in an earlier analysis of the co-relation between CKD & peripheral vascular disease or their inciting risks.

Not all studies had a positive co-relation between femoral IMT and chronic kidney disease like research of A. Lisowskaa et al, of Japan, from 2005 to 2009, with a sample size of 498,where it was found that there was a significant negative correlation between eGFR values of subjects with intima-media thickness complex in CCA and CB. This relationship in normal cases couldn't be proved. Femoral intima-media thickness and CKD also didn't have a strong relationship.

A study by Marta Gracia et al, from the NEFRONA group, done in Spain (2009 to 2011), with a study sample of 1553, it was found that there was a strong relationship between chronic renal disorder and atheromas in the femoral artery.

METHODOLOGY

Materials and methods:

Study Design: A cross-sectional study.

Study site: The Department of Radio Diagnosis at Jawaharlal Nehru Medical College, Belagavi, Karnataka.

Study population:

Subjects with CKD undergoing ultrasound scan at the Department of Radio-diagnosis at the KLE'S Dr. Prabhakar Kore Hospital & MRC, Belagavi.

7.2 Method of collection of data:

Inclusion criteria:

- All subjects with chronic kidney disease undergoing ultrasonography at Department of Radiology in KLE hospital Dr. Prabhakar Kore Hospital & MRC, Belagavi

- As stated by the International kidney Journals, CKD is defined as when the GFR is less than 60 ml per min per 1.73 m^2 for more than 3 months having renal insult or is devoid of it.

Exclusion criteria:

- Patients with past renal transplant
- Patients with a known case of renal malignancy based on their history and medical records.

- Patients diagnosed with hypertension or with a history of smoking are also risk factors for atherosclerosis.
- Patients who underwent surgical/interventional treatment of femoral arteries for atherosclerotic disease.

Sample size:

Prevalence rate of chronic kidney disease in Indian population in most of the studies done is very less, hence the sample size would be very large which is quite difficult to attain in our hospital. Therefore all diagnosed cases of CKD over a period of one year at KLE'S DR Prabhakar Kore Hospital & Medical Research Centre, BELAGAVI would be taken as the sample size. Average number of patients within the last three years span with CKD, referred to the department of radio-diagnosis, was found to be around 84-96 each year.The mean number of patients was found to be = 90.

My intended study was carried out on 99 patients visiting the OPD / IPD referred to USG scan to the department of radio diagnosis at KLE'S DR Prabhakar Kore Hospital & Medical Research Centre, BELAGAVI for a period of 12 month duration.

Statistical Analysis:

In the present cross-sectional analysis, the mean and standard deviation was determined for the continuous quantitative variables. For comparative purposes, if data was separated into two groups with respect to such qualitative characteristics, such as gender or some other qualitative characteristics, the continuous variables was compared using appropriate methods, such as ANOVA, correlation, regression, etc., that was used as needed.

Discrete variables were represented by a median. Suitable graphs were used to depict the comparison.

The Median was interpreted by discrete variables. Effective graphs were used to represent the comparison.

It will convey the categorical data in terms of prices, ratios, and percentages. The relation between the result, clinical and demographic characteristics were evaluated using either the Chi-square or the exact Fisher test.

The value of p less than 5% (0.05) was considered important for all the tests.

Study Duration: January 2020 to 31st December 2020.

Ethical considerations: This research was accepted by an institutional human ethics committee. All research participants received informed written consent and only those participants willing to sign the informed consent were included in the research. Before obtaining consent, the participants have clarified the risks and benefits involved in the research and the voluntary nature of participation. The confidentiality of the participants in this research was preserved.

METHODOLOGY: An informed written consent was received from all the subjects. A pre-structured proforma was used to gather clinical data.

A comprehensive history, related risk factors (smoking, hypertension, hyperlipidemia, obesity), and laboratory (random blood sugar) investigations were taken.

The above study population was subjected to femoral artery Doppler ultrasonography on GE VOLUSON machine (GE Healthcare, USA) fitted with a linear array transducer of 7.5-12 MHz high frequency.

EXAMINATION TECHNIQUE:

Patients were positioned supine with their legs extended. The examination was started with a transverse scan of the left and right thigh regions. Scanning was performed in the following areas: right and left femoral area,

The CFA & SFA were focused, & IMT would be measured on the transverse axis.

Data collection tools: Recorded all the necessary parameters in a structured research proforma.

The data gathered was analyzed and presented wherever possible in the form of tables, graphs, figures, and diagrams.

RESULTS

Study population:

99 CKD patients who were referred for femoral Doppler ultrasonography were prospectively evaluated in this study.

Table 1: Descriptive inspection of age distribution among the study group

(N =99)

Age groups	Number	Frequency
<=30yrs	10	10.10
31-40yrs	13	13.13
41-50yrs	19	19.19
51-60yrs	26	26.26
61-70yrs	23	23.23
71-80yrs	8	8.08
Total	99	100.00
Mean	52.39	
SD	15.89	

The study had most of the subjects from age of 51-60 years, trailed by 61-70-year age group. The mean age was 52.39 years.

Graph 1: Descriptive inspection of Age distribution among study group.

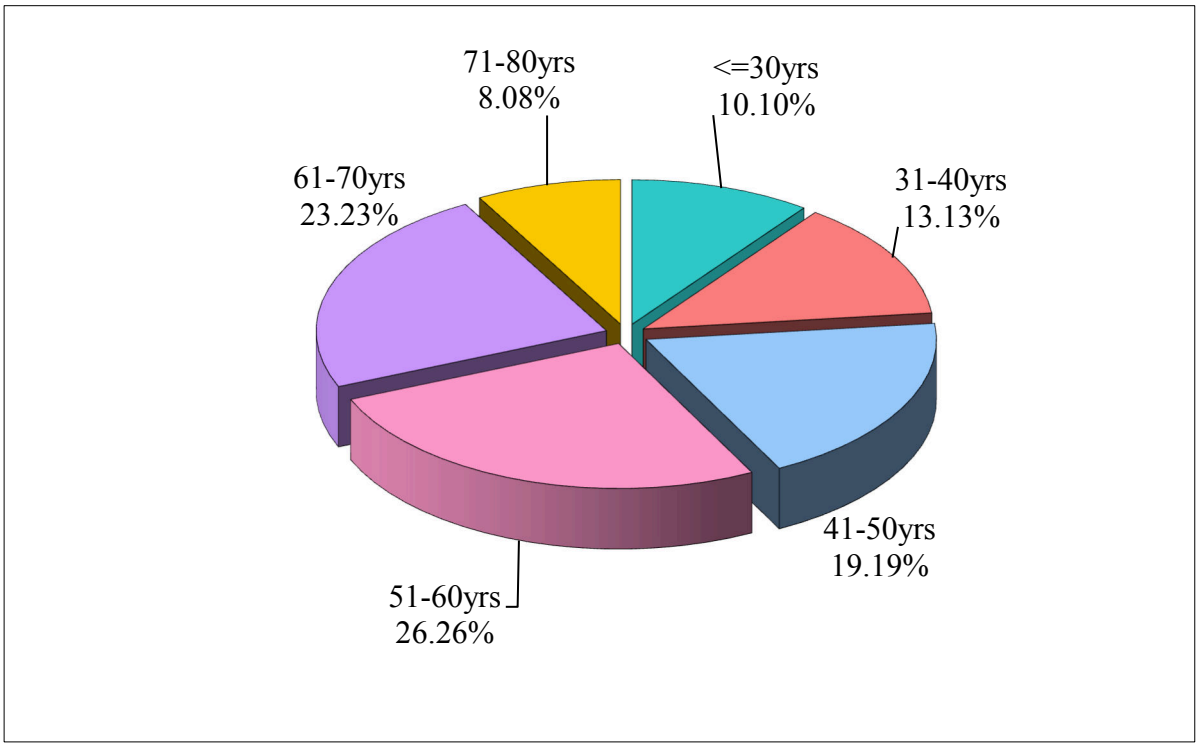
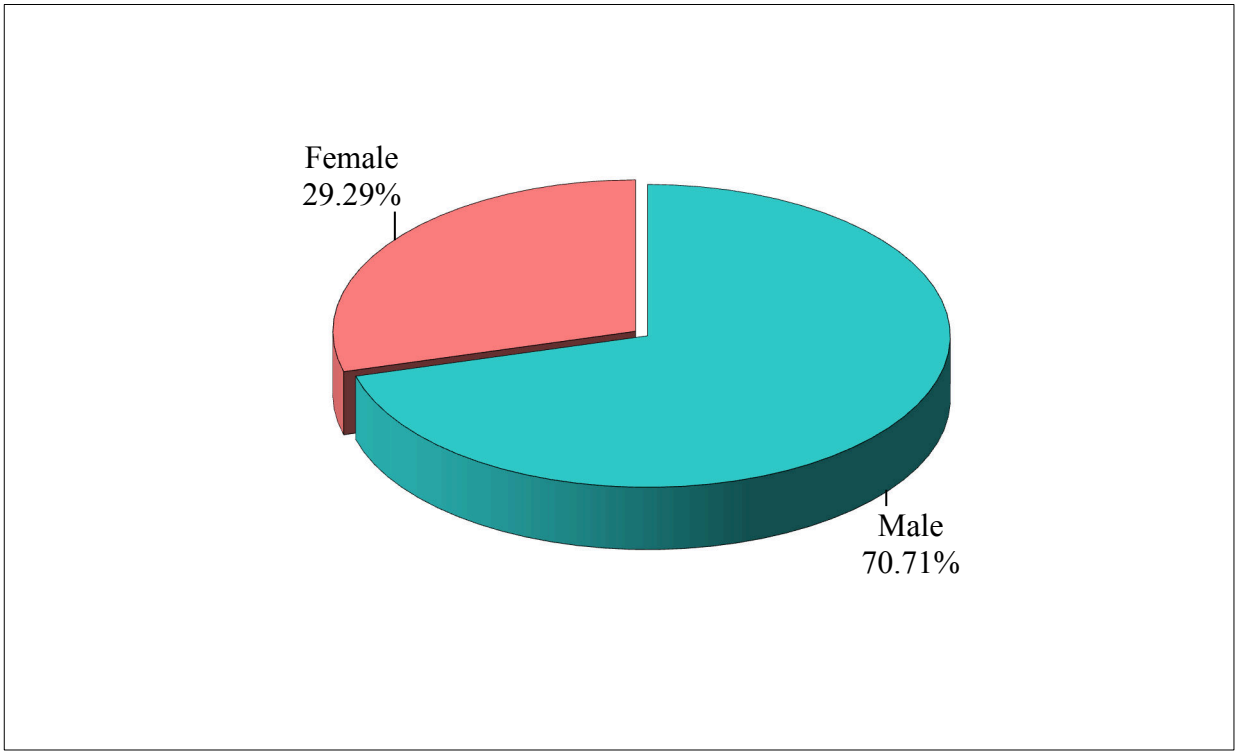


Table 2: Descriptive inspection of Gender wise distribution among study group.

Gender	Number	Frequency
Male	70	70.71
Female	29	29.29
Total	99	100.00

Graph 2: Graph showing gender distribution among study group.

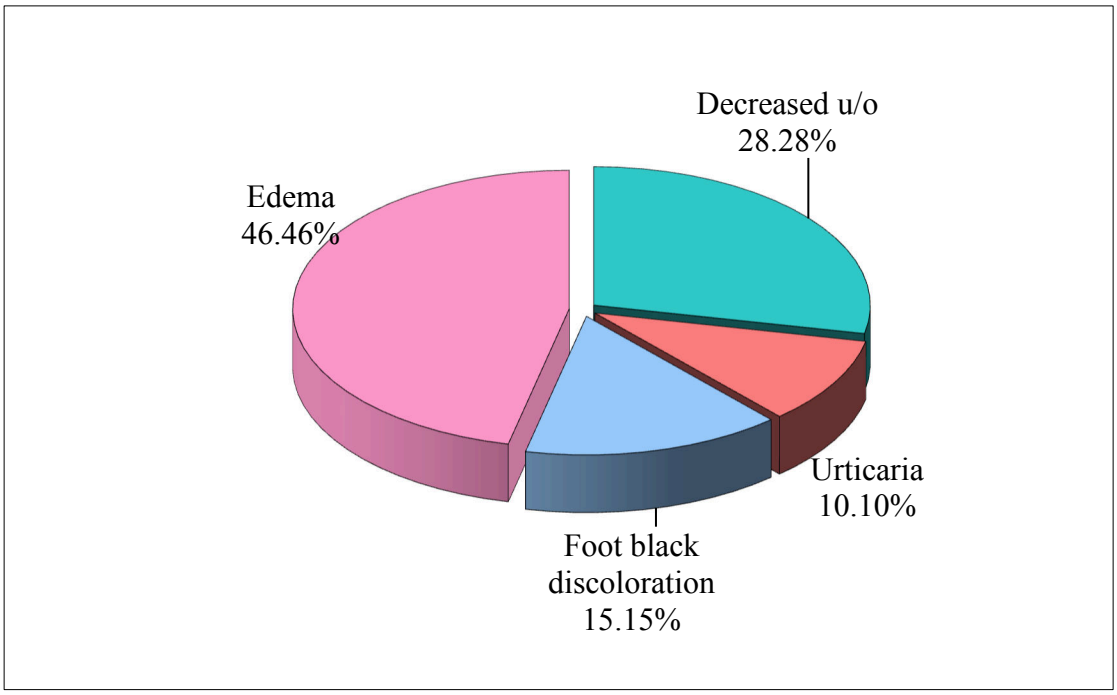


In the current study percentage of male patients were more (70.71%) as compared to the female patients (29.29%).

Table 3: Descriptive inspection of distribution with respect to clinical history in study population (N=99).

SYMPTOMS	NUMBER	FREQUENCY
EDEMA	46	46.46
URTICARIA	10	10.10
FOOT BLACK DISCOLORATION	15	15.15
DECREASED URINE OUTPUT	28	28.28
TOTAL	99	100.00

Graph 3: Graph showing distribution with respect to clinical history (N=99)

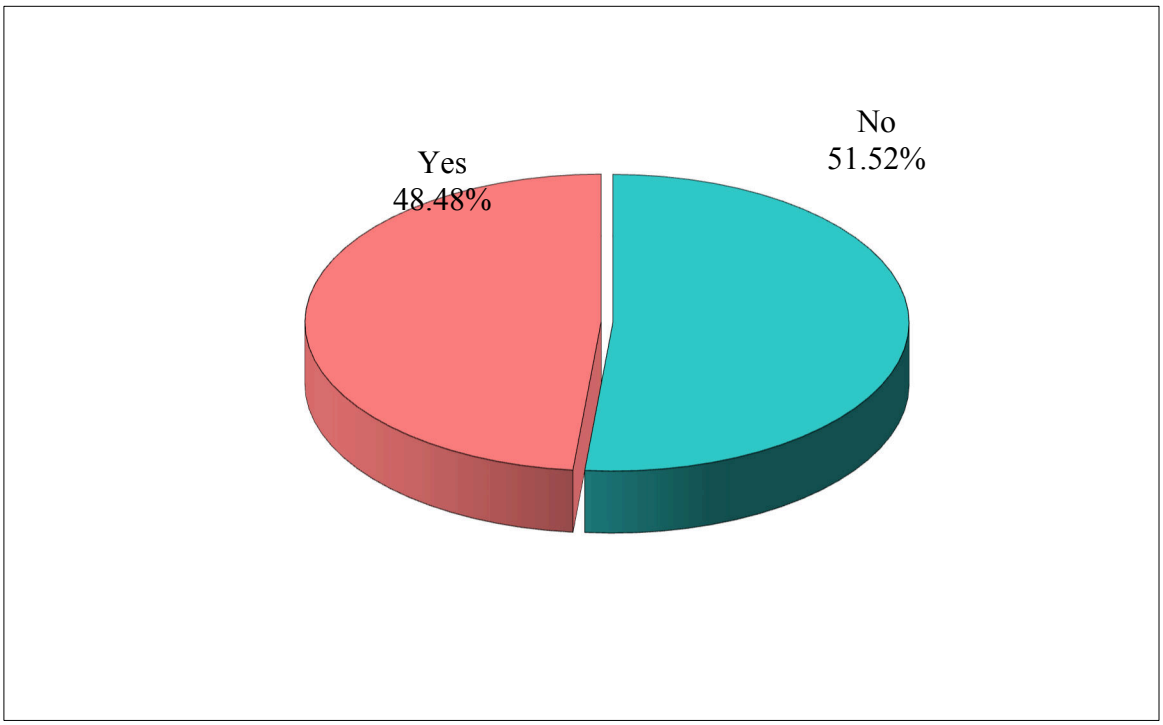


In the current research a greater number of patients presented with history of edema (46) and decreased urine output (28).

Table 4: Descriptive inspection of distribution with respect to prevalence of Diabetes mellitus (DM) in study population (N=99)

DM	Number	Frequency
No	51	51.52
Yes	48	48.48
Total	99	100.00

Graph 4: Graph showing distribution with respect to prevalence of Diabetes mellitus (DM) in study population (N=99).



The study had borderline high percentage of non-diabetics, the percentage being 51.52%, whereas diabetics in the study constituted about 48.48%.

Table 5: Descriptive inspection of distribution with respect to prevalence of raised IMT among diabetics in study population (N=99)

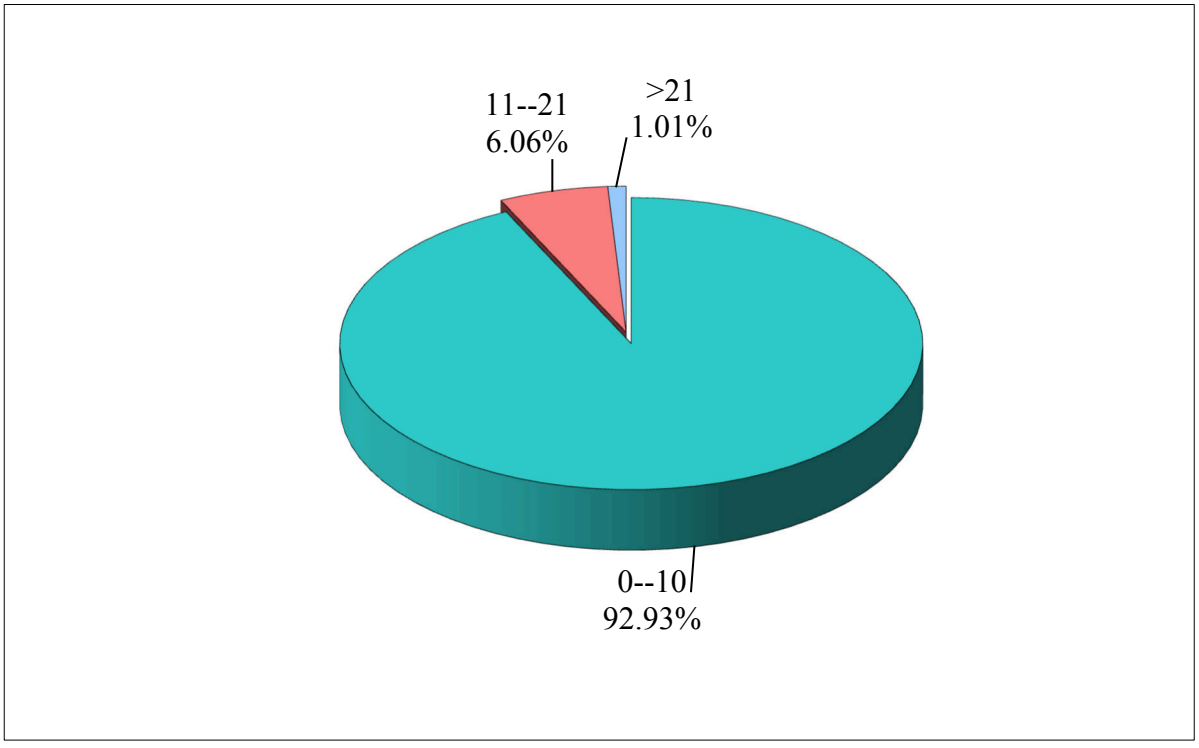
DM	Raised IMT	%	Not raised IMT	%	Total	%
No	33	64.71	18	35.29	51	51.52
Yes	36	75.00	12	25.00	48	48.48
Total	69	69.70	30	30.30	99	100.00
Chi-square=8.7710, p=0.1190						

In the present study it shows that of the 48 diabetic patients, 36 diabetic patients (75.0%) had raised IMT.

Table 6: Descriptive analysis of distribution in terms of prevalence of raised Creatinine levels (N=99)

Creatinine(mg/dl)	Number	Frequency
1.3-10	92	92.93
11-21	6	6.06
>21	1	1.01
Total	99	100.00

Graph 5: Graph showing distribution with respect to prevalence of raised Creatinine(N=99).

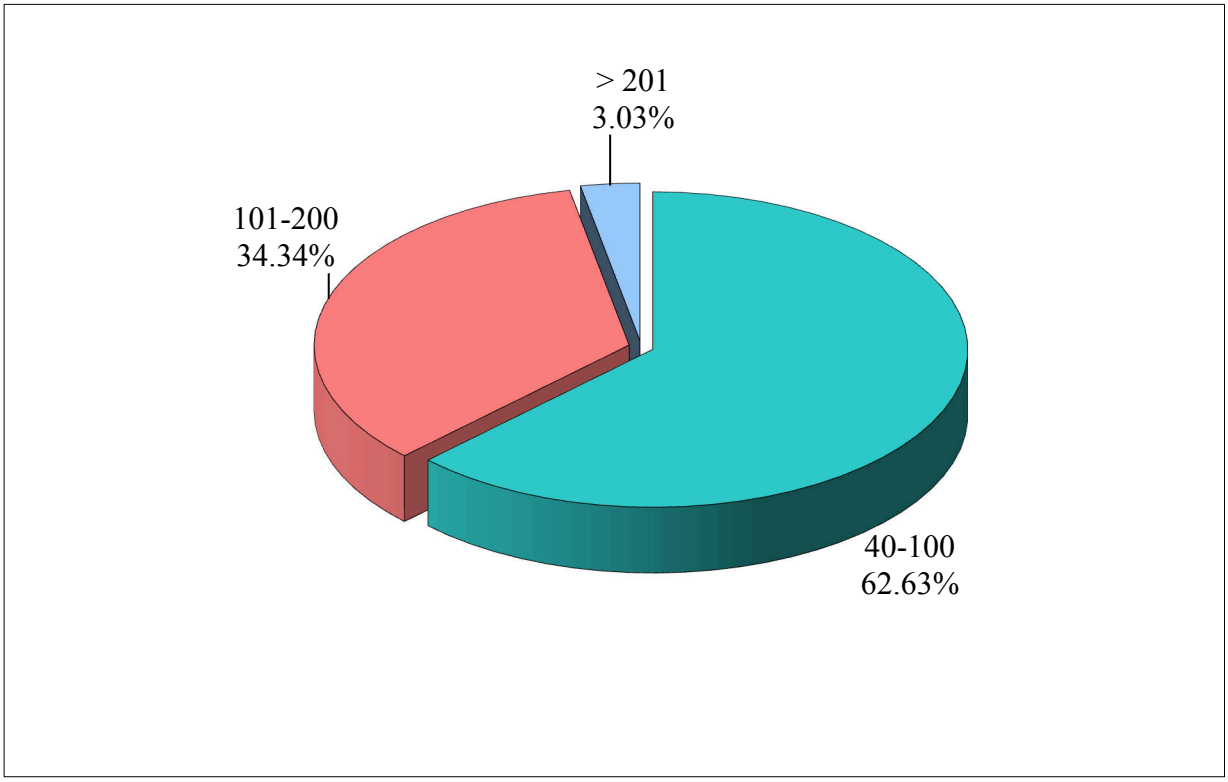


Maximum number of patients had creatinine in the range of 1.3-10 mg/dl. Just one patient had creatinine >21mg/dl.

Table 7: Descriptive analysis of distribution in terms of prevalence of raised Urea levels (N=99)

Urea(mg/dl)	Number	Frequency
40-100	62	62.63
101-200	34	34.34
> 201	3	3.03
Total	99	100.00

Graph 6: Graph showing distribution with respect to prevalence of raised Urea levels.

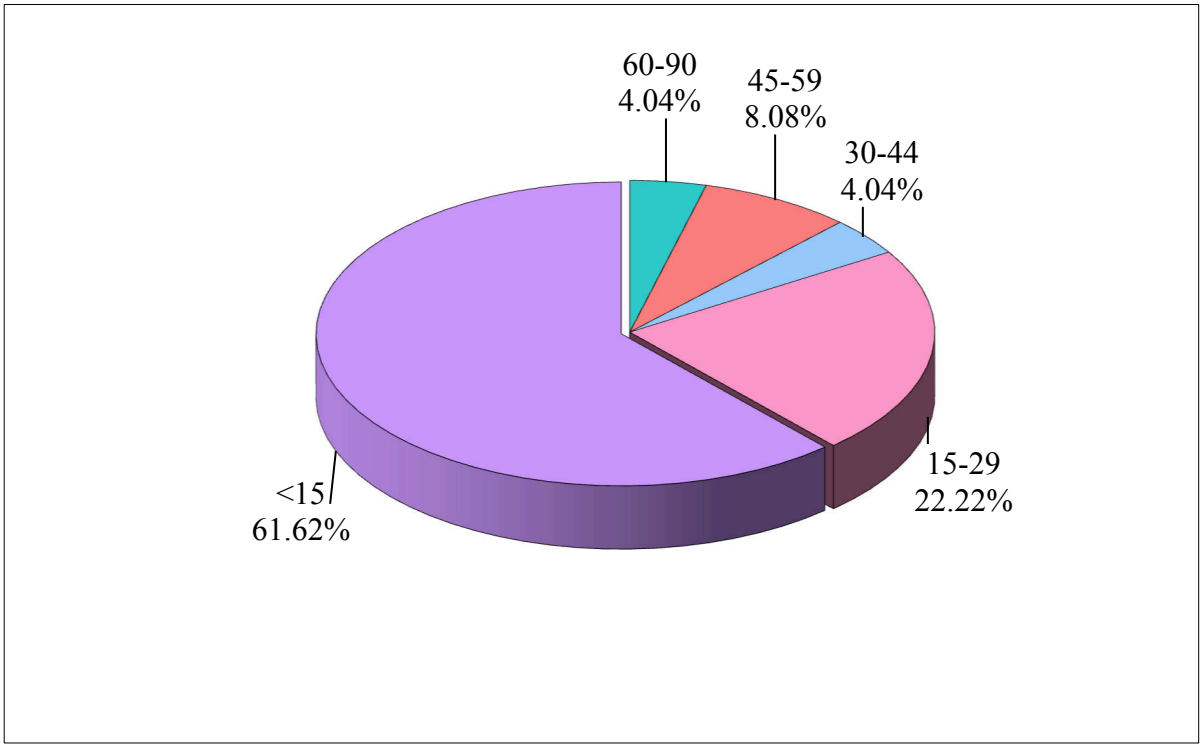


Maximum number of patients had urea in the range of 40-100 mg/dl. Just 3 patients had urea levels > 201 mg/dl.

Table 8: Descriptive analysis of distribution in terms of eGFR levels.

eGFR(mL/min/1.73m^2)	Number	Frequency
60-90	4	4.04
45-59	8	8.08
30-44	4	4.04
15-29	22	22.22
<15	61	61.62
Total	99	100.00

Graph 7: Distribution in terms of eGFR levels among subjects (N=99).

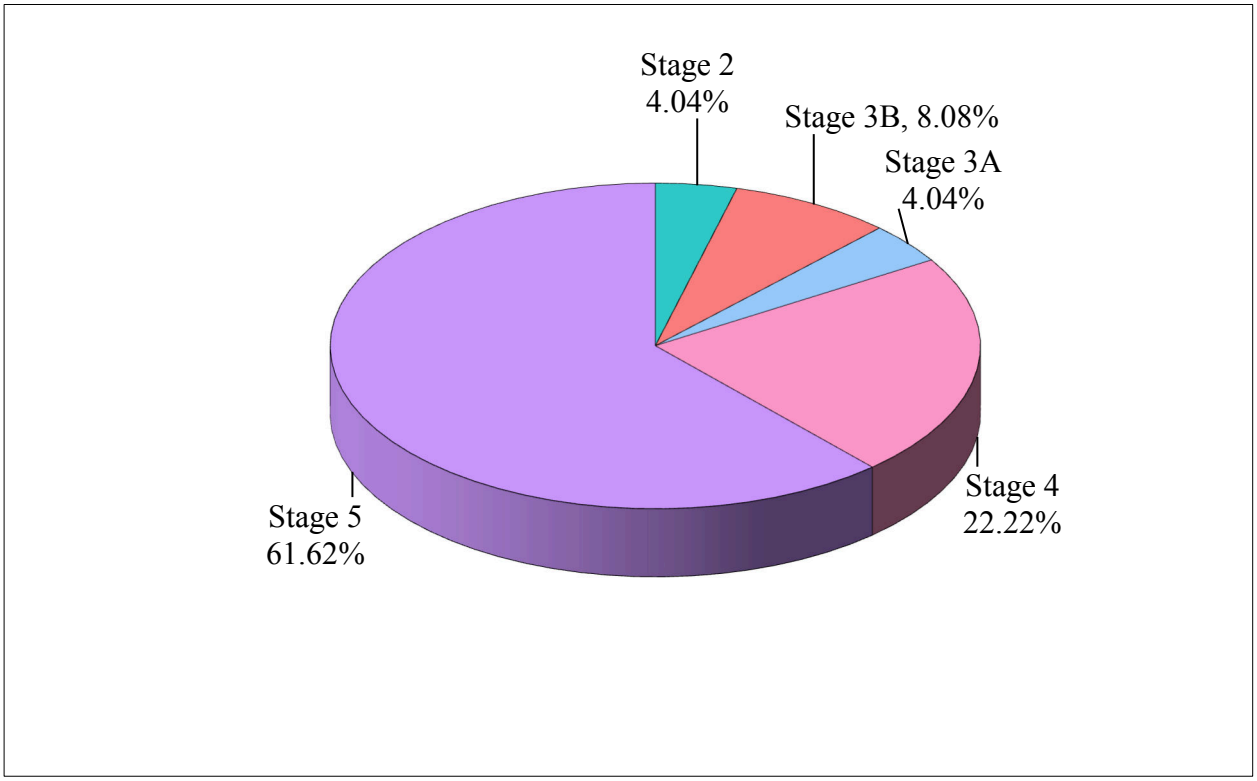


Maximum number (61) of patients had eGFR values < 15 mL per min per 1.73m^2. 4 patients had eGFR values between 60-90 mL per min per 1.73m^2 range.

Table 9: Descriptive analysis of distribution in terms of CKD stages.

CKD stages	Number	Frequency
Stage 2	4	4.04
Stage 3B	8	8.08
Stage 3A	4	4.04
Stage 4	22	22.22
Stage 5	61	61.62
Total	99	100.00

Graph 8: Distribution in terms of CKD stages among subjects (N=99).

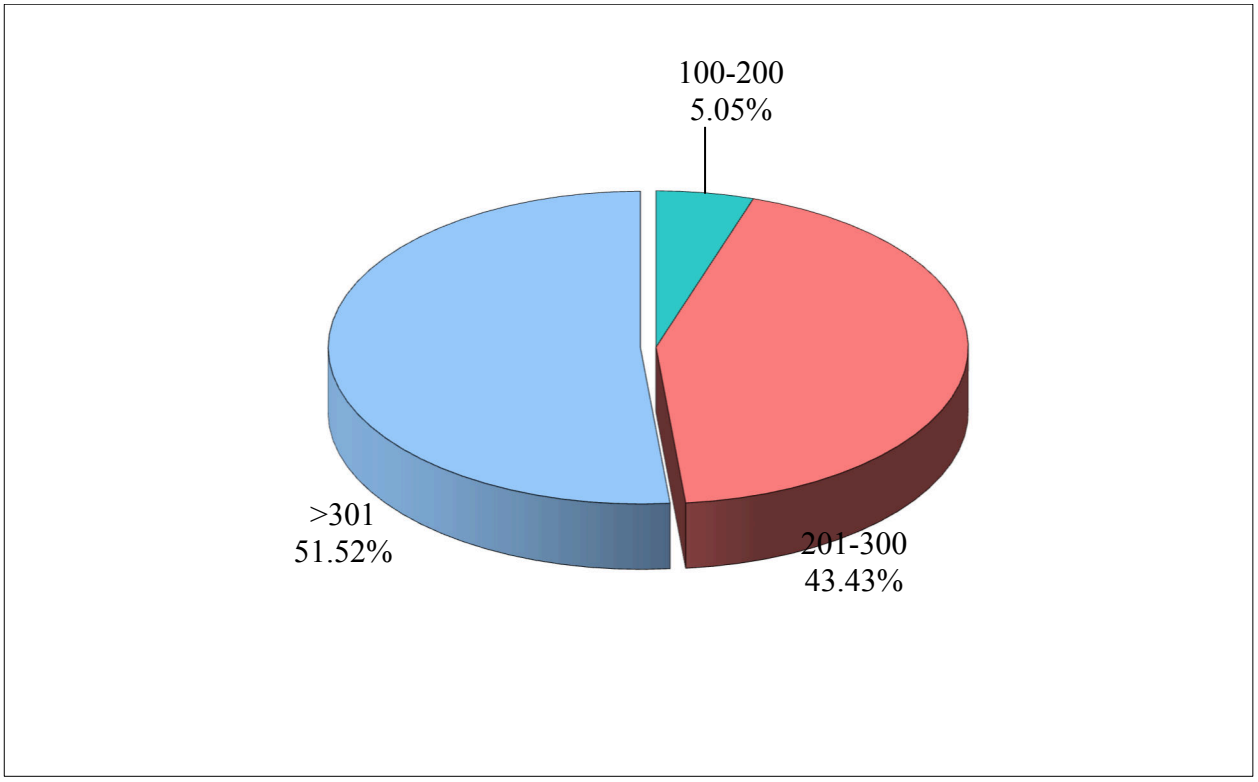


Maximum number (61) of subjects were in stage 5. Only 4 subjects were in stage 2.

Table 10: Descriptive analysis of distribution in terms of raised triglycerides (TG).

TG (mg/dl)	Number	Frequency
100-200	5	5.05
201-300	43	43.43
>301	51	51.52
Total	99	100.00

Graph 9: Distribution in terms of raised triglycerides (TG) among subjects.

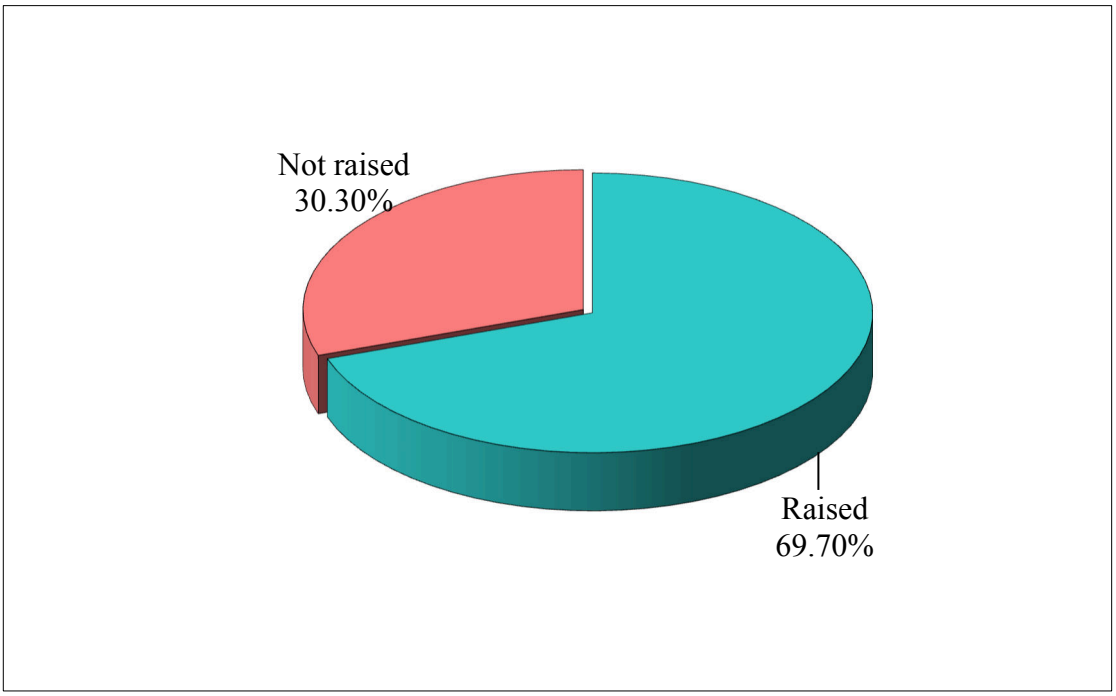


Maximum number of patients had triglycerides levels > 301mg/dl. Just 5 patients had triglycerides levels between 100-200 mg /dl.

Table 11: Descriptive analysis of distribution in terms of prevalence of raised IMT (N=99)

IMT (cm)	Number	Frequency
Raised	69	69.70
Not raised	30	30.30
Total	99	100.00

Graph 10: Distribution with respect to prevalence of raised IMT (N=99).

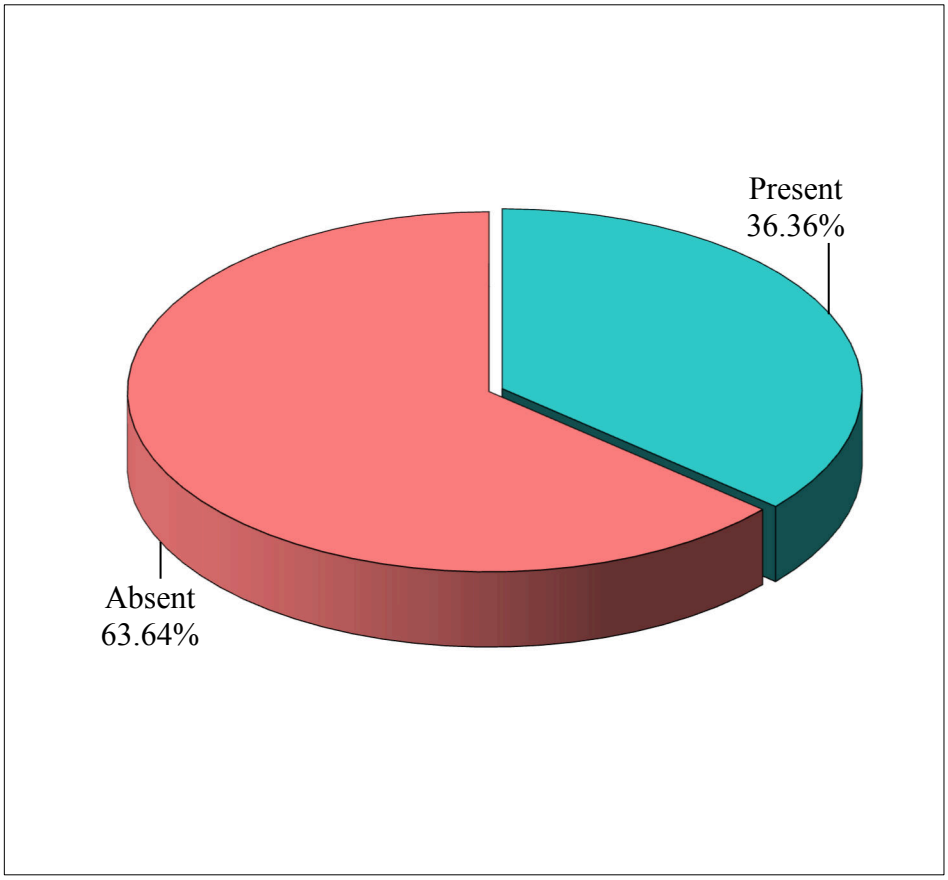


In the current research with sample size of 99, there were 30 (30.30%) cases who didn't have any atherosclerotic changes, 69 cases (69.70 %) had raised IMT suggesting a significant prevalence.

Table 12: Descriptive analysis of distribution in terms of prevalence of femoral wall calcification (N=99).

Wall calcification	Number	Frequency
Present	36	36.36
Absent	63	63.64
Total	99	100.00

Graph 11: Distribution with respect to prevalence of wall calcification (N=99).



Of the 99 cases, 36 (36.36%) patients had femoral artery wall calcification. However significant number (63.64%) didn't have wall calcification.

Table 13: Descriptive analysis of distribution in terms of prevalence of femoral wall calcification in subjects with raised IMT. (N=99).

Wall calcification	Raised IMT	%	Not raised IMT	%	Total	%
Present	31	86.11	5	13.89	36	36.36
Absent	38	60.32	25	39.68	63	63.64
Total	69	69.70	30	30.30	99	100.00
Chi-square=0.2620, p=0.6090						

The table suggests that of the 69 patients having raised IMT 31 patient had femoral wall calcification.

Table 14: Descriptive analysis of distribution in terms of prevalence of raised IMT among different age groups (N=99).

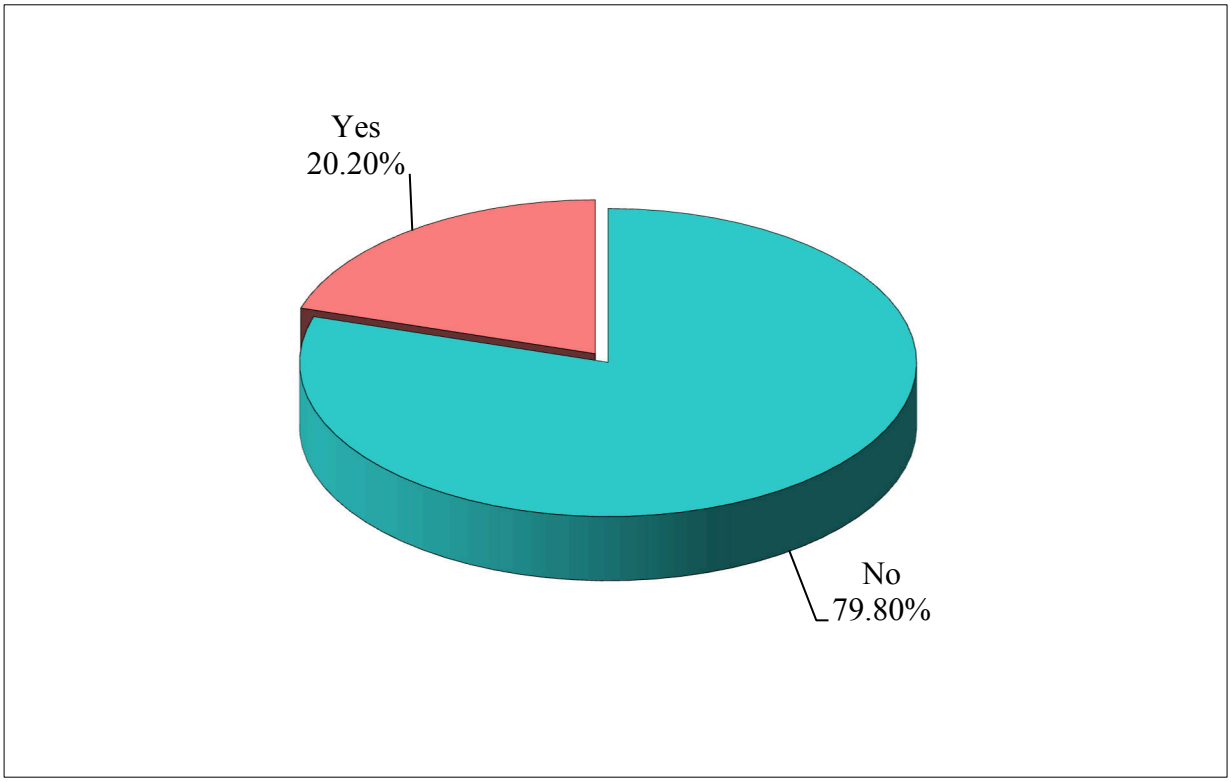
Age groups	Raised IMT	%	Not raised IMT	%	Total	%
<=30yrs	6	60.00	4	40.00	10	10.10
31-40yrs	8	61.54	5	38.46	13	13.13
41-50yrs	10	52.63	9	47.37	19	19.19
51-60yrs	18	69.23	8	30.77	26	26.26
61-70yrs	19	82.61	4	17.39	23	23.23
71-80yrs	8	100.00	0	0.00	8	8.08
Total	69	69.70	30	30.30	99	100.00
Chi-square=7.2170, p=0.0070,						

Maximum number (19) of subjects who had raised IMT were from age group of 61-70 years. However, all the patients of age group 71-80 years had raised Midlist number of patients with raised IMT were from age group 31-40 years.

Table 15: Descriptive analysis of distribution in terms of prevalence of PVD among subjects (N=99).

PVD	Number	Frequency
No	79	79.80
Yes	20	20.20
Total	99	100.00

Graph 12: Distribution in terms of prevalence of PVD among subjects

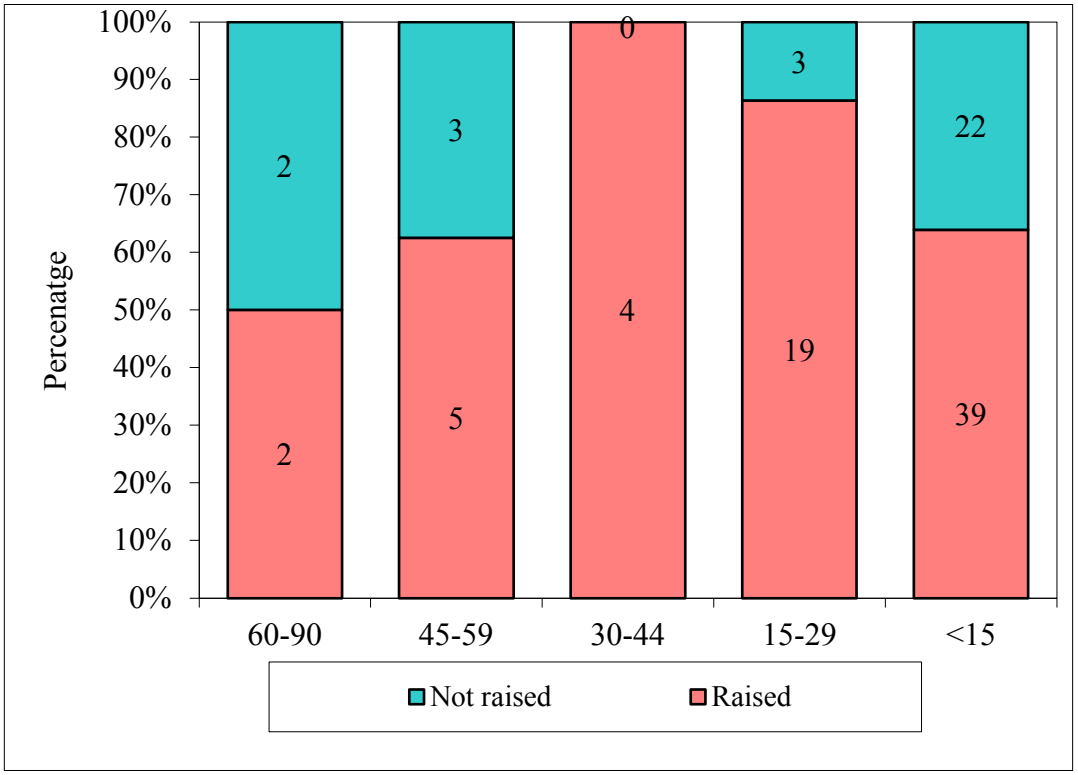


Of the 99 subjects about 20 patients had peripheral vascular disease. But majority (79.80%) didn't have any peripheral vascular disease.

Table 16: Descriptive analysis of association between eGFR and IMT (N=99).

eGFR(mL/min/1.73m^2)	Raised	%	Not raised	%	Total	%
60-90	2	50.00	2	50.00	4	4.04
45-59	5	62.50	3	37.50	8	8.08
30-44	4	100.00	0	0.00	4	4.04
15-29	19	86.36	3	13.64	22	22.22
<15	39	63.93	22	36.07	61	61.62
Total	69	69.70	30	30.30	99	100.00
Chi-square=6.5232, p = 0.1630						

Graph 13: Graphical representation of association between eGFR & IMT.

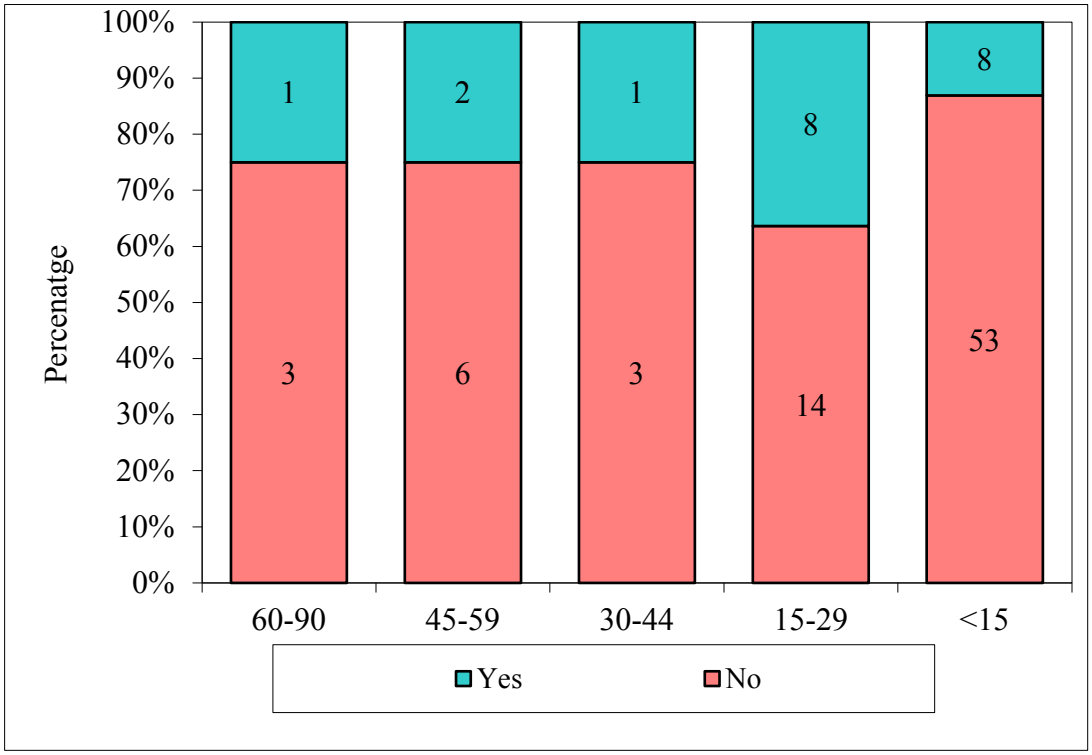


The study showed that all the patients with eGFR range 30-44 mL/min/1.73m^2 had raised IMT. And most of the patients (86.36%) with eGFR range 15-29 mL/min/1.73m^2 had raised IMT.

Table 17: Descriptive analysis of association between eGFR and PVD (N=99).

eGFR(mL/min/1.73m^2)	No	%	Yes	%	Total	%
60-90	3	75.00	1	25.00	4	4.04
45-59	6	75.00	2	25.00	8	8.08
30-44	3	75.00	1	25.00	4	4.04
15-29	14	63.64	8	36.36	22	22.22
<15	53	86.89	8	13.11	61	61.62
Total	79	79.80	20	20.20	99	100.00
Chi-square=5.6940, p = 0.2230						

Graph 14: Graphical representation of association between eGFR & PVD.

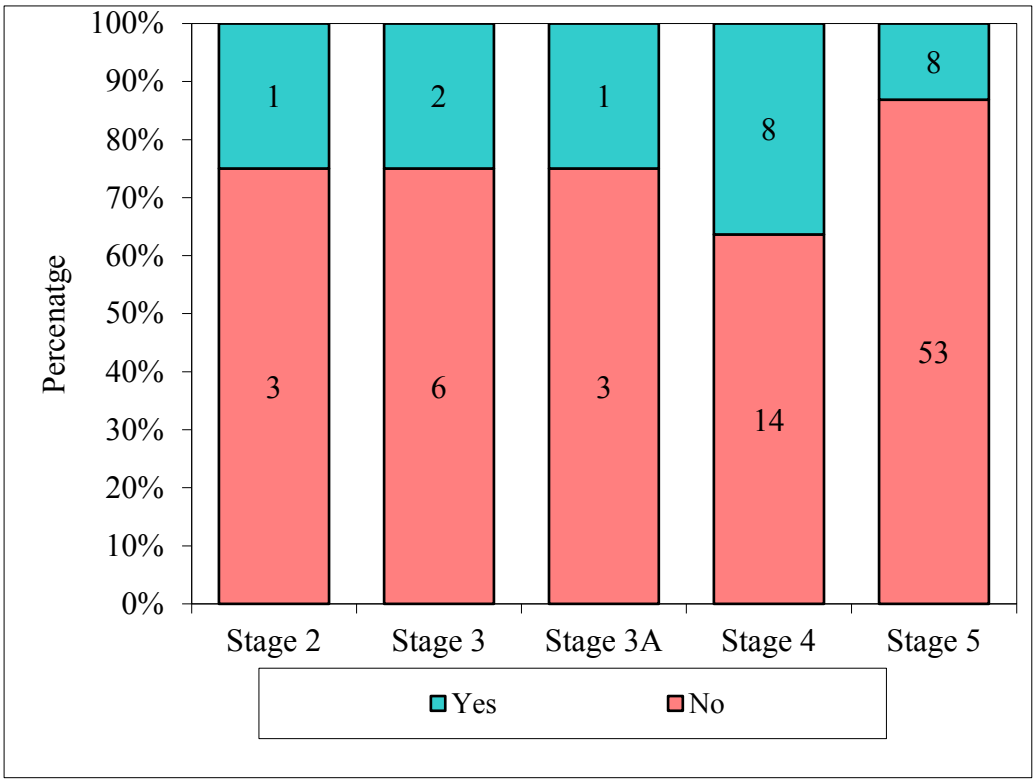


In the present study, it is evident that majority of cases with any eGFR range didn't have significant association with PVD.In the patients with eGFR < 15mL/min/1.73m2 range 86.89% of patients didn't have peripheral vascular disease.

Table 18: Descriptive analysis of association between CKD Stages and PVD.

CKD stages	No	%	Yes	%	Total	%
Stage 2	3	75.00	1	25.00	4	4.04
Stage 3	6	75.00	2	25.00	8	8.08
Stage 3A	3	75.00	1	25.00	4	4.04
Stage 4	14	63.64	8	36.36	22	22.22
Stage 5	53	86.89	8	13.11	61	61.62
Total	79	79.80	20	20.20	99	100.00
Chi-square=5.6940, p = 0.2230						

Graph 15: Graphical representation of association between CKD Stages & PVD

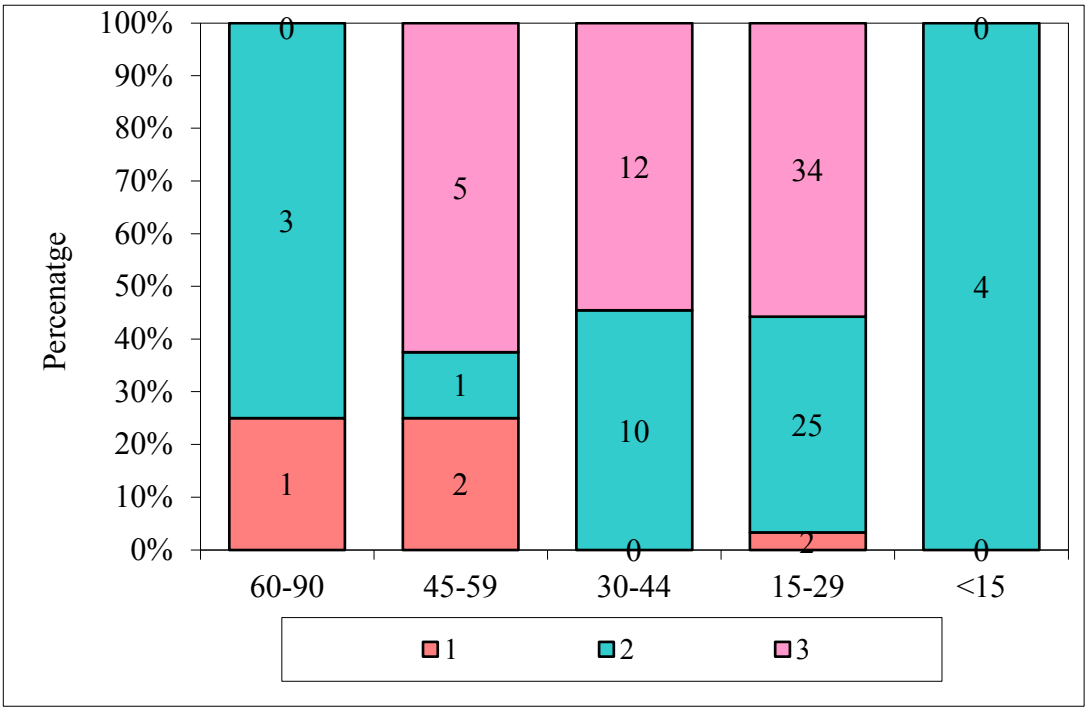


Similarly, the study showed that majority of cases with any CKD stages didn't have significant association with PVD. In the patients with CKD stage 5, 86.89% of patients didn't have peripheral vascular disease.

Table 19: Descriptive analysis of association between eGFR and TG (N=99).

eGFR(mL/min/1.73m^2)	100-200mg/dl	%	201-300mg/dl	%	>301mg/dl	%
60-90	1	25.00	3	75.00	0	0.00
45-59	2	25.00	1	12.50	5	62.50
30-44	0	0.00	10	45.45	12	54.55
15-29	2	3.28	25	40.98	34	55.74
<15	0	0.00	4	100.0	0	0.00
Total	5	5.05	43	43.43	51	51.52
Chi-square= 21.4390, p = 0.0060,						

Graph 16: Graphical representation of association between eGFR and TG

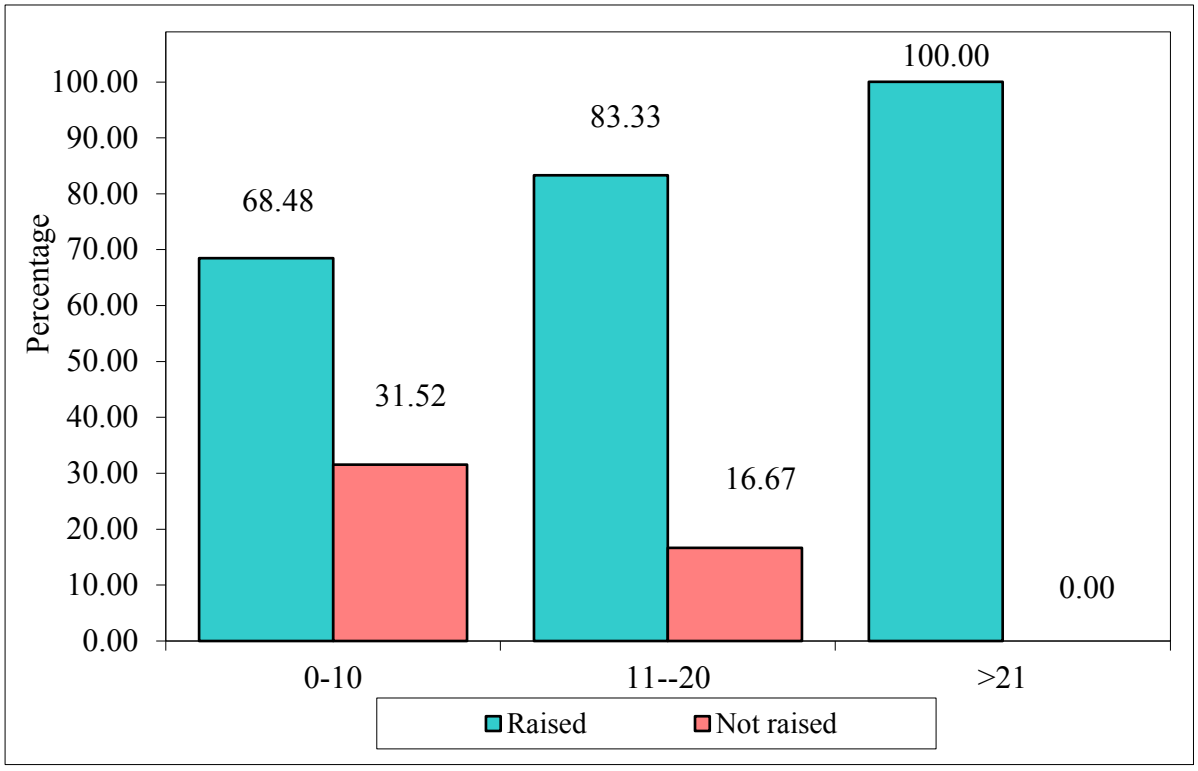


The table shows that in the study the patients with eGFR range 15-29 (mL/min/1.73m2) had maximum triglyceride levels.

Table 20: Descriptive analysis of association between Creatinine and IMT (N=99)

Creatinine(mg/dl)	Raised	%	Not raised	%	Total	%
0-10	63	68.48	29	31.52	92	92.93
11-21	5	83.33	1	16.67	6	6.06
>21	1	100.00	0	0.00	1	1.01
Total	69	69.70	30	30.30	99	100.00
Chi-square=1.0280, p = 0.5980						

Graph 17: Graphical representation of association between Creatinine and IMT

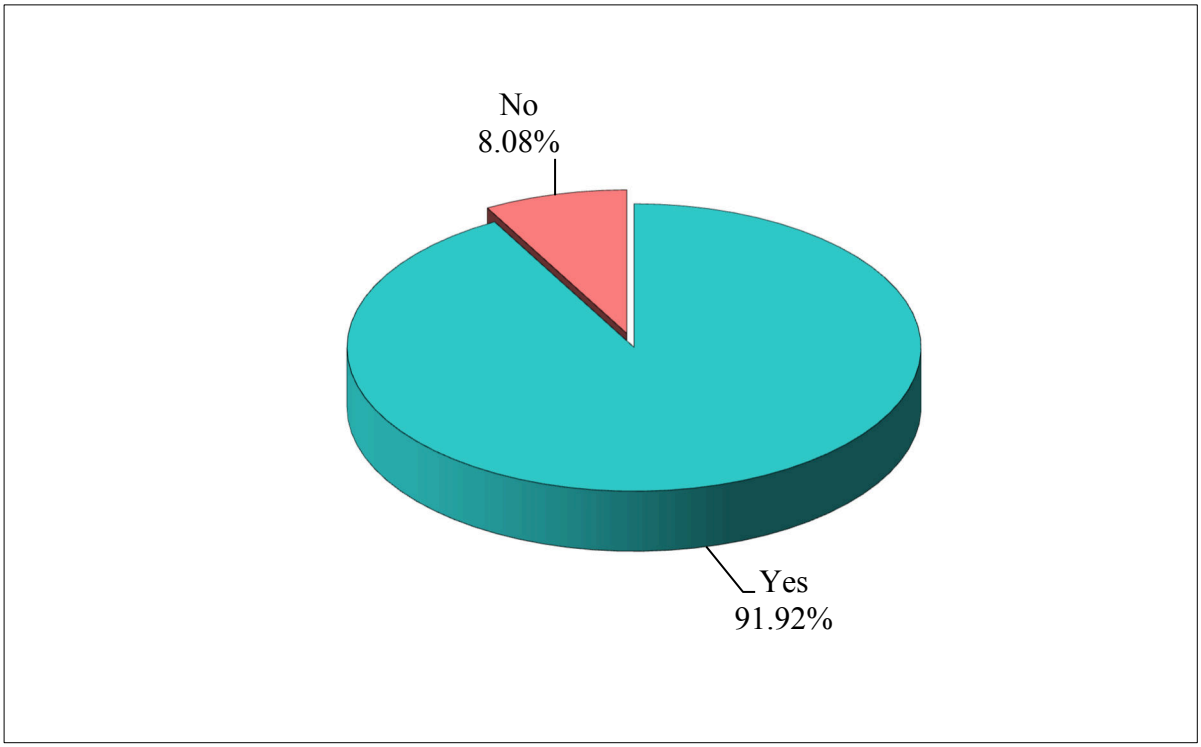


In the present study, the femoral IMT was raised in 68.48% of patients with creatinine range 0-10 mg/dl, 83.3 % of patient's creatinine range 11-20 mg/dl and in 1 patient in the creatinine value > 21 mg/dl.

Table 21: Descriptive analysis of distribution in terms of prevalence of Anemia among subjects (N=99).

HB low(gm/dl)	Number	Frequency
Yes	91	91.92
No	8	8.08
Total	99	100.00

Graph 18: Distribution in terms of prevalence of Anemia among subjects



Another significant finding in the study was that, about 91.92 % of the CKD subjects were anemic.

Table 22: Descriptive analysis of correlations among different numerical parameters by Karl Pearson's correlation coefficient (N=99). (*p<0.05)

Parameters	IMT	Urea	Creatinine	EGFR	HB	LDL/TG
IMT	-					
Urea	0.5143*	-				
Creatinine	0.3664*	0.6577*	-			
EGFR	-0.4313*	-0.5110*	-0.6076*	-		
HB	-0.2133*	-0.2367*	-0.4065*	0.2773*	-	
TG	0.2973*	0.2415*	0.2100*	-0.3175*	-0.0930	-

According to our study, urea levels had low degree of co relation with fIMT and with creatinine levels. The creatinine levels too had low degree of co relation with fIMT.

There was negative co-relation between eGFR with fIMT, Urea & creatinine.

Similarly, hemoglobin levels had negative co-relation with fixture & creatinine but had low degree of co relation with eGFR.

The triglyceride levels expressed low degree of co relation with fIMT, urea & creatinine and negative co -relation with hemoglobin levels.

Table 23: Descriptive analysis of summary of numerical parameters in the study

Parameters	Min	Max	Range	Mean	SD	Median
Age	15.00	83.00	68.00	52.42	15.95	56.00
IMT	0.02	0.13	0.11	0.08	0.02	0.07
Urea	40.00	258.00	236.00	91.37	54.12	78.00
Creatinine	1.30	29.58	28.38	5.61	4.02	4.60
EGFR	1.70	71.10	69.40	17.44	15.44	12.50
HB	4.50	15.00	10.50	9.98	1.99	9.90
TG	98.00	466.00	368.00	225.92	79.01	202.00

Lowest age of subject in the study group was 15 years and highest was 83 years. 52.42 years was the mean age.

Lowest IMT measured was 0.02 cm and the highest IMT was 0.11cm. Mean IMT was 0.08 cm.

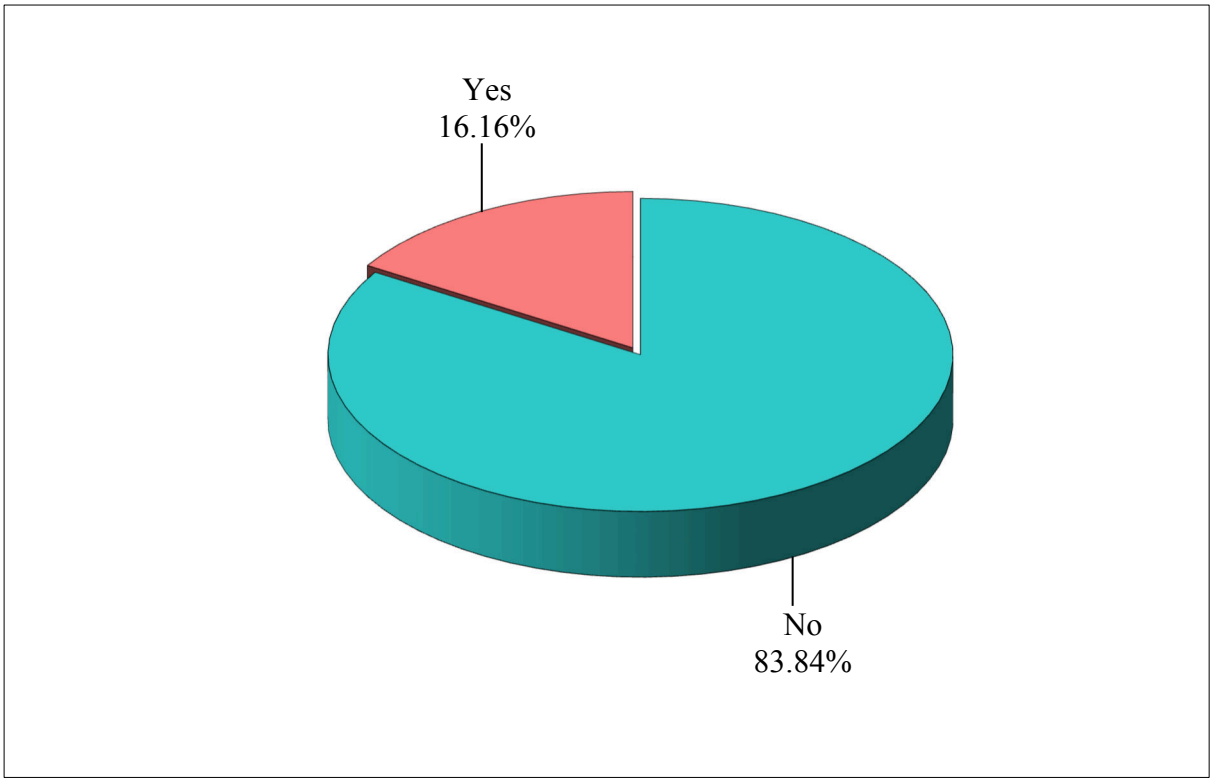
The lowest urea level of the patients was 22mg per dl and maximum value was 258mg per dl. The mean urea level of the patients was 91.37mg per dl. The lowest creatinine level was 1.2 mg per dl and the maximum value being 29.58 mg per dl. The mean value 5.61 mg/dl.

The lowest eGFR value recorded was 1.7 mL per min per 1.73m2 and highest being 71.10 mL per min per 1.73m2. Mean value of GFR being 17.44mL per min per $1.73m^2$. The lowest triglyceride level was 98.0 mg per dl & highest value found was 466.0 mg per dl. Mean value was 225.92 mg per dl.

Table 24: Descriptive analysis of distribution in terms of dialysis treatment among subjects (N=99).

On dialysis	Number	Frequency
No	83	83.84
Yes	16	16.16
Total	99	100.00

Graph 19: Distribution in terms of dialysis treatment among subjects (N=99).



The study included 83.84 % of subjects not undergoing hemodialysis treatment and had 16.16 % subjects undergoing hemodialysis treatment.

DISCUSSION

Chronic renal disorder is a stand-alone threat for atherosclerosis. Color Doppler ultrasonography is a non-invasive and cost-effective imaging modality that has a vital function in assessing the severity of atherosclerotic disease in PVD in CKD patients.

Age & Sex distribution:

In the current study, which included 99 individuals, the number of male patients was more, 70 cases (76.9%) when compared to the female patients who were 29 (29.9%).

A maximum number of cases in this study were from the age group of 50-60 i.e. 26 cases (26.26%) followed by the age group of 60-70 yrs. which had 23 cases (23.23%).

16 yrs. were the minimum age of the patient in our study and the maximum age was 83 yrs. The mean age is 52.39 yrs.

The maximum number (19) of subjects who had raised IMT were from the age group of 61-70 years. However, all the patients of age group 71-80 years had raised IMT, making this age group the most vulnerable age for atherosclerosis. Least number of patients with raised IMT were from age group 31-40 years.

Men were more affected as compared to women.

Research by Simon Hsu et al. showed that the prevalence of plaque was higher in males, which is consistent with our study.[76]

Symptomatology:

In our study, 46 patients (46.6%) had a symptom of edema in areas like the periorbital region and lower leg, whereas 28 (28.28%) patients had a symptom of decreased urine output.

Prevalence of atherosclerosis & raised IMT:

Mannheim consensus concluded that the plaque presence to be defined as if plaque that is encroaching the lumen is 0.5cm or more.

In this study out of 99 patients, 69 patients (69.70%) had raised IMT, whereas 30 patients (30.30%) didn't have raised IMT without evidence of any atherosclerotic plaques, making the prevalence of atherosclerosis in the given CKD population as 69.70%. The highest IMT in our subjects was 0.13cm. The mean IMT was 0.08cm.

This was in consistency with a research of Nariman et al., who had femoral IMT in chronic renal disorder subjects in comparison with normal individuals.[94]

The result was also matching with a study by Simon et al., who had a plaque prevalence of 46% among 256 patients with atherosclerosis. The mean common femoral artery intima-media thickness was 0.99 +/- 0.61 cm and the mean superficial femoral artery was 0.63 +/- 0.16 cm.

Though the prevalence of atherosclerosis in the CKD population was high (69.70%), the percentage of subjects having peripheral vascular disease was 20.20 %.

Raised IMT in diabetics:

In our study out of 99 subjects, 48 subjects had diabetes. Of the 48 diabetic patients, 36 diabetic patients (75.0%) had raised IMT, suggesting a high prevalence of atherosclerosis among diabetics.

The study by Le et al also had similar results wherein femoral artery was thickened in 38.2 % of diabetics.

Wall calcification of femoral artery:

It's noteworthy that, out of 99 subjects, 36.36 % of subjects had wall calcification along with atheromatosis, since it also plays a role in peripheral vascular disease.

Raised creatinine levels:

Out of the 99 subjects, the maximum number i.e., 92 (92.93%) subjects had creatinine values in the range of 1.3-10 mg/dl. 6 subjects (6.06%) had creatinine in the range of 11-21 mg/dl and only one subject had creatinine > 21 mg/dl.

The lower range of a few of the patients in the 92.93 percentile could be attributed to the ongoing hemodialysis treatment.

Raised Urea levels:

Of 99 subjects ,62 patients (62.63%) had urea levels in the range of 40-100 mg/dl,34 patients (34.34%) had urea levels in the range of 101-200 and lastly just 3 subjects (3.03 %) had urea levels > 201 mg/dl.

eGFR distribution among the cases:

Using the demographic data and creatinine values, the GFR was estimated using the recent CKD EPI formula[92].

The CKD EPI equation being:

$$\mathbf{GFR = 141 \times \min(S.\,creatinine/\kappa, 1)^{\alpha} \times \max(S.\,creatinine/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018\ [for\ female] \times 1.159\ [for\ African]}$$

$\kappa = 0.7$ in female and 0.9 in male,

$\alpha = -0.329$ in females and -0.411 for male.

According to calculation, maximum subjects had eGFR value less than 15mL/min/1.73m^2, the number being 61(61.62%). 22 (22.22 %) patients had GFR in the range 15- /min/1.73m^2. 4 (4.04%) patients had GFR 30-44mL per min per 1.73m^2. 8 (8.08%) subjects had 45-59 mL per min per 1.73m^2 and lastly 4 (4.04%) subjects had GFR 60-90 mL per min per 1.73m^2.

CKD stage distribution among the cases:

In accordance with eGFR values, the CKD stages were assigned.

Maximum number of subjects were in CKD stage 5, the number being 61(61.62%). 22 (22.22 %) subjects had CKD 4. 4 (4.04%) subjects had CKD 3A. 8 (8.08%) subjects were in stage 3B & lastly 4 (4.04%) subjects were in CKD Stage 2.

Hemodialysis status among the study subjects:

The study included 83.84 % of subjects not undergoing hemodialysis treatment and had 16.16 % of subjects undergoing hemodialysis treatment.

Distribution in terms of raised triglycerides (TG) among subjects:

The triglyceride profile of the cases was noted and it was seen that maximum subjects i.e., 51 (51.52 %) had triglyceride levels > 301 mg/dl. 43 (43.43 %) had in the range of 201-300 mg/dl and just 5 subjects had triglycerides in the range of 100-200 mg/dl.

Association between eGFR and IMT:

In the present study, 63.93 % of patients with eGFR < 15 mL/min/1.73m^2 had raised IMT,86.36 % of patients with eGFR range 15-29 mL/min/1.73m^2 had raised IMT, all of the (4) patients (100%) with eGFR range 30-44 mL/min/1.73m^2 had raised IMT.Also 62.50% of patients of eGFR range 45-59 mL/min/1.73m^2 had raised IMT. Lastly 50% of patients with eGFR range 60-90 mL/min/1.73m^2 had raised IMT.

This suggests that only groups with eGFR values 15-29 & 30-44 mL/min/1.73m^2 had a strong positive correlation.

This is in contradiction to the study by Hsu et al, who had a significant association with lower eGFR values and higher fIMT values[76]. However, the adjusted model in terms of age, sex, race, the association was no longer was significant.

Association between CKD Stages and IMT:

Similar results were obtained as stated above since CKD categorization into stages depends on the eGFR values. Our study showed that only CKD Stages 4 & 5 had

more prevalence of higher IMT. The rest of the CKD stages didn't have a higher prevalence of raised IMT.

This is in contradiction with the study by Hsu et al, who had higher IMT with greater stages of CKD. However, in fully adjusted groups the relationship was not significant[76].

Association between eGFR and PVD:

According to our results, 13.11 % of patients with eGFR < 15 mL/min/1.73m^2 had PVD ,36.36 % of patients with eGFR range 15-29 mL/min/1.73m^2 had PVD, 25% of the patients with eGFR range 30-44 , 45-59 & 60-90 mL/min/1.73m^2 had PVD .($p = 0.22$) This suggests that none of the eGFR patients groups had any significant co-relation with PVD.

Association between CKD and PVD:

Similar results were obtained as stated above since CKD categorization into stages depends on the eGFR values. Hence 3.11 % of patients with CKD Stage 5 had PVD,36.36 % of patients with Stage 4 had PVD, 25% of the patients with Stage 3A, 3B & 2 had PVD. ($p = 0.22$) This suggests that none of the CKD Stages had any significant co-relation with PVD.

Association between eGFR and Triglyceride levels:

The study showed that all the patients with eGFR < 15 mL/min/1.73m^2 had higher triglyceride ranges of 201-300 mg/dl with a p-value of 0.0060, suggesting a statistically significant association between, lower eGFR values and higher triglyceride levels.

Association between Creatinine and IMT:

According to our study, 63 % of the patients with creatinine levels 1.3-10 mg/dl had raised IMT, 83.33 % of patients with creatinine levels 11-20 mg/dl had raised IMT & lastly one patient with creatinine levels > 21 mg/dl had raised IMT.

Though the percentage of groups with raised creatinine had higher IMT, there was no evidence for the statistically strong association between the two parameters ($p = 0.59$).

Prevalence of Anemia among subjects:

Out of 99 subjects, 91 subjects including both males and females had low hemoglobin levels, suggesting a very high prevalence of anemia among CKD patients of our study.

Correlations among different numerical parameters by Karl Pearson's correlation coefficient (N=99) (*p<0.05):

According to our study, urea levels had a low degree of co-relation with fIMT and with creatinine levels. The creatinine levels too had a low degree of co-relation with fIMT.

There was a negative correlation between eGFR with fIMT, Urea & creatinine.

Similarly, hemoglobin levels had a negative co-relation with fIMT, urea & creatinine but had a low degree of co-relation with eGFR.

The triglyceride levels expressed a low degree of co-relation with fIMT, urea & creatinine and a negative correlation with hemoglobin levels.

LIMITATIONS.

Examination technique and small sample size are the limitations of the study. Large sample size would have helped in establishing a correlation between femoral intima-media thickness and atherosclerosis. And also, in determining the cut-off values for femoral intima-media thickness in atherosclerosis in chronic kidney disease patients.

Since the ultrasound technique depends on the skill of the examiner, there is a lot of intra and inter-observer variations in assessing IMT.

Also, there were a lot of unavoidable risk factors which were not matched in the study such as age, BMI, smoking habits, and hypertension which would have also been factors in raising the intima-media thickness.

Lastly, atherosclerosis was not confirmed by histopathology which is the most gold standard investigation for confirmation of the same.

CONCLUSION

- Colour Doppler ultrasonography is the safest and first-line investigation for evaluation of peripheral vessels since it's a non-invasive, economic, and devoid of any radiation.
- This study indicates that the prevalence of atherosclerosis is more common in men and was more common above 50 years of age. However, 71 to 80 years is the most vulnerable age group.
- This study establishes evidence of the atherosclerotic prevalence in the form of raised IMT in patients suffering from CKD. 86.36 % & 100 % was the prevalence in CKD 3B & 4 respectively in this study. The overall prevalence of atherosclerosis in the given study group was found to be 69.70 %.
- Not all CKD groups had significant co-relation with IMT except one with eGFR values 15-29 & 30-44 mL/min/1.73m^2 who had a strong positive correlation.
- This study establishes that there's no significant co-relation between eGFR and peripheral vascular disease among the subjects.
- This study indicates a higher prevalence of raised IMT among diabetics (75.0%).
- A significant association between lower eGFR values and higher triglyceride levels was found in the study.
- A very high prevalence (91.92 %) of anemia among CKD patients in the study was seen.

SUMMARY

- Atherosclerosis is one of the most common pathologies affecting the femoral arteries and CKD is one of the risk factors. This study was aimed to assess the prevalence and study relationship between atherosclerosis in femoral arteries among CKD patients.
- Chronic kidney disease (CKD) is strongly associated with peripheral artery disease (PAD). The prevalence of CKD worldwide is estimated to be 11-13%.
- The exact prevalence of CKD in India could not be estimated, however approximate prevalence is found to be 800 per million population.
- Detection of sub-clinical PAD may allow for early interventions or prevention of PAD in persons with CKD. Whether the presence of atherosclerotic plaque and femoral intima-media thickness (IMT) is associated with kidney function is unknown. Such study is not done previously in our institution; hence this study is being carried out.
- The study was a hospital-based cross-sectional study, conducted from January 2020 – December 2020 in patients referred to the radiology department of KLE'S Dr. Prabhakar Kore Hospital Belagavi for femoral Doppler ultrasonography.
- The sample consisted of 99 patients with CKD. Exclusion criteria were patients with past renal transplants and patients with a known case of renal malignancy based on their history and medical records.
- After obtaining informed consent baseline data was recorded on a self-designed proforma. Doppler ultrasonography of femoral arteries was performed in all the

participants using either GE VOLUSON P8 scanner 7.5 – 12 MHz high-frequency linear transducer.

- Patients were positioned supine with their legs extended and examined with a transverse scan of the right and left femoral area, the common femoral artery would be focused, and IMT would be measured on the transverse axis.
- 99 CKD cases were included in this study, who underwent femoral Doppler ultrasonography, 46 had a symptom of edema, and 22 had symptoms of decreased urine output.
- It was found that males were affected more as compared to females.
- Maximum numbers of cases with raised IMT were in the age group of 61-70 years, however all the subjects of age group of 71 to 80 years had raised IMT, making it the vulnerable age group.
- Out of 99 subjects, 69 patients had raised IMT and 30 patients had normal IMT. The prevalence of atherosclerosis in the given study group was found to be 69.70 %.
- Most of the subjects in the study were from CKD Stage 5.
- CKD Stages 4 & 5 had the highest prevalence of thickened IMTs.
- Higher prevalence of raised IMT among diabetics (75.0%).
- Not all CKD groups had significant co-relation with IMT except one with eGFR values of 15-29 & 30-44 mL/min/1.73m2 who had strong positive co-relation.
- None of the eGFR patient groups had any significant co-relation with PVD.
- None of the CKD Stages had any significant co-relation with PVD.
- A significant association between lower eGFR values and higher triglyceride levels was found in the study.
- Very high prevalence of anemia among CKD patients of our study.

- Though the percentage of groups with raised creatinine had higher IMT, there was no evidence for the statistically strong association between the two parameters.

- Limitations of the present study include:

  - Cross-sectional assessment.
  - Small sample size with intra & inter-observer variation in the technique.
  - Unavoidable risk factors like age, BMI, smoking habits, and hypertension.
  - Non-confirmation of atherosclerosis with histopathology (gold standard method).

- Recommendations for future study include:

  - Longitudinal assessment with larger sample size & control groups.
  - Use of confirmatory methods like histopathology.

BIBLIOGRAPHY

1. Kidney Disease| Improving Global Outcomes. Chapter 1: Definition and classification of CKD. Kidney Int Suppl (2011). 2013 Jan;3(1):19-62.
2. Agarwal SK, Srivastava RK. Chronic kidney disease in India: challenges and solutions. Nephron clinical practice. 2009;111(3):c197-203.
3. Subbiah AK, Chhabra YK, Mahajan S. Cardiovascular disease in patients with chronic kidney disease: a neglected subgroup. Heart Asia. 2016 Jul 1;8(2):56-61.
4. Swift H, Bordoni B. Anatomy, Bony Pelvis and Lower Limb, Femoral Artery. StatPearls [Internet]. 2021 Feb 7.
5. Gocmen-Mas N, Aksu F, Edizer M, Magden O, Tayfur V, Seyhan T. The arterial anatomy of the saphenous flap: a cadaveric study. Folia morphologica. 2012;71(1):10-4.
6. Kasapis C, Gurm HS. Current approach to the diagnosis and treatment of femoral-popliteal arterial disease. A systematic review. Current cardiology reviews. 2009 Nov 1;5(4):296-311..
7. Tzouma G, Kopanakis NA, Tsakotos G, Skandalakis PN, Filippou D. Anatomic variations of the deep femoral artery and its branches: clinical implications on anterolateral thigh harvesting. Cureus. 2020 Apr;12(4).
8. Tucker WD, Arora Y, Mahajan K. Anatomy, blood vessels.
9. Lnsis A. Atherosclenrosis. Nature. 2000;407:233-41.
10. Allawi AA. Chronic kidney disease and risk of coronary artery disease, a prospective Study. Al-Kindy College Medical Journal. 2013;9(1):1-8.
11. Singh AK, Farag YM, Mittal BV, Subramanian KK, Reddy SR, Acharya VN, Almeida AF, Channakeshavamurthy A, Ballal HS, Gaccione P, Issacs R. Epidemiology and risk factors of chronic kidney disease in India–results from the

SEEK (Screening and Early Evaluation of Kidney Disease) study. BMC nephrology. 2013 Dec;14(1):1-0.

12. Life expectancy at birth – Male (years) 2013 Country Ranks, By Rank SOURCE: CIA World Factbook. 2013
13. Palanca A, Castelblanco E, Perpiñán H, Betriu A, Soldevila B, Valdivielso JM, Bermúdez M, Duran X, Fernández E, Puig-Domingo M, Groop PH. Prevalence and progression of subclinical atherosclerosis in patients with chronic kidney disease and diabetes. Atherosclerosis. 2018 Sep 1;276:50-7
14. Prevalence and progression of subclinical atherosclerosis in patients with chronic kidney disease and diabetes,Atherosclerosis,Volume 276,2018,Pages 50-57,ISSN 0021-9150,
15. Stubbe J, Skov V, Thiesson HC, Larsen KE, Hansen ML, Jensen BL, Jespersen B, Rasmussen LM. Identification of differential gene expression patterns in human arteries from patients with chronic kidney disease. American Journal of Physiology-Renal Physiology. 2018 Jun 1;314(6):F1117-28.
16. Mathew RO, Bangalore S, Lavelle MP, Pellikka PA, Sidhu MS, Boden WE, Asif A. Diagnosis and management of atherosclerotic cardiovascular disease in chronic kidney disease: a review. Kidney international. 2017 Apr 1;91(4):797-807.
17. Valdivielso JM, Rodríguez-Puyol D, Pascual J, Barrios C, Bermúdez-López M, Sánchez-Niño MD, Pérez-Fernández M, Ortiz A. Atherosclerosis in chronic kidney disease: more, less, or just different?. Arteriosclerosis, thrombosis, and vascular biology. 2019 Oct;39(10):1938-66.

18. Moe SM, Chen NX. Mechanisms of vascular calcification in chronic kidney disease. Journal of the American Society of Nephrology. 2008 Feb 1;19(2):213-6.
19. Fang Y, Ginsberg C, Sugatani T, Monier-Faugere MC, Malluche H, Hruska KA. Early chronic kidney disease–mineral bone disorder stimulates vascular calcification. Kidney international. 2014 Jan 1;85(1):142-50.
20. Mathew RO, Bangalore S, Lavelle MP, Pellikka PA, Sidhu MS, Boden WE, Asif A. Diagnosis and management of atherosclerotic cardiovascular disease in chronic kidney disease: a review. Kidney international. 2017 Apr 1;91(4):797-807.
21. Coll B, Betriu A, Martínez-Alonso M, Amoedo ML, Arcidiacono MV, Borras M, Valdivielso JM, Fernández E. Large artery calcification on dialysis patients is located in the intima and related to atherosclerosis. Clinical Journal of the American Society of Nephrology. 2011 Feb 1;6(2):303-10.
22. Pai AS, Giachelli CM. Matrix remodeling in vascular calcification associated with chronic kidney disease. Journal of the American Society of Nephrology. 2010 Oct 1;21(10):1637-40.
23. Kendrick J, Chonchol M. The role of phosphorus in the development and progression of vascular calcification. American Journal of Kidney Diseases. 2011 Nov 1;58(5):826-34.
24. Valcheva P, Cardus A, Panizo S, Parisi E, Bozic M, Novoa JM, Dusso A, Fernández E, Valdivielso JM. Lack of vitamin D receptor causes stress-induced premature senescence in vascular smooth muscle cells through enhanced local angiotensin-II signals. Atherosclerosis. 2014 Aug 1;235(2):247-55.

25. Torremadé N, Bozic M, Panizo S, Barrio-Vazquez S, Fernandez-Martín JL, Encinas M, Goltzman D, Arcidiacono MV, Fernandez E, Valdivielso JM. Vascular Calcification Induced by Chronic Kidney Disease Is Mediated by an Increase of 1α-Hydroxylase Expression in Vascular Smooth Muscle Cells. Journal of Bone and Mineral Research. 2016 Oct;31(10):1865-76.
26. Alesutan I, Voelkl J, Feger M, Kratschmar DV, Castor T, Mia S, Sacherer M, Viereck R, Borst O, Leibrock C, Gawaz M. Involvement of vascular aldosterone synthase in phosphate-induced osteogenic transformation of vascular smooth muscle cells. Scientific reports. 2017 May 17;7(1):1-5.
27. Mokas S, Larivière R, Lamalice L, Gobeil S, Cornfield DN, Agharazii M, Richard DE. Hypoxia-inducible factor-1 plays a role in phosphate-induced vascular smooth muscle cell calcification. Kidney international. 2016 Sep 1;90(3):598-609.
28. Crouthamel MH, Lau WL, Leaf EM, Chavkin NW, Wallingford MC, Peterson DF, Li X, Liu Y, Chin MT, Levi M, Giachelli CM. Sodium-dependent phosphate cotransporters and phosphate-induced calcification of vascular smooth muscle cells: redundant roles for PiT-1 and PiT-2. Arteriosclerosis, thrombosis, and vascular biology. 2013 Nov;33(11):2625-32.
29. de Oca AM, Madueno JA, Martinez-Moreno JM, Guerrero F, Muñoz-Castañeda J, Rodriguez-Ortiz ME, Mendoza FJ, Almaden Y, Lopez I, Rodriguez M, Aguilera-Tejero E. High-phosphate-induced calcification is related to SM22α promoter methylation in vascular smooth muscle cells. Journal of Bone and Mineral Research. 2010 Sep;25(9):1996-2005.
30. Junyent M, Martínez M, Borràs M, Coll B, Valdivielso JM, Vidal T, Sarró F, Roig J, Craver L, Fernández E. Predicting cardiovascular disease morbidity and

mortality in chronic kidney disease in Spain. The rationale and design of NEFRONA: a prospective, multicenter, observational cohort study. BMC nephrology. 2010 Dec;11(1):1-8.

31. Junyent M, Martínez Alonso M, Borràs M, Betriu i Bars M, Coll B, Marco Mayayo MP, Sarró F, Valdivielso Revilla JM, Fernández i Giráldez E. Usefulness of imaging techniques and novel biomarkers in the prediction of cardiovascular risk in patients with chronic kidney disease in Spain: the NEFRONA project. Nefrologia, 2010, vol. 30, núm. 1, p. 119-126. 2010.
32. Kwan BC, Kronenberg F, Beddhu S, Cheung AK. Lipoprotein metabolism and lipid management in chronic kidney disease. Journal of the American Society of Nephrology. 2007 Apr 1;18(4):1246-61.
33. Florens N, Calzada C, Lyasko E, Juillard L, Soulage CO. Modified lipids and lipoproteins in chronic kidney disease: a new class of uremic toxins. Toxins. 2016 Dec;8(12):376.
34. Reiss AB, Voloshyna I, De Leon J, Miyawaki N, Mattana J. Cholesterol metabolism in CKD. American Journal of Kidney Diseases. 2015 Dec 1;66(6):1071-82.
35. Keane WF, Tomassini JE, Neff DR. Lipid abnormalities in patients with chronic kidney disease: implications for the pathophysiology of atherosclerosis. Journal of atherosclerosis and thrombosis. 2012:12849.
36. Betriu A, Martinez-Alonso M, Arcidiacono MV, Cannata-Andia J, Pascual J, Valdivielso JM, Fernández E, Investigators from the NEFRONA Study. Prevalence of subclinical atheromatosis and associated risk factors in chronic kidney disease: the NEFRONA study. Nephrology Dialysis Transplantation. 2014 Jul 1;29(7):1415-22.

37. Bermudez-Lopez M, Forne C, Amigo N, Bozic M, Arroyo D, Bretones T, Alonso N, Cambray S, Del Pino MD, Mauricio D, Gorriz JL. An in-depth analysis shows a hidden atherogenic lipoprotein profile in non-diabetic chronic kidney disease patients. Expert opinion on therapeutic targets. 2019 Jul 3;23(7):619-30.
38. Bermúdez-López M, Arroyo D, Betriu À, Masana L, Fernández E, Valdivielso JM. New perspectives on CKD-induced dyslipidemia. Expert opinion on therapeutic targets. 2017 Oct 3;21(10):967-76.
39. Ritz E, Wanner C. Lipid abnormalities and cardiovascular risk in renal disease. Journal of the American Society of Nephrology. 2008 Jun 1;19(6):1065-70.
40. Wang Z, Nicholls SJ, Rodriguez ER, Kummu O, Hörkkö S, Barnard J, Reynolds WF, Topol EJ, DiDonato JA, Hazen SL. Protein carbamylation links inflammation, smoking, uremia and atherogenesis. Nature medicine. 2007 Oct;13(10):1176-84.
41. Bermúdez-López M, Betriu À, Valdivielso JM, Bretones del Pino T, Arroyo D, Fernández E. Beyond the traditional lipid parameters in chronic kidney disease. Nefrología (English Edition). 2018 Mar 1;38(2):109-13.
42. Speer T, Zewinger S, Fliser D. Uraemic dyslipidaemia revisited: role of high-density lipoprotein. Nephrology Dialysis Transplantation. 2013 Oct 1;28(10):2456-63.
43. Swaminathan S, Shah SV. Novel inflammatory mechanisms of accelerated atherosclerosis in kidney disease. Kidney international. 2011 Sep 1;80(5):453-63.
44. Menon V, Sarnak MJ. The epidemiology of chronic kidney disease stages 1 to 4 and cardiovascular disease: a high-risk combination. American journal of kidney diseases. 2005 Jan 1;45(1):223-32.

45. Castillo-Rodríguez E, Pizarro-Sánchez S, Sanz AB, Ramos AM, Sanchez-Niño MD, Martin-Cleary C, Fernandez-Fernandez B, Ortiz A. Inflammatory cytokines as uremic toxins:"Ni son todos los que estan, ni estan todos los que son". Toxins. 2017 Apr;9(4):114.
46. Zoccali C, Vanholder R, Massy ZA, Ortiz A, Sarafidis P, Dekker FW, Fliser D, Fouque D, Heine GH, Jager KJ, Kanbay M. The systemic nature of CKD. Nature Reviews Nephrology. 2017 Jun;13(6):344-58.
47. Zimmermann J. Herrlinger S, Pruy A, Metzger T, and Wanner C. Inflammation enhances cardiovascular risk and mortality in hemodialysis patients. Kidney Int. 1999;55:648-58.
48. Pecoits-Filho R, Bárány P, Lindholm B, Heimbürger O, Stenvinkel P. Interleukin-6 is an independent predictor of mortality in patients starting dialysis treatment. Nephrology Dialysis Transplantation. 2002 Sep 1;17(9):1684-8.
49. Porażko T, Kuźniar J, Kusztal M, Kuźniar TJ, Weyde W, Kuriata-Kordek M, Klinger M. IL-18 is involved in vascular injury in end-stage renal disease patients. Nephrology Dialysis Transplantation. 2009 Feb 1;24(2):589-96.
50. Kalantar-Zadeh K, Brennan ML, Hazen SL. Serum myeloperoxidase and mortality in maintenance hemodialysis patients. American Journal of Kidney Diseases. 2006 Jul 1;48(1):59-68.
51. Merino A, Buendia P, Martin-Malo A, Aljama P, Ramirez R, Carracedo J. Senescent CD14+ CD16+ monocytes exhibit proinflammatory and proatherosclerotic activity. The Journal of Immunology. 2011 Feb 1;186(3):1809-15.

52. Sedelnikova OA, Redon CE, Dickey JS, Nakamura AJ, Georgakilas AG, Bonner WM. Role of oxidatively induced DNA lesions in human pathogenesis. Mutation Research/Reviews in Mutation Research. 2010 Apr 1;704(1-3):152-9.

53. Schumacher B, Garinis GA, Hoeijmakers JH. Age to survive: DNA damage and aging. Trends in Genetics. 2008 Feb 1;24(2):77-85.

54. Schiffrin EL, Lipman ML, Mann JF. Chronic kidney disease: effects on the cardiovascular system. Circulation. 2007 Jul 3;116(1):85-97.

55. Tatematsu S, Wakino S, Kanda T, Homma K, Yoshioka K, Hasegawa K, Sugano N, Kimoto M, Saruta T, Hayashi K. Role of Nitric Oxide–Producing and–Degrading Pathways in Coronary Endothelial Dysfunction in Chronic Kidney Disease. Journal of the American Society of Nephrology. 2007 Mar 1;18(3):741-9.

56. Di Marco GS, Hausberg M, Hillebrand U, Rustemeyer P, Wittkowski W, Lang D, Pavenstadt H. Increased inorganic phosphate induces human endothelial cell apoptosis in vitro. American Journal of Physiology-Renal Physiology. 2008 Jun;294(6):F1381-7.

57. Peng A, Wu T, Zeng C, Rakheja D, Zhu J, Ye T, Hutcheson J, Vaziri ND, Liu Z, Mohan C, Zhou XJ. Adverse effects of simulated hyper-and hypo-phosphatemia on endothelial cell function and viability. PLoS One. 2011 Aug 9;6(8):e23268.

58. Olmos G, Martínez-Miguel P, Alcalde-Estevez E, Medrano D, Sosa P, Rodríguez-Mañas L, Naves-Diaz M, Rodríguez-Puyol D, Ruiz-Torres MP, López-Ongil S. Hyperphosphatemia induces senescence in human endothelial cells by increasing endothelin-1 production. Aging Cell. 2017 Dec;16(6):1300-12.

59. Carmona A, Guerrero F, Buendia P, Obrero T, Aljama P, Carracedo J. Microvesicles derived from indoxyl sulfate treated endothelial cells induce endothelial progenitor cells dysfunction. Frontiers in physiology. 2017 Sep 8;8:666.
60. Shang F, Wang SC, Hsu CY, Miao Y, Martin M, Yin Y, Wu CC, Wang YT, Wu G, Chien S, Huang HD. MicroRNA-92a mediates endothelial dysfunction in CKD. Journal of the American Society of Nephrology. 2017 Nov 1;28(11):3251-61.
61. Schwarz U. Buzello M, Ritz E, Stein G, Raabe G, Wiest G, Mall G, Amann K. Morphology of coronary atherosclerotic lesions in patients with end-stage renal failure. Nephrol Dial Transplant. 2000;15:218-23.
62. Gross ML, Meyer HP, Ziebart H, Rieger P, Wenzel U, Amann K, Berger I, Adamczak M, Schirmacher P, Ritz E. Calcification of coronary intima and media: immunohistochemistry, backscatter imaging, and x-ray analysis in renal and nonrenal patients. Clinical Journal of the American Society of Nephrology. 2007 Jan 1;2(1):121-34.
63. Nakano T, Ninomiya T, Sumiyoshi S, Fujii H, Doi Y, Hirakata H, Tsuruya K, Iida M, Kiyohara Y, Sueishi K. Association of kidney function with coronary atherosclerosis and calcification in autopsy samples from Japanese elders: the Hisayama study. American Journal of Kidney Diseases. 2010 Jan 1;55(1):21-30.
64. Kato K, Yonetsu T, Jia H, Abtahian F, Vergallo R, Hu S, Tian J, Kim SJ, Lee H, McNulty I, Lee S. Nonculprit coronary plaque characteristics of chronic kidney disease. Circulation: Cardiovascular Imaging. 2013 May;6(3):448-56.

65. Xu D, Li J, Zou L, Xu Y, Hu D, Pagoto SL, Ma Y. Sensitivity and specificity of the ankle—brachial index to diagnose peripheral artery disease: a structured review. Vascular medicine. 2010 Oct;15(5):361-9.

66. Aboyans V, Criqui MH, Abraham P, Allison MA, Creager MA, Diehm C, Fowkes FG, Hiatt WR, Jönsson B, Lacroix P, Marin B. Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association. Circulation. 2012 Dec 11;126(24):2890-909.

67. Allison MA, Laughlin GA, Barrett-Connor E, Langer R. Association between the ankle-brachial index and future coronary calcium (the Rancho Bernardo study). The American journal of cardiology. 2006 Jan 15;97(2):181-6.

68. McDermott MM, Guralnik JM, Ferrucci L, Criqui MH, Greenland P, Tian L, Liu K, Tan J. Functional decline in lower-extremity peripheral arterial disease: associations with comorbidity, gender, and race. Journal of vascular surgery. 2005 Dec 1;42(6):1131-7.

69. McDermott MM, Guralnik JM, Ferrucci L, Criqui MH, Greenland P, Tian L, Liu K, Tan J. Functional decline in lower-extremity peripheral arterial disease: associations with comorbidity, gender, and race. Journal of vascular surgery. 2005 Dec 1;42(6):1131-7.

70. McDermott MM, Guralnik JM, Tian L, Liu K, Ferrucci L, Liao Y, Sharma L, Criqui MH. Associations of borderline and low normal ankle-brachial index values with functional decline at 5-year follow-up: the WALCS (Walking and Leg Circulation Study). Journal of the American College of Cardiology. 2009 Mar 24;53(12):1056-62.

71. EC NN, Piatto MJ, Paschôa AF, Schlaad SW, Van Bellen B. Intima-media thickness: correlation between carotids, vertebral artery, aorta and femoral

arteries. International angiology: a journal of the International Union of Angiology. 2014 Oct 6;34(3):269-75.

72. Flanigan DP, Ballard JL, Robinson D, Galliano M, Blecker G, Harward TR. Duplex ultrasound of the superficial femoral artery is a better screening tool than ankle-brachial index to identify at risk patients with lower extremity atherosclerosis. Journal of vascular surgery. 2008 Apr 1;47(4):789-93.
73. Carpenter M, Sinclair H, Kunadian V. Carotid intima media thickness and its utility as a predictor of cardiovascular disease: a review of evidence. Cardiology in review. 2016 Mar 1;24(2):70-5.
74. Bots ML, Evans GW, Tegeler CH, Meijer R. Carotid intima-media thickness measurements: relations with atherosclerosis, risk of cardiovascular disease and application in randomized controlled trials. Chinese medical journal. 2016 Jan 20;129(2):215.
75. Desbien AM, Chonchol M, Gnahn H, Sander D. Kidney function and progression of carotid intima-media thickness in a community study. American journal of kidney diseases. 2008 Apr 1;51(4):584-93.
76. Hsu S, Rifkin DE, Criqui MH, Suder NC, Garimella P, Ginsberg C, Marasco AM, McQuaide BJ, Barinas-Mitchell EJ, Allison MA, Wassel CL. Relationship of femoral artery ultrasound measures of atherosclerosis with chronic kidney disease. Journal of vascular surgery. 2018 Jun 1;67(6):1855-63.
77. Valdivielso JM, Rodríguez-Puyol D, Pascual J, Barrios C, Bermúdez-López M, Sánchez-Niño MD, Pérez-Fernández M, Ortiz A. Atherosclerosis in chronic kidney disease: more, less, or just different?. Arteriosclerosis, thrombosis, and vascular biology. 2019 Oct;39(10):1938-66.

78. Junyent M, Martínez M, Borràs M, Coll B, Valdivielso JM, Vidal T, Sarró F, Roig J, Craver L, Fernández E. Predicting cardiovascular disease morbidity and mortality in chronic kidney disease in Spain. The rationale and design of NEFRONA: a prospective, multicenter, observational cohort study. BMC nephrology. 2010 Dec;11(1):1-8.
79. Junyent M, Martínez Alonso M, Borràs M, Betriu i Bars M, Coll B, Marco Mayayo MP, Sarró F, Valdivielso Revilla JM, Fernández i Giráldez E. Usefulness of imaging techniques and novel biomarkers in the prediction of cardiovascular risk in patients with chronic kidney disease in Spain: the NEFRONA project. Nefrologia, 2010, vol. 30, núm. 1, p. 119-126. 2010.
80. Rigatto C, Levin A, House AA, Barrett B, Carlisle E, Fine A. Atheroma progression in chronic kidney disease. Clinical Journal of the American Society of Nephrology. 2009 Feb 1;4(2):291-8.
81. Wanner C, Amann K, Shoji T. The heart and vascular system in dialysis. The Lancet. 2016 Jul 16;388(10041):276-84.
82. Ortiz A, Covic A, Fliser D, Fouque D, Goldsmith D, Kanbay M, Mallamaci F, Massy ZA, Rossignol P, Vanholder R, Wiecek A. Epidemiology, contributors to, and clinical trials of mortality risk in chronic kidney failure. The lancet. 2014 May 24;383(9931):1831-43.
83. Gracia M, Betriu A, Martínez-Alonso M, Arroyo D, Abajo M, Fernandez E, Valdivielso JM. Predictors of subclinical atheromatosis progression over 2 years in patients with different stages of CKD. Clinical Journal of the American Society of Nephrology. 2016 Feb 5;11(2):287-96.
84. Bosma J, Dijksman LM, Lam K, Wisselink W, van Swijndregt AD, Vahl A. The costs and effects of contrast-enhanced magnetic resonance angiography and

digital substraction angiography on quality of life in patients with peripheral arterial disease. Acta radiologica. 2014 Apr;55(3):279-86.

85. Willner S. The Role of Imaging in Peripheral Arterial Disease. Peripheral Arterial Disease: A Practical Approach. 2018 Oct 17:85.
86. Olin JW, Kaufman JA, Bluemke DA, Bonow RO, Gerhard MD, Jaff MR, Rubin GD, Hall W. Atherosclerotic vascular disease conference: writing group IV: imaging. Circulation. 2004 Jun 1;109(21):2626-33.
87. Whelan JF, Barry MH, Moir JD. Color flow Doppler ultrasonography: comparison with peripheral arteriography for the investigation of peripheral vascular disease. Journal of clinical ultrasound. 1992 Jul;20(6):369-74.
88. Erickson SJ, Mewissen MW, Foley WD, Lawson TL, Middleton WD, Quiroz FA, Macrander SJ, Lipchik EO. Stenosis of the internal carotid artery: assessment using color Doppler imaging compared with angiography. American Journal of Roentgenology. 1989 Jun 1;152(6):1299-305.
89. Ayoola OO, Bolarinwa RA, Onakpoya OH, Onigbinde SO, Asaleye CM, Odedeyi AA. Intima-media thickness of the common carotid arteries as a marker of retinopathy and nephropathy in sickle cell disease. Ultrasonography. 2020 Jan;39(1):79.
90. Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, Adebayo OM, Afarideh M, Agarwal SK, Agudelo-Botero M, Ahmadian E. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet. 2020 Feb 29;395(10225):709-33.
91. Varma PP. Prevalence of chronic kidney disease in India-Where are we heading?. Indian journal of nephrology. 2015 May;25(3):133.

92. Levey AS, Stevens LA, Schmid CH, Zhang Y, Castro III AF, Feldman HI, Kusek JW, Eggers P, Van Lente F, Greene T, Coresh J. A new equation to estimate glomerular filtration rate. Annals of internal medicine. 2009 May 5;150(9):604-12.
93. Agarwal SK, Srivastava RK. Chronic kidney disease in India: challenges and solutions. Nephron clinical practice. 2009;111(3):c197-203..
94. Nezami N, Ghabili K, Shokouhi-Gogani B, Mirchi M, Ghojazadeh M, Safa J, Zomorrodi A, Gharadaghi A, Mojadidi MK, Tarzamni MK, Khajir G. The relationship between carotid and femoral artery intima-media thickness and histopathologic grade of atherosclerosis in patients with chronic kidney disease. Nephron. 2018;139(2):159-69.
95. Le TD, Nguyen NP, Nguyen ST, Nguyen HT, Tran HT, Nguyen TH, Nguyen CD, Nguyen GT, Nguyen XT, Nguyen BD, Trinh ST. The Association Between Femoral Artery Intima-Media Thickness and Serum Glucagon-Like Peptide-1 Levels Among Newly Diagnosed Patients with Type 2 Diabetes Mellitus. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2020;13:3561.

ANNEXURE I –

INFORMED CONSENT

TITLE OF THE STUDY: "RELATIONSHIP BETWEEN FEMORAL ARTERY INTIMA-MEDIA THICKNESS AND ATHEROSCLEROSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE, A ONE YEAR CROSS SECTIONAL STUDY''

PRINCIPAL INVESTIGATOR:

INTRODUCTION AND PURPOSE:

Chronic kidney disease (CKD) is an irreversible decline in kidney function which usually develops over a long period. CKD is linked with increased morbidity and mortality, reduced quality of life and increased medical costs. The prevalence of CKD worldwide is estimated to be 11-14%. The burden of CKD in India cannot be assessed precisely because of lack of proper data. The approximate prevalence of CKD in India is 800 per million population and more than 100, 000 new patients enter renal replacement programs annually in India. The prevalence of end-stage renal disease continues to increase globally

Atherosclerosis unless in a severe form is often asymptomatic, hence a direct examination of the vessel wall is needed to detect affected patients in the initial stages. Atherosclerosis is the most common risk factors of cardiovascular morbidity in CKD patients.

Chronic kidney disease (CKD) is strongly linked with peripheral artery disease (PAD). Detection of sub-clinical PAD may help in early interventions for prevention of PAD in patients with CKD. It is not known whether the presence

of atherosclerotic plaque and femoral intima-media thickness (IMT) are associated with kidney function.

Hence this study is aimed at finding the same in our set up.

PROCEDURE:

"**RELATIONSHIP BETWEEN FEMORAL ARTERY INTIMA-MEDIA THICKNESS AND ATHEROSCLEROSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE, A ONE YEAR CROSS SECTIONAL STUDY**''

at Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi" is being conducted by Post graduate in Radio diagnosis at J. N. Medical College Belagavi, Karnataka, J. N. Medical College, Belagavi.

We request you to participate in this study as you are eligible to be included. During the study you will be asked questions regarding your present and past medical history and you will be required to answer to the best of your knowledge. You will also be clinically examined as per the protocol drawn.

If you agree to participate in the study, please furnish the details pertaining to the study.

BENEFITS:

- Your atherosclerotic status in femoral artery can be known and can help you help prevent peripheral artery disease risk in advance if any.

RISKS/ COMPLICATIONS:

- No risk to the patient has been documented from ULTRASONOGRAPHY earlier.

ALTERNATIVES:

If you are not willing to take part in the study, your treatment or any other further investigations that you want to undergo, in future, in KLE will not be affected by your decision.

VOLUNTARY PARTICIPATION/WITHDRAWAL:

Taking part in this study is voluntary. You may choose not to take part in this study, or if I decide to take part, I can later change my mind and withdraw from the study. My decision will not change the present or future health care or other services that I receive. The study doctor or the sponsor may stop my participation in this study. I will tell if any important new findings that may change my willingness to continue to take part. If I choose not to take part in the study, I will receive the standard treatment for patients with my condition.

COSTS:

NIL (The study is to be conducted on the participants who are advised USG as an investigation for CKD by the referring consultant and the participants will bear the charges for it.)

Payment for Participation: No incentive will be paid to you for participating in this study.

COMPENSATION:

In the event that you become injured as a result of taking part in this study, treatment whatever available at KLE charitable hospital, Belagavi, will be offered to me. No reimbursement or compensation will be given.

CONFIDENTIALITY:

All information collected about you during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will identify you in this research record. Information from this study may be published but your identity will be kept confidential in any publication/ presentation.

CONSENT TO PARTICIPATE IN RESEARCH STUDY:

1. "I understand that I am participating in the study, which relationship between femoral artery intima-media thickness and atherosclerosis in patients with chronic kidney disease, a cross sectional study"-one-year study confirm that I have read and understood the information in the patient information sheet. Procedure is explained to me in detail along with information about the advantages and disadvantages of taking part in the study. I have been given the opportunity to discuss all aspects of the trial, to ask questions and hereby consent to participation in the trial outlined above.
2. I understand that the decision to take part in this study is completely voluntary and I am aware that I can choose to withdraw from the study at any point of time.
3. I consent to the photographing or recording of the procedure to be performed including appropriate portions of my body, for medical, scientific or educational purposes provided my identity is not revealed in the pictures or by the descriptive texts accompanying them.
4. I understand that there is no significant risk involved in the test that would be done in this study.
5. No guarantee or assurance has given by anyone as to the results that may be obtained.
6. My signature on this form signifies that I have willingly decided to participate after understanding the above information."

Participant's Name/ legally authorized representative _____

Signature _____

Name and signature of witness _____

Name and signature of interviewer _____

Date: _____

Place: _____

ANNEXURE II -ETHICAL CLEARANCE LETTER

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 292 **Date: 24/12/2019**

To,

BS0119011
PG student in Radio-diagnosis,
J. N. Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"RELATIONSHIP BETWEEN FEMORAL ARTERY INTIMA-MEDIA THICKNESS AND ATHEROSCLEROSIS IN PATIENTS WITH CHRONIC KIDNEY DISEASE – A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"**, is ethical and justifiable.

The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Anita Dalal)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Bellad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

ANNEXURE III-PROFORMA

PROFORMA FOR DATA COLLECTION

NAME OF THE PATIENT: _____

AGE (IN YEARS) _____ **OP/IP NO _____**

MOBILE NUMBER: _____ **GENDER: M / F**

ADDRESS: HOUSE NO.:
_____

WARD/GALLI: _____

VILLAGE _____ **TALUK: _____** **DISTRICT: _____**

PH NO.: _____

USG NUMBER: _____

OCCUPATION:

MONTHLY INCOME:

SOCIO ECONOMIC STATUS:

EDUCATION:

CHIEF COMPLAINTS: **DURATION**

1)

2)

3)

HISTORY OF PRESENTING ILLNESS **DURATION**

1)

2)

3)

PAST HISTORY

1)

2)

PERSONAL HISTORY:

SMOKING	PRESENT / ABSENT
ALCOHOLISM	PRESENT / ABSENT
OCCUPATION	

FAMILY HISTORY

PHYSICAL AND LABORATORY EXAMINATION:

HEIGHT	...m
WEIGHT	…Kgs
BMI	……
PULSE	……
RANDOM BLOOD SUGAR	……

CVS:

RS:

RENAL:

PROVISIONAL DIAGNOSIS:

FINAL DIAGNOSIS:

ULTRASONOGRAPHY FINDINGS:

INTIMA MEDIA TICKNESS (IMT):

ARTERY	R (cm)	L (cm)
CFA/SFA		

WALL CALCIFICATION: PRESENT/ ABSENT.

ANNEXURE IV: FIGURES

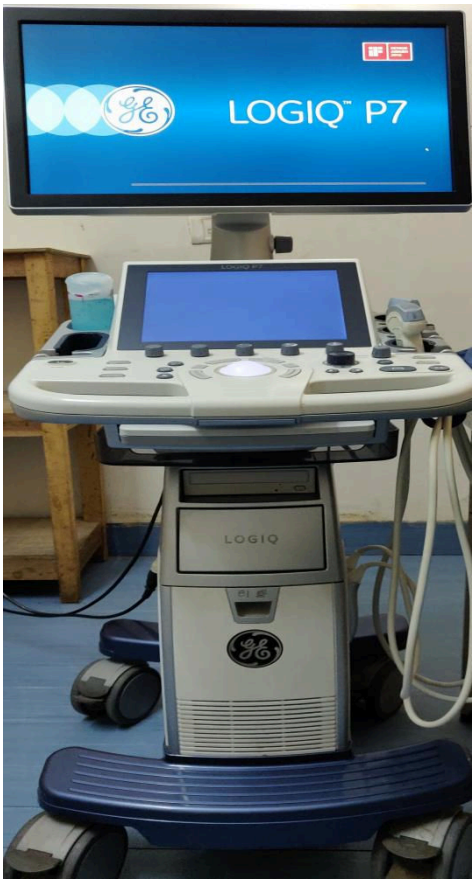


Fig 5: GE VOLUSON USG machine used for the study

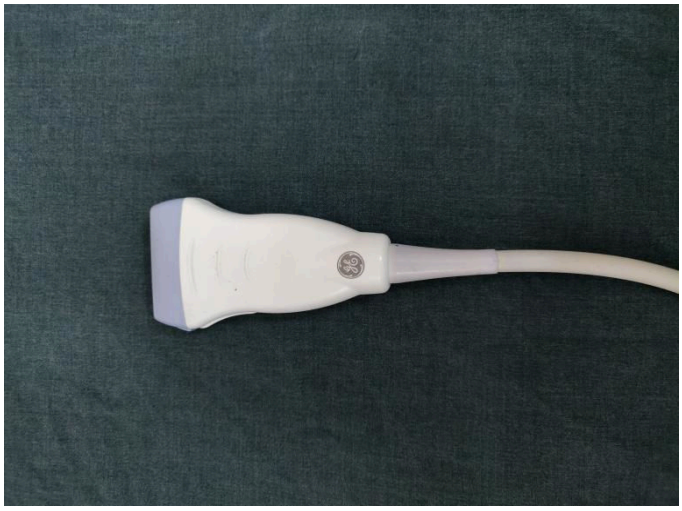


Fig 6: High frequency linear array transducer used for the study.

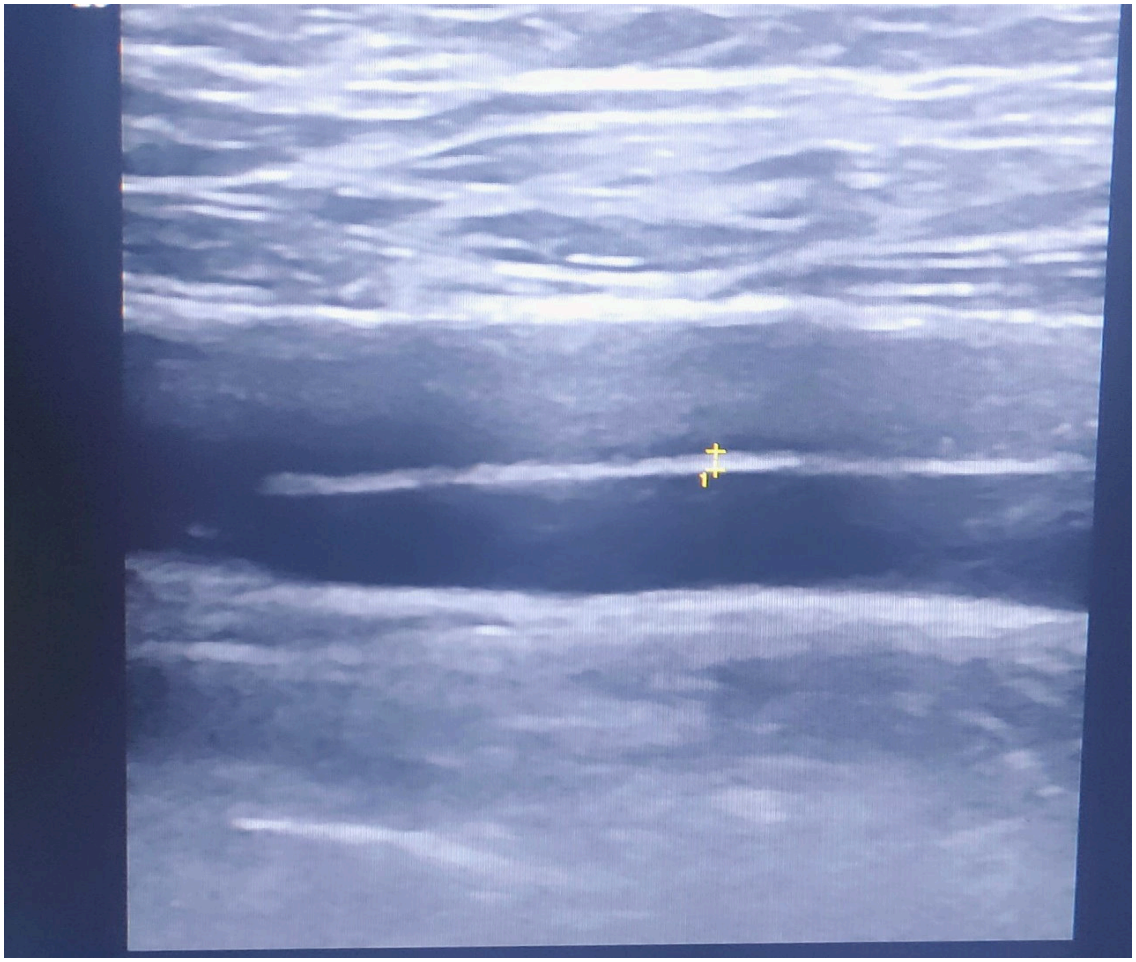


Fig 7: USG image showing normal anatomy of common femoral artery and its bifurcation into superficial and deep femoral arteries.

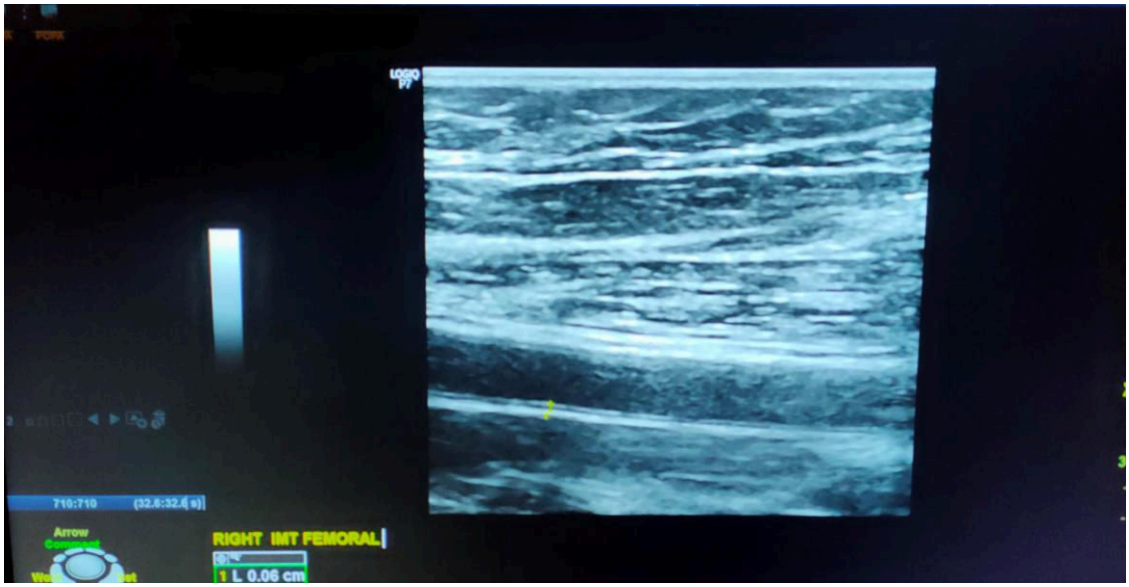


Fig 8: B mode USG image showing intima media thickness measurement.

PHOTOGRAPHS OF CASES

Case 1: A 79-year-old non-alcoholic male, case of CKD was referred for lower limb color doppler evaluation in view of peripheral vascular disease. Incidentally, raised femoral intima media thickness was noted. The IMT measured 0.10 cms.

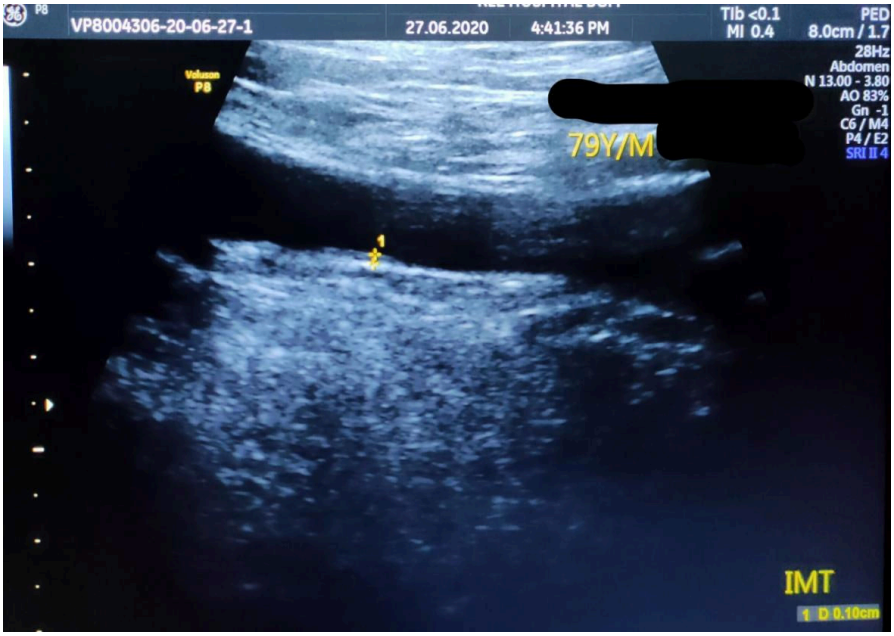


Fig 9: B mode USG image showing raised IMT measurement.

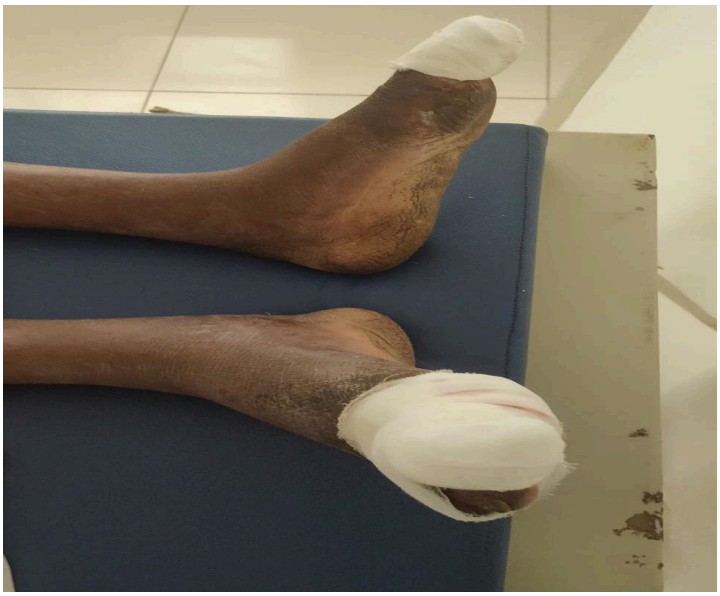


Fig 10: Picture of above described patient with bandaged foot for arterial ulcers suggesting PAD.

Case 2: A 34-year-old female, case of stage 4 CKD was referred for abdominal & pelvic ultrasound in view of decreased urine output. The femoral artery intima of the right-side leg was measured. The IMT measured 0.05 cms.

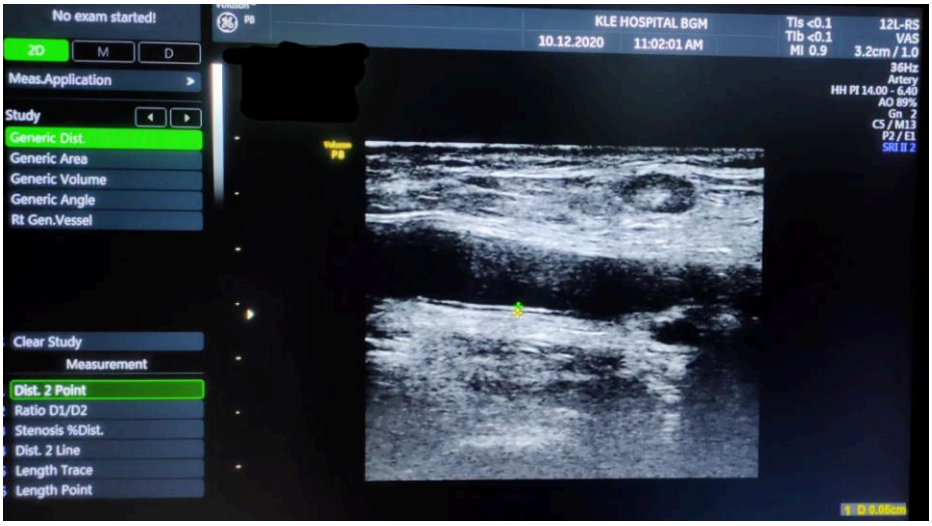


Fig11: USG image showing normal IMT measurement even with CKD.

Case 3: A 58-year-old male, case of CKD stage 3 was referred for abdominal & pelvic ultrasound in view of abdominal distention and edema. The femoral artery intima of the left side leg was measured. The IMT measured 0.08 cms.

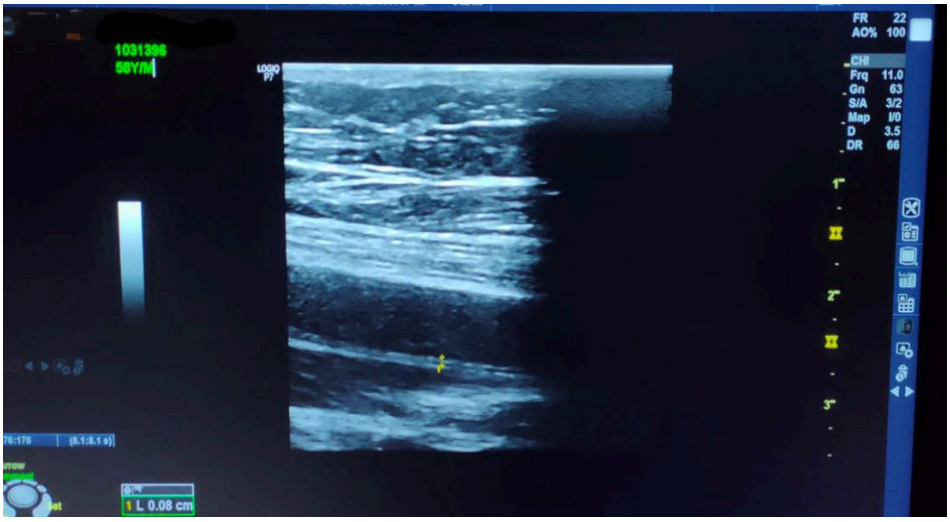


Fig 9: B mode USG image showing raised IMT measurement.

Case 4: A 48-year-old female was referred for abdominal & pelvic ultrasound in view of decreased urine output and raised creatinine. The patient was in CKD stage 3A. The femoral artery intima of the left side leg was measured. The IMT measured 0.07 cms.

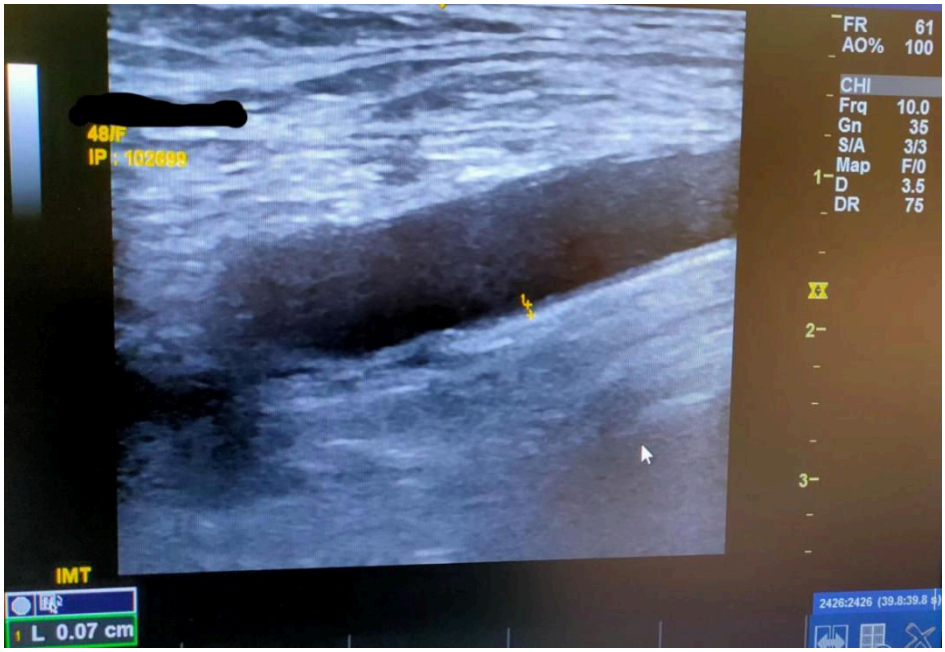


Fig 12: B mode USG image showing of femoral artery with raised IMT measurement.

ANNEXURE – V

KEY TO MASTER CHART

CKD	**Chronic kidney disease**
PVD	**Peripheral vascular disease**
EGFR	**Estimated Glomerular filtration rate**
DM	**Diabetes mellitus**
U/O	**Urine output**
TG	**Triglycerides**
HB	**Hemoglobin**
IP	**In patient**
OP	**Out patient**

	1	2	3	4	5
Age	31 - 45 Yrs.	45 - 60 Yrs.	> 60 Yrs.		
Gender	Male	Female			
Femoral IMT (cut-off: 0.06 cm & above)	Raised	Not raised			
CKD Stage	I	II	IIIA	IIIB	IV
PVD	Present	Absent			
Anemia **M: < 13.5 gm/dl** **F: 12.0 gm/dl**	Present	Absent			
Urea levels (mg/dl)	Up-to 100	101-200	>201		
Creatinine levels (mg/dl)	Up-to 10	11-20	21-30		
TG (mg/dl)	100-200	201-300	>301		
DM	Yes	No			
On Dialysis	Yes	No			
Symptoms	Decreased u/o	Urticaria	Foot black discoloration	Edema	
Wall Calcification	Present	Absent			

ANNEXURE – VI

MASTER CHART

NAME	IP/OP No.	AGE	SYMPTOMS	SEX	IMT	WALL CALCIFICATION	UREA	CREATINE	CKD STAGE	EGFR	PVD	HB	LDL/TG	DM	ON DIALYSI
GANGAPPA	1010515	57	DECREASED U/O	M	0.1	PRESENT	56	6	5	9.5	N	9.8	223	N	Y
SHANKAR	1019509	83	DECREASED U/O	M	0.11	PRESENT	221	11	5	9.9	N	9.7	153	N	Y
CHANDRAKANT	1016393	79	DECREASED U/O	M	0.1	PRESENT	57	9.8	5	4.5	N	11.1	164	N	Y
ANNASAB	1033678	57	DECREASED U/O	M	0.05	PRESENT	112	5.6	5	10.4	N	5.6	189	N	Y
MARUTI	1029383	58	URTICARIA	M	0.07	ABSENT	43	2.3	3	30.2	N	10.9	234	N	N
YUVRAJ	1029383	36	DECREASED U/O	M	0.06	ABSENT	45	3.3	4	22.8	N	11	166	N	Y
SHANTABAI	1025565	65	FOOT BLACK DISCOLORATION	F	0.09	PRESENT	172	8.4	5	4.5	Y	9.8	111	N	Y
NASIMA	1026995	48	FOOT BLACK DISCOLORATION	F	0.07	ABSENT	40	1.3	3A	48.6	Y	12.3	176	Y	N
MALLAWA	6560580	42	FOOT BLACK DISCOLORATION	F	0.07	ABSENT	41	3	4	21	Y	8.9	189	Y	Y
DEEPAK	1026677	38	DECREASED U/O	M	0.08	ABSENT	44	3.6	4	23	N	9.9	276	Y	Y
SHRIKANT N	6578922	48	DECREASED U/O	M	0.04	ABSENT	57	1.3	2	64.5	N	10	116	Y	N
RAMESH	1029777	48	DECREASED U/O	M	0.07	ABSENT	150	15.8	5	3.1	N	7.8	174	Y	Y
SAVITA K	1028814	30	DECREASED U/O	F	0.05	ABSENT	108	7.1	5	7.1	N	10.6	188	Y	Y
SHIVALINGAYYA	1030106	56	DECREASED U/O	M	0.1	PRESENT	163	17	3	2.7	N	5.8	220	N	N
PAVANANJANEYA	1030517	62	DECREASED U/O	M	0.06	ABSENT	110	6.7	5	8.1	N	9.9	331	Y	Y
RAKESH	5111363	45	FOOT BLACK DISCOLORATION	M	0.09	PRESENT	43	2	3	39.1	Y	7.6	115	N	N
RAMACHANDRA	5119969	57	DECREASED U/O	M	0.07	ABSENT	45	2.3	3	30.4	N	9	244	N	N
SRIRAM	1042488	35	DECREASED U/O	M	0.08	ABSENT	111	3.6	4	20.6	N	11.2	166	Y	Y
NARYANI	1058597	48	DECREASED U/O	M	0.05	ABSENT	140	8.7	5	6.5	N	6.7	178	Y	Y
SHOBHA	1042872	40	DECREASED U/O	F	0.08	ABSENT	132	4	5	13.2	N	13.9	198	Y	Y
BASAVARAJ P	1031396	58	FOOT BLACK DISCOLORATION	M	0.08	PRESENT	47	1.7	3	43.5	Y	14.3	110	Y	N
FAKIRA K	1030771	58	DECREASED U/O	M	0.09	ABSENT	127	3.7	4	17	N	11.1	156	N	Y
LAXMKANT	1042409	43	DECREASED U/O	M	0.1	ABSENT	136	9.9	5	5.7	N	10.1	378	Y	Y
SATYAPPA	1042183	67	DECREASED U/O	M	0.12	ABSENT	156	5.6	5	9.7	N	12	279	N	Y
ANUSHRI	31143	16	URTICARIA	F	0.06	ABSENT	42	2.8	4	24.1	N	11.1	464	Y	Y
MANIK B	31178	52	FOOT BLACK DISCOLORATION	M	0.11	PRESENT	156	4	4	16.1	Y	10.6	330	N	Y
ASHOK K	1331332	60	EDEMA	M	0.1	PRESENT	83	4.7	4	12.5	N	10.7	311	N	Y
RAJU B	1043661	42	EDEMA	M	0.09	ABSENT	213	4.8	5	13.9	N	10.5	289	Y	Y
GURUSIDAPPA	4792934	23	EDEMA	M	0.05	ABSENT	78	4.3	4	18.1	N	11.2	244	N	Y
MAHADEV	5681741	38	EDEMA	M	0.09	ABSENT	98	5.4	5	12.4	N	11.2	170	N	Y
CHANDRASHEKAR S	1042133	62	EDEMA	M	0.05	ABSENT	66	3.3	4	19	N	10	276	Y	Y
MARUTI	1042889	32	FOOT BLACK DISCOLORATION	M	0.07	ABSENT	258	29.58	5	1.7	Y	7.9	333	N	Y
NISARAHMAD	1044841	65	EDEMA	M	0.1	PRESENT	95	5.3	5	10.5	N	9	374	Y	Y
OMKAR SUTAR	1026790	24	FOOT BLACK DISCOLORATION	M	0.08	ABSENT	56	3.6	4	22.3	Y	11.7	267	Y	Y
SATISH	1047475	71	EDEMA	M	0.06	PRESENT	151	2.3	4	27.5	N	14	329	Y	Y
SUMITRA	1042356	60	EDEMA	F	0.07	ABSENT	190	3.8	5	12.2	N	11	267	Y	Y
MAHADEV	1056338	42	FOOT BLACK DISCOLORATION	M	0.05	ABSENT	99	4.9	5	13.5	N	8.9	289	N	Y
RAMESH	1056286	61	EDEMA	M	0.12	ABSENT	112	7.9	5	6.6	N	11.1	466	Y	Y
BASAYYA	1052789	60	EDEMA	M	0.07	ABSENT	54	4.8	5	12.2	N	7.9	330	Y	Y
SIDDALINGAPPA	1057252	78	EDEMA	M	0.09	PRESENT	45	4.4	5	12	N	10	221	Y	Y

YALLANNA	1053393	56	URTICARIA	M	0.1	ABSENT	42	1.4	2	67.2	N	9.3	189	Y	N
RAJU A	1052973	44	URTICARIA	M	0.05	ABSENT	43	2.2	3	35.1	N	14	156	N	N
BASANGOUDA	1042730	57	EDEMA	M	0.06	ABSENT	78	5.9	5	9.7	N	9.9	278	Y	Y
RAJABI	1042399	67	EDEMA	F	0.08	PRESENT	42.3	8	5	4.7	N	7.9	298	N	Y
SUMUKH	1034772	46	EDEMA	M	0.06	ABSENT	70	2.9	4	24.8	N	7	244	Y	Y
RUDRAVVA	1024392	77	EDEMA	F	0.08	PRESENT	122	4	5	10.2	N	10.8	279	Y	Y
SANAPPA	1045299	46	URTICARIA	M	0.04	ABSENT	41.1	2.1	3	36.6	N	11.2	389	Y	N
IQBAL	5118732	56	URTICARIA	M	0.05	ABSENT	41	2.2	3	32.3	N	9.8	289	Y	N
GURUNATH	5119373	66	EDEMA	M	0.07	ABSENT	89	3.2	4	19.1	N	10.9	345	Y	Y
YASMEEN	1056288	69	FOOT BLACK DISCOLORATION	F	0.1	PRESENT	45	2.8	4	16.6	Y	8.3	378	Y	Y
SIDDAVVA	1053880	65	EDEMA	F	0.06	ABSENT	172	12.2	5	2.9	N	11.6	258	N	Y
NASEEMA MULLA	1062334	60	EDEMA	F	0.08	ABSENT	167	10.1	5	3.7	N	10.7	217	N	Y
RAJSHEKAR	1068902	54	EDEMA	M	0.09	ABSENT	119	8.7	5	6.2	N	11.1	287	Y	Y
KAMALNATH	1062236	68	FOOT BLACK DISCOLORATION	M	0.1	PRESENT	178	10	5	4.8	Y	7.9	301	Y	Y
TEHSIN	1062289	56	EDEMA	F	0.07	ABSENT	46	9.8	5	4	N	11.1	288	Y	Y
MAHANING	1054222	69	EDEMA	M	0.11	PRESENT	166	8.8	5	5.5	N	8.8	321	Y	Y
RAVI SHET	1025679	55	EDEMA	M	0.08	PRESENT	78	4.5	5	12.7	N	11.7	287	Y	Y
SHARAWWA	1023789	78	EDEMA	F	0.08	PRESENT	88	8.8	5	3.9	N	8.9	290	N	Y
ASLAM	1053378	70	EDEMA	M	0.05	PRESENT	57	2.6	4	23.9	N	11.9	189	N	Y
GOURAWWA	1053893	69	EDEMA	F	0.11	ABSENT	98	3.3	4	18.2	N	7.9	270	N	Y
STEPHEN M	1062342	56	EDEMA	M	0.04	ABSENT	69	5.9	5	9.8	N	6.8	121	Y	Y
RENUKA	1056333	38	EDEMA	F	0.05	ABSENT	44	2.3	4	26.2	N	11.3	156	N	Y
PAUL IGUARDO	1043899	60	FOOT BLACK DISCOLORATION	M	0.07	PRESENT	60	4.2	5	14.4	Y	10.2	223	Y	Y
KALAVATHI	1034782	45	EDEMA	F	0.06	ABSENT	43.3	2.2	4	26.3	N	8.9	167	Y	Y
BEERAPPA	1035890	67	EDEMA	M	0.06	PRESENT	56	3.4	4	17.7	N	7.9	174	Y	Y
KALKAPPA	1056222	68	EDEMA	M	0.09	PRESENT	121	6.6	5	7.9	N	9.3	212	Y	Y
CHANNABASAVA	1034992	59	EDEMA	M	0.07	PRESENT	111	5.6	5	10.2	N	9.4	288	Y	Y
SAKINA	1045299	34	EDEMA	F	0.03	ABSENT	77	4.3	5	12.6	N	8.8	245	Y	Y
IRANGOUDA	1042292	70	EDEMA	M	0.07	PRESENT	119	3.4	4	17.3	N	9.7	189	Y	Y
MARGARET	1052389	79	EDEMA	F	0.06	PRESENT	80	3.3	5	12.7	N	10.2	178	N	Y
SIDDAVVA	1059477	65	EDEMA	F	0.06	PRESENT	45	2.8	4	17	N	11.6	156	N	Y
YAMANAVVA	1076533	65	EDEMA	F	0.06	PRESENT	41	1.8	5	14	N	12.9	111	N	Y
SHIVALINGESHWAR	1069982	62	FOOT BLACK DISCOLORATION	M	0.12	PRESENT	181	7	5	19	Y	8.4	201	N	Y
SHIVRUDRA	1062332	38	DECREASED U/O	M	0.11	ABSENT	145	8.8	5	6.9	N	9.8	255	N	Y
MAHALING	1067893	45	DECREASED U/O	M	0.11	ABSENT	167	9.2	5	5	N	8	270	N	Y
MOULANA	1046229	66	DECREASED U/O	M	0.12	PRESENT	177	9.9	5	4.9	N	8.9	202	Y	Y
ANUJ	1025339	23	DECREASED U/O	M	0.12	ABSENT	156	7.6	5	9.1	N	11.3	211	N	Y
SULTAN	1037352	35	DECREASED U/O	M	0.1	ABSENT	78	5	5	13.9	N	12.5	198	N	Y
FAKIRESHWAR	1063536	56	DECREASED U/O	M	0.09	ABSENT	89	4.6	5	13.2	N	14	179	N	Y
VAMSI	1035363	40	DECREASED U/O	M	0.06	ABSENT	65	5.6	5	11.7	N	7.9	170	N	Y
JAYA	1036353	59	DECREASED U/O	F	0.11	PRESENT	98	6.4	5	6.6	N	9.9	221	N	Y
SHOBHAKKA	1034627	60	DECREASED U/O	F	0.08	ABSENT	111	3.9	5	11.8	N	9.5	172	N	Y

BHARATHI	1042888	34	DECREASED U/O	F	0.08	ABSENT	150	4.5	5	12	N	8.6	200	N	Y
SUNIL	1056889	20	URTICARIA	M	0.04	ABSENT	41	1.8	3A	53	N	10.9	187	N	N
FREDRICH PINTO	1054288	70	EDEMA	M	0.07	PRESENT	41	5.4	5	9.9	N	11.1	151	N	Y
KAMALA	1055556	59	EDEMA	F	0.04	PRESENT	44	3.5	5	13.6	N	13	167	N	Y
PEERSAB	1052882	66	EDEMA	M	0.06	PRESENT	46	6	5	8.9	N	9.5	189	Y	Y
MAHALSA	1065890	80	EDEMA	M	0.06	PRESENT	48	3.9	5	13.7	N	10.1	111	Y	Y
PUNITH	1062222	18	URTICARIA	M	0.05	ABSENT	67	1.7	3A	57.6	N	9.6	98	N	N
RAKAPPA	1062111	50	EDEMA	M	0.09	ABSENT	99	9.5	5	5.7	N	7.6	167	N	Y
GOUDAPPA	1056028	49	FOOT BLACK DISCOLORATION	M	0.1	ABSENT	101	11	5	4.8	Y	4.5	190	N	Y
SUMITH	1024567	15	EDEMA	M	0.04	ABSENT	41	1.5	2	68.4	N	8.4	111	N	N
SOMNATH	1027900	26	URTICARIA	M	0.02	ABSENT	41	1.9	3A	47.6	N	15	101	N	N
INDIRA	1052881	38	EDEMA	F	0.06	ABSENT	67	6.3	5	7.7	N	9.9	178	N	Y
SUNITA PATIL	1026372	42	EDEMA	F	0.06	ABSENT	48	5.4	5	9.1	N	9.7	156	N	Y
AMEENA NADAF	562820	44	EDEMA	F	0.08	ABSENT	94	4.9	5	10.1	N	10.1	191	N	Y
CHARLES DSOUZA	557920	55	EDEMA	M	0.09	ABSENT	60	7.9	5	6.9	N	9.1	201	N	Y
S MUJAWAR	559892	19	URTICARIA	M	0.03	ABSENT	42	1.6	2	61.5	N	13	121	N	N
YADUVEER	529282	43	FOOT BLACK DISCOLORATION	M	0.13	ABSENT	186	12.3	5	4.4	Y	4.7	301	Y	Y