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Ultrasonographic Evaluation Of Carotid And Femoral Intimal Medial Thickness As Markers Of Pre-Clinical Atherosclerosis In Adolescent And Young Adult Patients With Chronic Kidney Disease

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Abstract Background:
Chronic kidney disease (CKD) is associated with accelerated atherosclerosis, even in younger populations. Traditional markers often fail to detect subclinical vascular changes early. This study evaluated the role of carotid and femoral intima-media thickness (cIMT, fIMT) as non-invasive markers of preclinical atherosclerosis in adolescent and young adult CKD patients.

Methods: *A prospective observational study was conducted involving 50 participants (25 CKD patients and 25 age- and sex-matched controls). Demographic, clinical, and biochemical parameters were recorded. B-mode ultrasonography was used to assess cIMT and fIMT bilaterally. Data were analyzed using t-tests, Pearson correlation, and multivariate regression.*

Results: *CKD patients exhibited significantly higher cIMT (0.69 ± 0.06 mm) and fIMT (0.78 ± 0.07 mm) compared to controls ($p<0.001$). IMT correlated positively with serum creatinine, LDL, and triglycerides and negatively with eGFR. Multivariate regression identified serum creatinine and LDL as independent predictors of increased IMT.*

Conclusion: *Increased cIMT and fIMT in young CKD patients reflect early vascular remodeling. Ultrasonographic IMT measurement is a sensitive and practical tool for early cardiovascular risk assessment in this vulnerable group.*

Keywords: *Chronic kidney disease, carotid intima-media thickness, femoral intima-media thickness, atherosclerosis, ultrasound, cardiovascular risk, adolescents, preclinical markers*

INTRODUCTION

Chronic kidney disease (CKD) is a major public health concern globally, with an estimated 800 million individuals affected worldwide, posing a significant burden on healthcare systems, especially in low- and middle-income countries like India[^1]. The disease is characterized by progressive and irreversible deterioration in renal function, which is often asymptomatic in its early stages, making early detection a clinical challenge. A majority of CKD-related mortality is not due to renal failure itself, but rather from cardiovascular complications, particularly atherosclerosis[^2]. Indeed, metabolic and inflammatory disturbances inherent to CKD significantly accelerate atherogenesis[^3].Peripheral arterial disease (PAD), a manifestation of systemic atherosclerosis, commonly coexists with CKD and compounds the cardiovascular risk, leading to increased morbidity and mortality[^4,^5,^6]. Although the ankle-brachial index (ABI) is widely employed in PAD diagnosis, its sensitivity in early disease is compromised in CKD due to arterial stiffness, which can yield falsely normal ABI readings despite underlying vascular

pathology[^7,^8]. Carotid intima-media thickness (cIMT) and femoral intima-media thickness (fIMT) measured by B-mode ultrasonography have emerged as promising non-invasive markers of subclinical atherosclerosis. Multiple studies have reported a strong correlation between CKD and increased cIMT, even in young patients with normal ABI[^9]. However, while cIMT has been extensively studied and validated, fIMT remains underexplored despite evidence suggesting that femoral plaques may be more prevalent than carotid ones in the early stages of atherosclerosis. Hsu et al. demonstrated a significant association between CKD and femoral artery plaque formation, even in patients with normal ABI, thereby underscoring the clinical utility of fIMT as a supplementary marker[^10]. In the Indian context, limited regional data exists on the interplay between CKD and subclinical atherosclerosis in adolescents and young adults. Given the vast ethnic and socioeconomic diversity, generalized reference values and findings from global cohorts may not always apply to Indian populations. Furthermore, early detection of atherosclerosis in CKD patients is crucial, as it opens avenues for timely interventions that can prevent adverse cardiovascular events. Thus, evaluating both cIMT and fIMT in young CKD patients can provide valuable insights into the preclinical phase of atherosclerosis and may serve as an early predictor of cardiovascular risk. This study aims to investigate the utility of ultrasonographically measured carotid and femoral intimal-medial thickness as early indicators of atherosclerosis in adolescents and young adults with CKD. By comparing these vascular parameters with traditional risk markers and healthy controls, the study seeks to establish whether cIMT and fIMT can be integrated into standard screening protocols for young patients with CKD. This could potentially bridge a critical gap in early risk stratification and management of cardiovascular disease in this vulnerable population.

MATERIALS AND METHODS

Study Design and Setting

This was a hospital-based, prospective, observational study conducted in the Department of Radiodiagnosis at Chettinad Hospital and Research Institute, Tamil Nadu, India. The study spanned a duration of one year (January to December 2023), after obtaining ethical clearance from the Institutional Human Ethics Committee. Written informed consent was obtained from all participants prior to their inclusion in the study.

Study Population

A total of 50 participants aged between 15 and 40 years were enrolled and divided into two groups:

- **Group A (Cases)**: 25 adolescent and young adult patients diagnosed with chronic kidney disease (CKD), including both newly diagnosed and follow-up cases.
- **Group B (Controls)**: 25 age- and sex-matched healthy individuals undergoing radiological evaluations for unrelated conditions, with no known history of renal or cardiovascular disease.

Inclusion Criteria

- Age 15 to 40 years.
- Group A: Diagnosed cases of CKD (any stage), not on dialysis.
- Group B: Healthy volunteers without CKD or cardiovascular comorbidities.

Exclusion Criteria

- Patients with a history of diabetes mellitus or established cardiovascular disease.
- Patients on hemodialysis.
- Individuals with congenital or systemic inflammatory disorders.
- Inadequate acoustic windows for vascular ultrasound evaluation.

Clinical and Biochemical Evaluation

All participants underwent detailed clinical assessment including height, weight, body mass index (BMI), blood pressure, and comprehensive history (including comorbidities and family history). Biochemical parameters assessed included:

- Serum creatinine
- Estimated glomerular filtration rate (eGFR)
- Serum uric acid
- Total cholesterol
- LDL, HDL, and triglycerides

Ultrasonographic Evaluation

High-resolution B-mode ultrasonography was performed using a GE LOGIQ P9 machine equipped with a 7–13 MHz linear array transducer. The following arterial segments were examined bilaterally:

- **Common carotid artery (CCA)** • **Common femoral artery (CFA)**

The intima-media thickness (IMT) was measured at 1 cm proximal to the carotid bifurcation and in the distal superficial femoral artery in longitudinal plane. Three measurements were taken at each site, and the mean value was calculated for both carotid (cIMT) and femoral (fIMT) arteries.

Data Analysis

All collected data were entered into Microsoft Excel and analyzed using SPSS software (version 25.0). Descriptive statistics were used to summarize the demographic and clinical data. Mean IMT values were compared between groups using independent t-tests. Correlations between IMT values and biochemical parameters were evaluated using Pearson's correlation coefficient. A p-value of <0.05 was considered statistically significant.

RESULTS

The present study included a total of 50 participants, divided equally into a CKD group (n=25) and a control group (n=25). The baseline characteristics of the two groups are detailed in **Table 1**. There were no statistically significant differences in age or BMI between the groups (p=0.42 and p=0.35, respectively). However, systolic and diastolic blood pressures were significantly higher in CKD patients compared to controls (SBP: 134.5 mmHg vs. 122.8 mmHg, p=0.01; DBP: 86.3 mmHg vs. 80.1 mmHg, p=0.03), indicating a higher cardiovascular risk profile among CKD subjects. The core objective of the study was to assess vascular changes using intima-media thickness. As shown in **Table 2**, both carotid (cIMT) and femoral (fIMT) intima-media thickness values were significantly elevated in the CKD group compared to controls. The mean cIMT in CKD subjects was 0.69 mm compared to 0.54 mm in controls (p=0.001), while the mean fIMT was 0.78 mm versus 0.62 mm, respectively (p=0.0001). These findings strongly suggest early subclinical atherosclerotic changes in CKD patients even in younger age groups. Biochemical profiling revealed significant dyslipidemia among CKD patients, as outlined in **Table 3**. Total cholesterol, LDL, and triglyceride levels were notably higher in the CKD group (p=0.02, 0.01, and 0.03, respectively), while HDL levels were significantly lower (38.2 mg/dL vs. 48.9 mg/dL, p=0.005). This dyslipidemic pattern is consistent with known pro-atherogenic profiles associated with CKD. Correlational analyses were performed to explore associations between IMT and biochemical parameters. In **Table 4**, cIMT showed a strong positive correlation with serum creatinine (r=0.62, p=0.001) and an inverse correlation with eGFR (r=-0.59, p=0.002), reinforcing the relationship between declining renal function and early vascular changes. Additionally, significant correlations were observed with total cholesterol (r=0.41, p=0.03), LDL (r=0.52, p=0.008), and triglycerides (r=0.39, p=0.04). A similar trend was noted for femoral IMT in **Table 5**. fIMT was positively correlated with serum creatinine (r=0.65, p=0.0005) and negatively correlated with eGFR (r=-0.63, p=0.001). It also demonstrated moderate positive correlations with lipid parameters such as total cholesterol (r=0.45, p=0.02), LDL (r=0.49, p=0.01), and triglycerides (r=0.36, p=0.05). These findings suggest that both carotid and femoral arteries undergo early atherosclerotic changes in parallel with biochemical derangements in CKD. To determine independent predictors of IMT, a multivariate regression analysis was conducted combining both cIMT and fIMT as outcomes (**Table 6**). Serum creatinine emerged as the strongest independent predictor (β=0.33, p=0.002), followed

by LDL (β=0.29, p=0.005) and systolic blood pressure (β=0.21, p=0.03). Although age and BMI were positively associated, they did not reach statistical significance (p=0.09 and p=0.06, respectively).

Table 1: Baseline Clinical and Demographic Parameters

Parameter	CKD Group (n=25)	Control Group (n=25)	p-value
Age (years)	29.4	28.7	0.42
BMI (kg/m²)	23.1	22.4	0.35
SBP (mmHg)	134.5	122.8	0.01
DBP (mmHg)	86.3	80.1	0.03

Table 2: Comparison of Intima-Media Thickness Values

Artery	CKD Group (n=25)	Control Group (n=25)	p-value
Carotid IMT (mm)	0.69	0.54	0.001
Femoral IMT (mm)	0.78	0.62	0.0001

Table 3: Lipid Profile Comparison

Parameter	CKD Group (n=25)	Control Group (n=25)	p-value
Total Cholesterol (mg/dL)	202.4	180.6	0.02
LDL (mg/dL)	128.7	110.3	0.01
HDL (mg/dL)	38.2	48.9	0.005
Triglycerides (mg/dL)	168.5	132.7	0.03

Table 4: Correlation of cIMT with Biochemical Parameters (CKD Group)

Parameter	Pearson Correlation (r)	p-value
Serum Creatinine	0.62	0.001
eGFR	-0.59	0.002
Total Cholesterol	0.41	0.03
LDL	0.52	0.008
Triglycerides	0.39	0.04

Table 5: Correlation of fIMT with Biochemical Parameters (CKD Group)

Parameter	Pearson Correlation (r)	p-value
Serum Creatinine	0.65	0.0005
eGFR	-0.63	0.001
Total Cholesterol	0.45	0.02
LDL	0.49	0.01
Triglycerides	0.36	0.05

Table 6: Multivariate Regression for Predictors of Increased IMT

Predictor	Beta Coefficient	p-value
Age	0.12	0.09
BMI	0.18	0.06
Serum Creatinine	0.33	0.002
LDL	0.29	0.005

SBP	0.21	0.03

DISCUSSION

This study investigated the potential of carotid and femoral intima-media thickness (cIMT and fIMT) as early ultrasonographic markers for subclinical atherosclerosis in adolescents and young adults with chronic kidney disease (CKD). The findings provide robust evidence that both cIMT and fIMT are significantly elevated in CKD patients compared to healthy controls, suggesting early vascular remodeling and atherosclerotic changes in this population. The observed increase in cIMT among CKD participants aligns with previous literature that recognizes carotid artery wall thickening as a reliable surrogate marker for early atherosclerosis and cardiovascular risk in high-risk populations [11]. Baroncini et al. demonstrated increased cIMT values in hypertensive adolescents, highlighting the sensitivity of IMT in detecting vascular abnormalities even at younger ages [12]. Similarly, Umeh et al. reported significantly elevated cIMT values in hypertensive adults, further substantiating the link between vascular changes and systemic conditions like hypertension and CKD [13]. Our findings are further supported by Kollias et al., who noted a direct correlation between higher cIMT and central adiposity, blood pressure, and glucose levels among adolescents [14]. These parameters are often altered in CKD patients, and the present study reiterates that traditional risk factors in combination with renal dysfunction lead to a compounded effect on arterial wall thickness. Gao et al. employed structural equation modeling and emphasized that age, systolic blood pressure, and glucose levels were key predictors of increased cIMT, a finding echoed in our regression analysis where serum creatinine, LDL, and SBP emerged as significant independent predictors [15]. Though the carotid artery is most commonly studied, our results also demonstrate a marked increase in femoral IMT among CKD patients, which has received relatively less attention in literature. This is consistent with findings by Litwin et al., who documented increased fIMT in hypertensive children, suggesting muscular arteries may also undergo early pathological remodeling in the presence of systemic risk factors [17]. Furthermore, studies such as that by Hsu et al. have shown femoral artery plaque formation to be more prevalent than carotid plaques in CKD, even in patients with a normal anklebrachial index, underscoring the need to incorporate fIMT assessment in routine screening [9].The present study also established significant positive correlations between both cIMT and fIMT with traditional atherogenic markers such as total cholesterol, LDL, and triglycerides. These associations were statistically significant, reiterating the role of dyslipidemia in endothelial dysfunction and atherogenesis. Leite et al. corroborated that even moderate increases in body mass and triglyceride levels among adolescents are significantly associated with higher cIMT [19]. Additionally, the inverse relationship between eGFR and IMT values, as observed in our study, further emphasizes that vascular alterations may begin even before substantial renal decline or overt symptoms manifest. This aligns with the findings of Cai et al., who showed a direct relationship between cIMT and pulse pressure index (PPI) in newly diagnosed hypertensive individuals [18]. The multivariate regression model used in our study highlighted serum creatinine and LDL as key predictors of arterial wall thickening. These findings mirror those of Sesti et al., who showed that endothelial dysfunction, as assessed by acetylcholine-induced vasodilation, is significantly worse in individuals with elevated cIMT and lower IGF-1 levels [16]. Our data suggest that such vascular dysfunction in CKD could be multifactorial—attributable to a mix of traditional cardiovascular risk factors and CKD-specific metabolic disturbances such as hyperuricemia, endothelial inflammation, and uremic toxin accumulation. From a clinical perspective, this study suggests that the use of high-resolution B-mode ultrasonography to measure cIMT and fIMT can offer a non-invasive, costeffective, and reliable method for early detection of atherosclerotic risk in CKD patients. Unlike ABI, which loses sensitivity in stiff vessels typical of CKD, IMT evaluation can detect preclinical changes and aid in early risk stratification [8, 10].

One of the strengths of our study is the inclusion of a relatively young CKD population (15–40 years), a group typically overlooked in cardiovascular risk screening despite increasing evidence of early vascular

involvement. The limitations, however, include a relatively small sample size and the cross-sectional nature of the study, which restricts the ability to infer causality. Moreover, histopathological validation of atherosclerosis and long-term follow-up for cardiovascular outcomes would enhance the clinical relevance of the findings.

In conclusion, this study affirms that CKD independently contributes to vascular changes measurable by IMT and supports incorporating ultrasonographic screening of cIMT and fIMT into the routine evaluation of young CKD patients. Early detection of vascular alterations in this population can guide timely lifestyle modifications and pharmacologic interventions aimed at reducing cardiovascular morbidity and mortality.

CONCLUSION

This study establishes carotid and femoral intima-media thickness as promising non-invasive markers for detecting subclinical atherosclerosis in young CKD patients. Both cIMT and fIMT were significantly higher in CKD subjects compared to controls and showed strong correlations with serum creatinine, lipid parameters, and blood pressure. Serum creatinine and LDL emerged as independent predictors of increased IMT. These findings highlight the urgent need for early vascular screening in CKD patients, especially in younger age groups, to facilitate timely intervention and mitigate long-term cardiovascular complications. Ultrasonographic IMT measurement should be considered a valuable tool in risk stratification protocols.

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