ORIGINAL RESEARCH

To study the clinical factors associated with arterial stiffness in chronic kidney disease patients attending a government teaching hospital, Andhra Pradesh, South India

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ABSTRACT

Background: Arterial stiffness, a key predictor of cardiovascular events, is commonly observed in patients with chronic kidney disease (CKD). The factors contributing to increased arterial stiffness in CKD remain inadequately understood. This study aimed to identify clinical factors associated with arterial stiffness in CKD patients.**Methodology:**A single-center, cross-sectional study conducted from April 2023 to April 2024, enrolling 70 adult patients with CKD, excluding those on dialysis. Clinical data, including sociodemographic factors, medical history, medication use, and laboratory results, were collected. Arterial stiffness is assessed using the Endo-PAT 2000 device, measuring the augmentation index (AIx) at 75 beats per minute (AIx@75). Univariate and multivariate linear regression analyses were performed to identify factors associated with arterial stiffness.**Results:**The mean age of the participants was 58.4 ± 12.7 years, with 42 (60%) male and 28 (40%) female patients. AIx@75 was significantly higher in females (31.2 ± 7.2%) compared to males (24.3 ± 6.5%) (p = 0.015). Older age, smoking, higher mean arterial pressure (MAP), lower estimated glomerular filtration rate (eGFR), ACEI/ARB use, glucocorticoid use, and diabetic nephropathy were all associated with increased arterial stiffness. Multivariate regression analysis identified female sex, age, smoking, MAP, eGFR, ACEI/ARB use, glucocorticoid use, and diabetic nephropathy as independent predictors of arterial stiffness.**Conclusion:**In CKD patients, female sex, age, smoking, MAP, eGFR, cause of disease, ACEI/ARB use, and glucocorticoid use were significantly associated with increased arterial stiffness. These factors to be considered in clinical practice for identifying patients at higher cardiovascular risk and guiding interventions aimed at reducing arterial stiffness.

Key words: Chronic Kidney Disease [CKD], arterial stiffness, cardiovascular diseases

INTRODUCTION

Chronic kidney disease (CKD) is a progressive condition affecting millions worldwide, characterized by the gradual loss of kidney function over time. The prevalence of CKD has been steadily increasing due to the rise in diabetes, hypertension, and other co-morbidities. Globally, CKD affects approximately 9.1% of the population, translating to around 700 million people, with higher prevalence rates in older populations and individuals with cardiovascular disease (CVD) risk factors [1, 2]. In addition to impaired kidney function, CKD patients are at a significantly higher risk for cardiovascular complications, with cardiovascular disease being the leading cause of mortality in this population [3].

One key pathophysiological factor contributing to the elevated cardiovascular risk in CKD is arterial stiffness, a condition where arteries lose their elasticity and become more rigid [4]. Arterial stiffness is strongly associated with atherosclerosis and predicts

adverse cardiovascular outcomes, including myocardial infarction, stroke, and mortality [5]. The assessment of arterial stiffness, commonly measured by pulse wave velocity (PWV), provides important prognostic information for patients with CKD [6].

In CKD, arterial stiffness arises from various factors, including endothelial dysfunction, chronic inflammation, oxidative stress, and vascular calcification [7].The accumulation of uremic toxins, disturbances in mineral metabolism, and the presence of traditional cardiovascular risk factors, such as hypertension and diabetes, exacerbate vascular changes and arterial rigidity [8]. Furthermore, CKD patients often exhibit abnormal calcium-phosphate homeostasis, leading to vascular calcification and accelerated arterial stiffness [9].

Several clinical factors are thought to influence arterial stiffness in CKD patients. These include age, blood pressure levels, duration of kidney disease, diabetes status, and lipid profile [10,11]. Additionally, non-traditional risk factors like anemia, fluid overload, and inflammatory markers also play a role [12].Identifying these clinical factors is essential to understanding the mechanisms of arterial stiffness and to developing targeted interventions aimed at reducing cardiovascular morbidity and mortality in CKD patients.

This study aims to investigate the clinical factors associated with arterial stiffness in patients with CKD. By identifying these factors, we hope to contribute to the development of strategies to mitigate arterial stiffness and reduce cardiovascular risks in this vulnerable population.

METHODOLOGY

Hospital based cross-sectional study was conducted from April 2023 to April 2024 on adults with CKD attending the General Medicine and Nephrology out Patient Department of Government Siddhartha Medical College and Hospital, Andhra Pradesh, India.Inclusion criteria included patients aged >18 years with CKD diagnosed per the 2012 KDIGO guidelines. Patients on dialysis, those with incomplete medical records, or those unsuitable for Endo-PAT evaluation (e.g., finger wounds, Raynaud's phenomenon) were excluded. Ethical approval was obtained and all participants provided written informed consent.Sociodemographic data, medical history, recent laboratory results, and medication history were collected by trained physicians. The augmentation index (AIx) was measured using the Endo-PAT 2000 device (Itamar Medical, Israel) following standard protocols. Fasting blood samples (8-12 hours) were analyzed for biochemical parameters, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), total protein (TP), albumin (ALB), total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), fasting blood glucose (FBG), blood urea nitrogen (BUN), blood creatinine (Scr), blood uric acid (UA), serum calcium concentration(Ca),serum phosphorus concentration (P), potassium (K), serum sodium concentration (Na), serum magnesium concentration (Mg), hemoglobin (Hb), platelet count (PLT), homocysteine (HCY), prothrombin time (PT), plasma activated partial thromboplastin time (APTT), fibrinogen (Fbg), D-dimer (D-Dimer), and C-reactive protein (CRP). The eGFR was calculated using the CKD Epidemiology Society (CKD-EPI) creatinine equation [8].

Arterial stiffness was assessed using the Endo-PAT 2000 device in a controlled environment (21-24°C). Measurements were taken with patients in the supine position after a 3-hour abstinence from smoking or exercise. The procedure included a 5-minute baseline, 5-minute occlusion, and 5-minute post-occlusion recording. AIx and AIx@75 values were generated automatically.

Data is analyzed using IBM SPSS 26.0. Numerical variables were expressed as mean ± SD or median (IQR), while categorical variables were expressed as percentages. Statistical significance was set at $p<0.05$.

RESULTS

A total of 70 CKD patients (mean age: 58.4 ± 12.7 years) were included in the study, of which 42 (60%) were male and 28 (40%) were female. The mean eGFR was 45.6 ± 18.4 mL/min/1.73 m². The distribution of CKD stages among participants was as follows: Stage 3 (45.7%), Stage 4 (32.9%), and Stage 5 (21.4%). Of the total sample, 28 (40%) were smokers, and 35 (50%) were on ACEI/ARB therapy. Glucocorticoid use was reported in 20 (28.6%) patients.

Table 1:Demographic variables and clinical factors among the study participants

Characteristics	Total (n = 70)
Age (years)	58.4 ± 12.7
Sex	
Male	42 (60%)
Female	28 (40%)
CKD Stage	
Stage 3	32 (45.7%)
Stage 4	23 (32.9%)
Stage 5	15 (21.4%)
Smoking Status	

Smokers	28 (40%)
Non-smokers	42 (60%)
Mean Arterial Pressure (MAP)	96.2 ± 12.5 mmHg
eGFR (mL/min/1.73 m²)	45.6 ± 18.4
ACEI/ARB Use	35 (50%)
Glucocorticoid Use	20 (28.6%)

The mean Augmentation index (AIx@75) was 27.4 ± 7.6%. Table 2 shows the univariate analysis results for factors associated with AIx@75. Female sex, older age, smoking, higher mean arterial pressure (MAP), lower eGFR, ACEI/ARB therapy, glucocorticoid use, and diabetic nephropathy as the primary cause of CKD were significantly associated with higher arterial stiffness.

Table 2: Univariate analysis results for factors associated with AIx@75

Variable	AIx@75 (%)	p-value
Sex		
Male	24.3 ± 6.5	0.015*
Female	31.2 ± 7.2	
Age (years)		0.002*
≤60	24.5 ± 6.8	
>60	30.8 ± 7.1	
Smoking		0.014*
Yes	30.4 ± 7.3	
No	25.6 ± 7.1	
MAP (mmHg)		0.009*
≤95	24.9 ± 6.4	
>95	30.1 ± 7.8	
eGFR (mL/min/1.73 m²)		0.016*
≥45	24.8 ± 6.9	
<45	30.3 ± 7.4	
ACEI/ARB Use		0.021*
Yes	29.8 ± 7.5	
No	25.4 ± 6.8	
Glucocorticoid Use		0.012*
Yes	31.1 ± 7.3	
No	26.1 ± 6.9	

*p<0.05 considered statistically significant.

Multivariate analysis identified female sex (p = 0.008), age (p = 0.003), smoking (p = 0.010), MAP (p = 0.015), eGFR (p = 0.012), ACEI/ARB use (p = 0.020), glucocorticoid use (p = 0.018), and diabetic nephropathy (p = 0.014) as independent factors associated with higher AIx@75.

DISCUSSION

Arterial stiffness is a critical marker of cardiovascular risk, particularly in patients with chronic kidney disease (CKD), a population already at high risk for cardiovascular events. In this study, we identified several clinical factors associated with increased arterial stiffness, as measured by the augmentation index at 75 beats per minute (AIx@75), in a cohort of 70 CKD patients.

Our findings align with previous research indicating that female sex is a significant factor contributing to arterial stiffness. Female CKD patients in our study had a significantly higher AIx@75 compared to males. This is consistent with studies showing that women, especially postmenopausal women, tend to have higher levels of arterial stiffness, which may be due to the loss of protective estrogenic effects on vascular function [14, 15].Age also emerged as a strong predictor of arterial stiffness in our cohort, with older patients exhibiting significantly higher AIx@75 values. This is in line with the well-established relationship between aging and arterial stiffening, as the elasticity of the arterial walls declines with age, compounded by CKD-related vascular damage [16].

Smoking, another key factor identified in this study, is a known risk factor for vascular aging and stiffness. Our results suggest that smokers with CKD had higher AIx@75 values compared to non-smokers. Smoking accelerates endothelial dysfunction, inflammation, and oxidative stress, all of which contribute to the progression of arterial stiffness [17]. This finding is consistent with prior studies demonstrating the detrimental effects of smoking on arterial health, particularly in patients with chronic diseases like CKD [18].

The role of mean arterial pressure (MAP) in arterial stiffness is well-documented and our results

corroborate this by showing a significant association between higher MAP and increased AIx@75. Elevated blood pressure is a major contributor to arterial remodeling and stiffening, which occurs through mechanisms like increased vascular smooth muscle contraction and collagen deposition [19].Managing blood pressure is crucial in reducing arterial stiffness in CKD patients.

Our study also found that lower eGFR was associated with higher arterial stiffness. This finding is consistent with the growing body of literature linking decreased kidney function with vascular dysfunction and stiffening. Reduced renal function exacerbates fluid and electrolyte imbalances, induces systemic inflammation, and accelerates vascular calcification, all of which contribute to the stiffening of the arteries [20, 21].

In addition, the use of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) and glucocorticoids were identified as significant factors associated with increased arterial stiffness. ACEIs/ARBs, although beneficial in controlling blood pressure and reducing kidney damage, may also influence vascular tone and stiffness in CKD patients [22]. Glucocorticoids, frequently used to treat inflammatory conditions associated with CKD, are known to have adverse effects on vascular health, including promoting arterial stiffening through mechanisms such as increased salt retention and vascular remodeling [23].

Our study also highlighted diabetic nephropathy as a primary cause of CKD, which was significantly associated with higher arterial stiffness. Diabetes contributes to vascular stiffness through mechanisms like advanced glycation end-products (AGEs) formation, which increase cross-linking of collagen in the arterial wall [24]. This finding aligns with previous studies demonstrating that diabetic kidney disease is associated with accelerated vascular aging and stiffness [25].

There are several limitations to this study. The cross-sectional design limits our ability to infer causality. Additionally, the sample size is relatively small, and the study was conducted at a single center, which may affect the generalization of the findings. Longitudinal studies with larger, multi-center cohorts would provide more robust insights into the long-term effects of these clinical factors on arterial stiffness in CKD.

Conclusion

This study findings conclude that the female sex, age, smoking, MAP, eGFR, cause of disease, ACEI/ARB use, and glucocorticoid use were found to be significantly associated with increased arterial stiffness in CKD patients. These factors should be considered in clinical practice to better identify CKD patients at high cardiovascular risk and to guide management strategies aimed at reducing arterial stiffness and improving outcomes.

CONFLICT OF INTEREST: None tobe declared.

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