ORIGINAL ARTICLE

Abdominal Aortic Calcifications in Patients with Chronic Kidney Disease: A Single Center Study in Lahore, Pakistan

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ABSTRACT

Objective: To determine the prevalence of abdominal aortic calcification in patients diagnosed with chronic kidney disease stage III to V.

Study Design: Cross-sectional study.

Place and Duration of Study: The study was carried out at the Department of Nephrology, Fatima Memorial Hospital Lahore, Pakistan from December 2022 to December 2023.

Methods: A total of 295 patients diagnosed with chronic kidney disease stages III to V were included. The lateral view of the lumbar radiograph was carried out in the standing position. All the X-rays were confidentially submitted to the Central Radiology Department where a consultant Radiologist interpreted the X-ray in the light of the Abdominal Aortic Calcification Score. Significant Abdominal Aortic Calcification (AAC) was designated as per the Operation ACC score interpreted and reported by the consultant Radiologist. Chronic kidney disease (CKD) and Aortic Calcification were designated.

Results: Abdominal aortic calcification was found in 89 (30.17%) patients. Male gender was significantly associated with the presence of abdominal aortic calcification ($\chi 2 = 50.019$, df = 1, *P*-value 0.001).

Conclusion: We concluded that there is a moderately high frequency (30%) of abdominal aortic calcification in patients with chronic kidney disease.

Keywords: *Cardiovascular Disease, Chronic Kidney Disease, Kidney Disease, Vascular Calcification.*

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Introduction

A total of 8-16% of the world population has been diagnosed with the chronic kidney disease.[1] Although the exact prevalence of this disease is not known in Pakistan, in a survey conducted in Karachi, 25.3% showed a decrease in the glomerular filtration rate (GFR) and 5% patients were diagnosed with moderate CKD, glomerular filtration rate being less than 60 ml/min.[2] A survey-based study conducted on 1023 subjects by Ahmed et al estimated the occurrence of chronic kidney disease stage III and IV as 14% of the study population.[3] In the neighboring country, India, the occurrence of chronic kidney disease is 17.2% and approximately 6% were diagnosed with stage 3 or more.[4] It will be safe to state that, considering a similar population, our CKD prevalence is likely to be similar.

Abdominal Aortic Calcification (AAC) is associated with a high risk of cardiovascular events as compared to people without abdominal aortic calcification.[5] Aortic calcification can be detected by the lateral view of the lumbar radiograph and Kidney Disease Improving Global Outcomes also recommends it.[6]

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AAC has been suggested to be a surrogate for coronary artery disease (CAD).[7] It may be so since the pathophysiology (hyperlipidemias, atherosclerosis, calcium deposition) is similar. In patients with CKD and without CAD, the presence of AAC may be a valuable finding for the urgent evaluation of CKD. Early detection of AAC will improve the optimal treatment for CKD patients.[8]

There is an increased prevalence of abdominal aortic calcification among CKD patients, which ranges from 18.5% to 94.4%.[9,10] However, these studies did not specifically study patients with end-stage kidney disease. In Pakistan, no study has been conducted to date to assess the incidence of AAC in local patients. This study was conducted to determine the prevalence of AAC in patients diagnosed with chronic kidney disease stage III to V.

Methods

A descriptive cross-sectional study was carried out at the Department of Nephrology, Fatima Memorial Hospital Lahore, Pakistan from December 2022 to December 2023 after obtaining permission from the Ethical Review Committee of the hospital vide letter no: 12/48 held on dated: 13th January 2021. We used non-probability, consecutive sampling to enroll 295 patients (expected AAC prevalence of 26%, with a 5% level of significance and 5% margin of error). The inclusion criteria were: age (18 – 80 years), serum CKD stages III to V, and intact PTH level of more than 300 IU/L. Patients unable to stand up and unwilling to participate were excluded.

We defined CKD as any eGFR (CKD-EPI equation utilizing creatinine) below 60 with further triage into CKD stages III (eGFR: 30 – 59), IV (eGFR: 15 – 29) and V (eGFR: <15). The presence of calcification was graded per segment using L1-L4 on the lateral view of the lumbar radiograph. The grading was between 0 and 3 for both the anterior and posterior aortic walls individually. These scores were used to calculate the AAC Score (0-24 score). Less than 6.5 points were taken to be significant. After taking informed consent, these patients underwent a lateral view of the Lumbar Radiograph in the standing position. All the X-rays were confidentially submitted to the Central Radiology Department where a consultant Radiologist interpreted the X-ray in the light of AAC Score.

All the data was stored in MS Excel 2016 and analyzed on R Statistical Computing Software (Version 4.3.2). The packages used for analysis and visualizations were: tidyverse, stats and tableone.

The descriptive including quantitative variables (age and duration of CKD) were calculated as mean±SD and categorical parameters (gender: nominal variable with values "Male" and "Female", CKD Stage: ordinal variable with values III, IV, V and presence or absence of AAC (binary variable, based on the AAC Score more or less than 6, respectively)) were given as frequencies and percentages. Chi-Square test was performed for assessing categorical variables and T-test was used to present quantitative variables. We also carried out logistic modeling to check the effect of numerical variables on the presence of AAC. A *P*-value of < 0.5 was considered to be significant.

Results

The demographics of the cohort are given in Table-1. The mean ages of males and females were 41.01 $\pm$ 15.40 and 43.54 $\pm$ 14.96, respectively. We conducted the Shapiro-Wilk Test and F-Test for homogeneity of variances which concluded that although the population distribution was non-normal, there was no significant difference in the ages of males and females. An independent samples T-Test confirmed the findings from F-Test (t = -1.3067, df = 167.16, *P*-value = 0.1931.). The presence of AAC was explained by the CKD Stage as shown by Pearson's Chi-Square test (X-squared = 6.4279, df = 2, *P*-value = 0.04) (Figure.1). To see the effect of gender on the presence of AAC, we used Pearson's Chi Square test with Yates' Continuity correction (X-squared = 6.6244, df = 1, *P*-value = 0.01), however after sub-setting the data and repeating the test for males and females separately we found that only the male gender was significantly associated with the presence of AAC (Females: X-squared = 2.5862, df = 1, *P*-value=0.1078, Males: X-squared = 50.019, df = 1, *P*-value=0.001).

Logistic regression modeling was done to note the effect of numerical variables (age, CKD duration) on the presence or absence of AAC. Based on our model the coefficient for CKD duration was statistically significant (*P*=0.001), indicating that there is strong evidence that CKD duration has a significant effect on

Table-1: Characteristics of the cohort	
Total Number of Patients (n)	295
Age in years (mean ± SD)	41.76 ± 15.40
Gender (n (% age))	M: 208 (70.5), F: 87 (29.5)
CKD Stage n (% age of the total cohort)	
III	148 (50.2)
IV	90 (30.5)
V	57 (19.3)
CKD duration in years (mean ± SD)	5.09 ± 1.85
Abdominal Aortic Calcification present n(%)	89 (30.2)

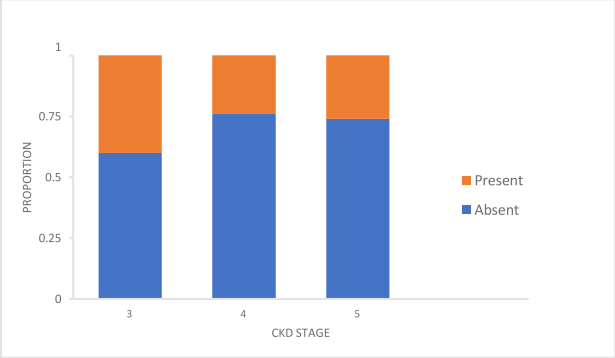

Fig.1: Distribution of Abdominal Aortic Calcifications by CKD Stages

AAC presence. Age did not show a significant effect on the presence of AAC (*P*=0.433).

Discussion

Cardiovascular events are very frequent in patients diagnosed with chronic kidney disease.[11] Changes in bone and mineral metabolism is one of its causes. For example, hyperphosphatemia, elevated FGF23, hyperparathyroidism, and hypercalcemia increase the risk of cardiovascular morbidity and mortality.[12,13] It has been suggested that disturbances in bone and mineral metabolism cause vascular calcification.[14,15] Studies conducted reported the increased severity and duration in CKD patients as compared to same-age healthy individuals.[16] Vascular calcification usually occurs due to cardiovascular events in patients dependent upon dialysis and healthy individuals.[16-19] It is recommended to use plain radiographs to assess AAC to select apt treatment.[20] However, scarce data is available to evaluate the prognostic value of AAC in non-dialysis CKD patients.[8] The prevalence of AAC (30.17%) in our study is lower than the prevalence rates reported elsewhere. According to studies, AAC is mostly common in the elderly population i.e. older than 60 years.[21] We were unable to bring out that relationship in our cohort, however, it needs to be kept in mind that ours was a younger cohort with mean ages for both males and females in their early 40s. On the other hand, considering this prevalence in a young cohort may also be thought-provoking about the current state of management of CKD patients.

The relationship between the male gender and the presence of AAC is also intriguing. We were unable to find a clear precedence in the previous studies. Males may be at a higher risk because of a generally higher risk for atherosclerosis as seen in cardiovascular trials at least up to the sixth or seventh decade, when females surpass them in terms of cardiovascular events.[22] This age was not represented sufficiently in our cohort (male participants above 60 years of age 11.52%, and 4.74% in females), hence we are unable to reliably comment upon this. However, it may be interesting to know if this relationship between ages and AAC holds for higher age ranges, for which further studies may be warranted. In a study by Chen et al. the high prevalence of AAC in males significantly increased six times when followed up for 25 years.[23] However, in this study the risk in women also increased eight times which is in contrast to our study findings suggesting male gender as risk factor for AAC. Furusawa et al also reported no significant difference in the prevalence of AAC between both genders.[24]

A study done in the Thai population reported that the prevalence of aortic calcification was lower in

these patients with chronic kidney disease as compared to studies done globally and in the Caucasian population specifically.[25] The reason for this discrepancy was reported due to changes in ethnicity and dietary lifestyle. These factors influence the lower risk of aortic calcification.

Our findings indicated a significant association between the presence of AAC and the duration of kidney disease. Ma et al. also reported that advancement in CKD staging also accelerated the development of AAC with pulse pressure level and PTH levels as predictors of disease prognosis.[26] In a research by Leow et al. , AAC was regarded as a significant predictor of CKD staging and its advancement and future mild and severe cardio events.[22]

AAC may be a risk marker for cardiovascular outcomes. Once developed it may lead to ischemia of the downstream vascular territories and intermittent claudication may be a manifestation as well. The treatment depends upon the control of atherosclerotic risk factors (diabetes, hypertension, hyperlipidemia). Recently, one of the trials using exercise training reported a lack of significant benefit of endurance exercise of the AAC score, which underlines the resistant nature of these lesions once developed.[27] In a study by Maruyama et al., AAC was reported as an independent predictor of cardiovascular events even after adjusting for standard risk factors of CVD including advanced age, family history, diabetes, BMI, smoking, SBP, and dyslipidemia.[28] Another 5-year follow-up study showed that AAC was a significant denominator in overall mortality and cardiovascular mortality in patients undergoing hemodialysis.[29] Suh et al showed that in pre-dialysis patients with chronic kidney disease with AAC score was an independent risk factor for adverse cardiac outcomes.[8]

The purpose of this study was to find out the frequency of AAC in a adequately sampled cohort of patients representing the later stages of CKD. The authors feel that they have succeeded in fulfilling the stated objective of this study. However, our study is limited in broader aspect. We only included patients with late-stage CKD, we did not measure the degree of AAC through the AAC index in patients. This study may be a springboard for later studies to explore relationships between various other factors influencing the development of AAC as well as to discover the relationship of AAC with cardiovascular outcomes.

Conclusion

The prevalence of abdominal aortic calcifications in patients with chronic kidney disease stage III to V is moderately high.

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Conflict of Interest: The authors declare no conflict of interest

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Authors Contribution

MD: Idea conception, data collection
OS: Study designing, manuscript writing and proofreading
MBB: Data collection, data analysis, results and interpretation
AHS: Idea conception
AK: Data analysis, results and interpretation
SAAS: Study designing