Original Article

Fibroblast Growth Factor-23 in Pre-Dialysis Chronic Kidney Disease Patients and its Correlation with Carotid Artery Calcification

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Abstract

Introduction: Fibroblast growth factor 23 (FGF-23) is a phosphate metabolism regulator in patients with chronic kidney disease (CKD). The present study is aimed to examine the FGF-23 level in pre-dialysis patients with CKD and its correlation with carotid artery calcification (CAAC). **Methods:** This cross-sectional study included patients with CKD and controls. The patients were compared with controls having similar distribution of age and sex to determine serum FGF-23 level in Indian healthy adult population. Detailed medical history, physical examination, and investigations were done for each patient. Atherosclerotic risk factors, cardiovascular comorbidities, and drug history were recorded. Carotid calcification was observed using carotid ultrasound. **Results:** In total, 62 patients with a mean age of 50.0 years were enrolled. Majority of the patients had hypertension (66.1%), followed by diabetes (27.4%) and dyslipidemia (3.2%). Mean serum corrected calcium levels were significantly higher in patients with CAAC compared to the patients without CAAC (9.21 ± 1.34 vs. 8.53 ± 0.93 mg/dL; $P = 0.014$). The FGF-23 levels were significantly higher in patients with CAAC compared to those without CAAC (396.0 vs. 254.0 pg/mL; $P = 0.008$). CAAC was found to be present in both early and late stages of CKD. Multivariate analysis showed that log FGF-23 and serum corrected calcium remained as independent determinants of CAAC. The prevalence of CAAC increased with the ascending quartiles of FGF23. **Conclusion:** In conclusion, FGF-23 was found to be independently associated with CAAC in CKD.

Keywords: *Calcium, carotid artery calcification, FGF23, iPTH, phosphorus, pre-dialysis*

Introduction

Chronic kidney disease (CKD) is a worldwide public health problem with an estimated affected population of 8%–16%. In India, the prevalence of CKD has been observed to be 17.2%, with around 6% having CKD stage 3 or worse with varying etiologies all over the country.[1-3] Fibroblast growth factor-23 (FGF-23) is an important regulator of phosphate metabolism in patients with CKD that acts by stimulating urinary phosphate excretion and reducing dietary phosphate absorption by inhibition of the synthesis of 1,25-dihydroxy vitamin D ($1,25(OH)_2D$).[4-6] It is a bone-derived 251-amino acid protein, primarily secreted by osseous tissue found in different species, including humans.

Mineral and bone disorder (MBD) is one of the major complications of CKD and is associated with higher risk of cardiovascular disease (CVD) and mortality. The clinical spectrum of CKD–MBD includes secondary hyperparathyroidism and its consequences, adynamic bone disease with increased fracture risk, vascular and cardiac calcification, and osteomalacia. FGF-23 has been identified as an independent biomarker for CKD–MBD. Investigations report that in adults with CKD, the plasma level of FGF-23 initially increases and is associated with the progression of CKD, disordered mineral metabolism, left ventricular hypertrophy, and mortality, whereas the decrease in plasma level of FGF-23 is associated with increasing levels of $1,25\ (OH)_2D$, hyperphosphatemia, ectopic calcification, and mortality.[7-12]

Cardiovascular calcification is a complex and active pathological process involving abnormal deposition of calcium phosphate salt within vascular tissues and is highly predominant in patients with CKD.[5] CVD is the most common cause of mortality and morbidity in patients with CKD, and cardiovascular calcification is one of the strongest interpreters of cardiovascular

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risk. A recent Italian study in CKD patients demonstrated vascular inflammation as one of the leading causes of cardiovascular calcification in patients with CKD.[13] Several methods have been used for prevention and control of cardiovascular calcification in patients with CKD, which generally target the control of phosphate and calcium homeostasis.[14] A positive relationship exists between the concentration of FGF-23 and cardiovascular risk, mortality, and cardiovascular calcification.[15-18] However, the pathophysiological role of FGF-23 in CKD and cardiovascular outcomes remains controversial.

A paucity of data exists in Indian patients with CKD about the relevance of FGF-23 level. The present study aimed to determine the levels of FGF-23 in patients with CKD and their association with carotid artery calcification (CAAC).

Materials and Methods

Study design

This cross-sectional observational study was conducted at the Department of Internal Medicine and Nephrology, Vardhman Mahavir Medical College and Safdarjung Hospital, New Delhi, India, during 2016–2018. The study was carried out in accordance with the principles of the Declaration of Helsinki and was approved by the Institutional Ethics Committee. All the patients provided written informed consent before enrollment.

Study population

Patients of either sex and age above 18 years with CKD not on dialysis were included in this study. The patients who were on phosphate binders or active vitamin D supplements and had pre-diagnosed comorbidities with elevated FGF-23 were excluded, like autosomal dominant hypophosphatemic rickets, X-linked hypophosphatemic rickets, etc. For this, we took detailed history of patients regarding any skeletal deformities. The patients were compared with controls having similar distribution of age and sex to determine serum FGF-23 level in Indian healthy adult population. As there is no reference level of serum FGF-23 in healthy Indian adult population at present, we took 30 age- and sex-matched healthy adults as controls to determine serum FGF-23 levels in healthy Indian adult population in our study. FGF level >222 pg/mL has been considered as elevated in our study. Detailed medical history, physical examination, and investigations were done for each patient. Atherosclerotic risk factors (history of smoking, dyslipidemia, hypertension, and diabetes mellitus), cardiovascular comorbidities, and drug history (phosphate binders and vitamin D supplements) at presentation were recorded. Diagnosis and staging of CKD was done by the National Kidney Foundation and the Kidney Disease Outcomes Quality Initiative (NKF/KDOQI) (2002) classification criteria, which made estimated glomerular filtration rate (eGFR) a defining component, and eGFR was calculated using the four-variable Modification of Diet in Renal Disease (MDRD) system.

eGFR (in mL/min/1.73 m^2) = 186 × (serum creatinine/88.4) − 1.154 × (age) − 0.203 × (0.742 if female) × (1.210 if black).

Laboratory investigation was performed to determine the levels of complete blood count (CBC), serum creatinine (Scr), fasting plasma glucose (FPG), hemoglobin (Hb), and serum corrected calcium and phosphorus. Serum intact parathyroid hormone (iPTH), serum levels of $1,25(OH)_2D$, and FGF-23 levels were measured in serum samples by using the enzyme-linked immunosorbent assay (ELISA) kit. Microscopic examination and routine analysis of urine was done.

Carotid ultrasound

Gray-scale ultrasound of bilateral carotid arteries was carried out in ultrasound laboratory with a 10-MHz linear array transducer (Philips HD 11XE). The patient was made to lie down supine with head slightly hyperextended and rotated 45° away from the side being examined. Entire extent of common carotid arteries, internal and external carotid arteries in the neck, was examined in longitudinal and transverse planes. Carotid arteries' calcification was seen as a highly echogenic nodule on the vessel wall or within a plaque and posterior shadowing.

Statistical analysis

Categorical variables were presented as proportions and compared using Pearson's Chi-square test. Continuous variables were presented as mean (standard deviation) or median and range and compared using independent sample *t*-test or Mann–Whitney U test (for comparison between two groups), depending upon the distribution of data. Comparison of continuous variables between more than two groups was done using one-way analysis of variance (ANOVA) or Kruskal–Wallis test, depending upon the distribution of data. Univariate and multivariate logistic regression analyses were used to assess the association of serum FGF-23 with carotid calcification. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 21.0. A P value of <0.05 was considered statistically significant.

Results

A total of 62 patients were enrolled in this study; 37 (59.7%) were men and 25 (40.3%) were women; 17.7% were smokers. Majority of the patients had hypertension (66.1%) followed by diabetes (27.4%) and dyslipidemia (3.2%). The mean levels of Hb, serum corrected calcium, phosphorus, and FPG levels were 9.4 g/dL, 8.7 mg/dL, 5.5 mg/dL, and 105.3 mg/dL, respectively. The median levels of Scr, eGFR, calcium phosphorus products, serum intact iPTH, $1,25(OH)_2D$, and FGF-23 were 3.9 (2.7–6.8) mg/dL, 14.8 (7.8–24.1)

mL/min/1.73 m^2, 41.6 (35.7–54.3) mg^2/dL^2, 181.6 (88.6–927.0) pg/mL, 17.9 (3.2–31.5) ng/mL, and 265.5 (165.4–397.6) pg/mL, respectively. The median FGF-23 level in healthy adult control group was 222.0 (116.0–238.0) pg/mL [Table 1]. The FGF-23 levels were higher in patients with CKD compared to healthy individuals (265.0; [range: 165.4–397.6] vs. 222.0 [range: 116.0–238.0] pg/mL; $P = 0.064$).

CAAC was found in 15 (24.2%) patients. There was no significant difference in age distribution, sex, rates of smoking, hypertension, diabetes, dyslipidemia, and biochemical parameters including Hb, eGFR, P, Ca–P product, iPTH, and 1,25(OH) $_2$D between the patients with and without CAAC. Mean serum corrected calcium levels were significantly higher in patients with CAAC compared to patients without CAAC (9.21 ± 1.34 vs. 8.53 ± 0.93 mg/dL; $P = 0.014$). The FGF-23 levels were significantly higher in patients with CAAC compared to those without CAAC (396.0 vs. 254.0 pg/mL; $P = 0.008$) [Table 2].

There was only one patient in CKD stage 1–2, with the mean age being significantly higher (60.0 years) compared to patients in CKD stage 3 (43.5 years), stage 4 (56.7 years), and stage 5 (47.1 years) ($P = 0.03$). There was no significant difference in body mass index (BMI) ($P = 0.303$), male sex ($P = 0.681$), hypertension ($P = 0.307$), diabetes ($P = 0.258$), dyslipidemia ($P = 0.258$), and smoking ($P = 0.173$) between those in CKD stage 1–2 and those with advanced stage of CKD. The mean levels of serum corrected calcium decreased and phosphorus levels increased in patients with end-stage kidney disease (ESKD) compared to those in patients with CKD stages 1–4. The median levels of calcium–phosphorus product and serum intact iPTH increased and the median levels of 1,25(OH) $_2$D decreased in patients with ESKD. There was no significant difference in the FGF-23 levels between stage <2 and stage 5 ($P = 0.818$). CAAC was found to be present in both early and late stages of CKD [Table 3].

Age and sex, serum corrected calcium, log FGF-23, and iPTH were significantly associated with CAAC. Multivariate analysis showed that log FGF-23 and serum corrected calcium remained independent determinants of CAAC [Table 4]. The prevalence of CAAC increased with the ascending quartiles of FGF-23. The mean levels of Hb, serum corrected calcium, and phosphorus and the median levels of calcium–phosphorus product, eGFR, iPTH, and 1,25(OH) $_2$D were found to be diffusely distributed along with increasing quartiles of FGF-23 [Table 5].

Table 1: Baseline characteristics, laboratory and radiological parameters

Parameters	Total (*n*=62)
Age (years), mean (SD)	50.0 (13.9)
Sex, *n* (%)	
Men	37 (59.7)
Women	25 (40.3)
BMI (kg/m^2)	20.4 (17.9-23.4)
Smokers, *n* (%)	11 (17.7)
Hypertension, *n* (%)	41 (66.1)
Diabetes, *n* (%)	17 (27.4)
Dyslipidemia, *n* (%)	2 (3.2)
Hemoglobin (g/dL), mean (SD)	9.4 (1.9)
Serum creatinine (mg/dL)	3.9 (2.7-6.8)
eGFR (mL/min/1.73 m^2)	14.8 (7.8-24.1)
Serum corrected calcium (mg/dL), mean (SD)	8.7 (1.1)
Phosphorus (mg/dL), mean (SD)	5.5 (2.0)
Calcium-phosphorus product (mg^2/dL^2)	41.6 (35.7-54.3)
FPG (mg/dL), mean (SD)	105.3 (27.8)
iPTH (pg/mL)	181.6 (88.6-927.0)
1,25(OH)$_2$D (ng/mL)	17.9 (3.2-31.5)
FGF-23 (pg/mL)	265.5 (165.4-397.6)
FGF-23 of control group (pg/mL)	(*n*=30)
	222.0 (116.0-238.0)
CAAC, *n* (%)	15 (24.2)

1,25(OH) 2D=1,25-dihydroxyvitamin D, BMI=body mass index, CAAC=carotid artery calcification, eGFR=estimated glomerular filtration rate, FGF=fibroblast growth factor, FPG=fasting plasma glucose, IQR=interquartile range, iPTH=parathyroid hormone, SD=standard deviation. Data shown as median (IQR), unless otherwise specified

Discussion

The present cross-sectional observational study was conducted on 62 pre-dialysis patients with CKD to determine the association between serum FGF-23 levels and CAAC. Moreover, efforts were taken to access FGF-23 level in 30 healthy adults to determine the normal FGF-23 levels in Indian population. The major findings of this study demonstrate CAAC to be a common occurrence (about 25%) in CKD. The median levels of FGF-23 were significantly higher in CKD and CAAC compared to those without CAAC. However, there was no association between CAAC and traditional risk factors of atherosclerosis such as diabetes, hypertension, smoking, and dyslipidemia. The mean serum corrected calcium levels and FGF-23 levels were significantly higher in patients with CAAC compared to the patients without CAAC. The mean levels of serum corrected calcium significantly decreased, while the phosphorus levels increased with the progression of CKD. Furthermore, the findings showed the presence of CAAC in both early and late stages of CKD; however, its prevalence increased with the ascending quartiles of FGF-23.

Evidence suggests a positive correlation between FGF-23 and peripheral and aortic calcification in patients in pre-dialysis and those undergoing hemodialysis; however, a study by Inaba *et al*. has reported negative correlation between FGF-23 and peripheral calcification.[5,18-21]

The present study showed a preponderance of men, and this concurs with previously reported studies.[5,22,23] Higher

Table 2: Clinical characteristics of the patients with and without carotid artery calcification

Parameters	CAAC (-) (*n*=47)	CAAC (+) (*n*=15)	*P*
Clinical profile			
Age (years)			0.347
>18-≤40	15 (31.9)	3 (20.0)	
≥41-≤60	23 (48.9)	7 (46.6)	
≥61	9 (19.1)	5 (33.3)	
Men	29 (61.7)	8 (53.3)	0.565
Smoking	8 (17.0)	3 (20.0)	1.000
Hypertension	33 (70.2)	8 (53.3)	0.229
Diabetes	11 (23.4)	6 (40.0)	0.210
Dyslipidemia	1 (2.1)	1 (6.7)	0.428
Biochemical profile			
Hb (g/dL), mean (SD)	9.3 (1.8)	9.8 (2.3)	0.345
eGFR (mL/min/1.73 m^2), median (IQR)	14.3 (7.4-21.3)	21.4 (12.6-30.3)	0.122
Serum corrected calcium (mg/dL), mean (SD)	8.5 (0.9)	9.2 (1.3)	0.014
Phosphorus (mg/dL), mean (SD)	5.3 (1.9)	5.9 (2.5)	0.645
Ca-P product (mg^2/dL^2), median (IQR)	41.3 (35.5-47.3)	54.3 (35.8-59.2)	0.141
iPTH (pg/mL), median (IQR)	207.0 (88.6-1234.7)	149.0 (67.6-184.3)	0.936
$1,25(OH)_2D$ (ng/mL), median (IQR)	19.4 (2.9-32.9)	16.8 (8.4-29.9)	0.278
FGF-23 (pg/mL), median (IQR)	254.0 (155.1-310.4)	396.0 (270.0-437.4)	0.008

1,25(OH) 2D=1,25-dihydroxyvitamin D, CAAC=carotid artery calcification, Ca-P=calcium-phosphorus, eGFR=estimated glomerular filtration rate, FGF=fibroblast growth factor, Hb=hemoglobin, IQR=interquartile range, iPTH=parathyroid hormone, SD=standard deviation. Data shown as *n* (%), unless otherwise specified

Table 3: Clinical characteristics of patients according to CKD stage

Parameters	CKD stage 1-2 (*n*=1)	CKD stage 3 (*n*=9)	CKD stage 4 (*n*=21)	CKD stage 5 (*n*=31)	*P*
Biochemical profile					
Hb (g/dL), mean (SD)	11.4	10.9 (1.5)	10.3 (1.3)	8.4 (1.8)	<0.001
Serum corrected calcium (mg/dL), mean (SD)	9.1	8.6 (1.4)	8.9 (0.8)	8.5 (1.1)	0.608
Phosphorus (mg/dL), mean (SD)	4.4	4.6 (1.8)	4.4 (0.7)	6.4 (2.3)	0.87
Ca-P product (mg^2/dL^2) median (IQR)	39.6	35.7 (29.8-48.3)	36.9 (34.5-42.8)	46.8 (41.3-60.5)	0.187
iPTH (pg/mL), median (IQR)	40.8	184.4 (62.7-242.3)	157.0 (94.6-422.8)	207.0 (89.2-1123.3)	0.34
$1,25(OH)_2D$ (ng/mL), median (IQR)	25.6	12.1 (4.3-31.6)	20.8 (12.3-31.9)	11.5 (2.0-33.2)	0.489
FGF-23 (pg/mL), median (IQR)	271.0	249.2 (198.7-55.6)	256.0 (163.2-353.3)	267.0 (164.0-397.2)	0.818
CAAC, *n* (%)	-	4 (44.4)	6 (28.6)	5 (16)	0.302

1,25(OH) 2D=1,25-dihydroxyvitamin D, CAAC=carotid artery calcification, Ca-P=calcium-phosphorus, CKD=chronic kidney disease, FGF-23=fibroblast growth factor-23, Hb=hemoglobin, IQR=interquartile range, iPTH=parathyroid hormone, SD=standard deviation. Data shown as *n* (%), unless otherwise specified

prevalence of hypertension and diabetes was observed in the overall population. The difference between the study population and healthy adults was found to be statistically insignificant, which may be due to the small sample size or dietary history of phosphorus intake in healthy adults which may alter the serum FGF-23 levels. Studies report that FGF-23 levels were higher in CKD patients.[12,23] Similarly, Chathoth *et al*. reported that the elevation of FGF-23 levels was nearly 40-fold in patients with stage 5 CKD compared to controls.[24] They also showed twofold, threefold, and eightfold elevation of phosphate, iPTH, and alkaline phosphatase in this stage, respectively. Conversely, in the present study, there was no significant difference in the FGF-23 levels between stage 1-2 and stage 5 due to the small sample size.

Carotid ultrasound showed the presence of CAAC in around one-quarter of the overall patient population belonging to the age group of 51–70 years. In contrast to this study, CAAC was found in 66% of the patients reported by Nakayama *et al*.[5]., which may be due to the large sample size of that study. However, in the present study, there was no statistically significant difference in the age and sex distribution of patients between the group with CAAC and the group without CAAC. Similarly, there was no statistically significant association between CAAC and hypertension, diabetes, smoking, dyslipidemia, and BMI. On the other hand, Nakayama *et al*. showed a significant correlation between CAAC and age, hypertension, diabetes, and smoking. Furthermore, like the present study, there was no significant correlation between CAAC and

Table 4: OR for carotid artery calcification in patients with chronic kidney disease

Parameters	Age- and sex-adjusted univariate logistic regression		
	OR	95% CI (lower-upper)	*P*
Clinical profile			
Log BMI (kg/m^2)	126.728	0.00-3.79E+10	0.12
Smoking	1.219	0.278-5.334	0.793
Hypertension	0.485	0.147-1.596	0.234
Diabetes	2.182	0.635-7.495	0.215
Dyslipidemia	3.286	0.193-55.992	0.411
Biochemical profile			
Hemoglobin (g/dL)	1.168	0.849-1.607	0.340
Serum corrected calcium (mg/dL)	1.945	1.029-3.676	0.041
Phosphorus (mg/dL)	1.145	0.877-1.496	0.318
Log FGF-23 (pg/mL)	60.255	2.488-1458.976	0.012
Log Ca-P product (mg^2/dL^2)	22.282	0.395-1257.232	0.131
Log eGFR ((mL/min/1.73 m^2)	3.700	0.524-26.106	0.189
Log iPTH (pg/mL)	0.334	0.120-0.925	0.035
Log 1,25(OH)$_2$D (ng/mL)	1.161	0.451-2.984	0.757
Adjusted multivariate logistic regression			
Log FGF-23 (pg/mL)	180.769	4.572-7146.541	0.006
Log iPTH (pg/mL)	0.312	0.096-1.008	0.052
Serum corrected calcium (mg/dL)	2.560	1.227-5.341	0.012

1,25(OH) 2D=1,25-dihydroxyvitamin D, BMI=body mass index, Ca-P=calcium-phosphorus, CI=confidence interval, eGFR=estimated glomerular filtration rate, FGF=fibroblast growth factor, OR=odds ratio, iPTH=parathyroid hormone

Table 5: Clinical characteristics of the CKD patients according to the quartiles of FGF-23 levels

Parameters	FGF-23 quartile 1 (*n*=16) (FGF-23=30.9-165.5)	FGF-23 quartile 2 (*n*=15) (FGF-23=165.5-265.5)	FGF-23 quartile 3 (*n*=16) (FGF-23=265.5-397.6)	FGF-23 quartile 4 (*n*=15) (FGF-23=397.6-1093.5)	P
Clinical profile					
Age (years)	49.4 (14.1)	49.1 (17.1)	49.1 (13.6)	52.7 (11.6)	0.828
Men, n (%)	8 (50.0)	8 (53.3)	10 (62.5)	11 (73.3)	0.554
BMI (kg/m^2)	20.3 (1.4)	20.4 (1.3)	20.0 (1.6)	20.2 (1.4)	0.931
Hypertension, *n* (%)	15 (93.7)	9 (60.0)	8 (50.0)	9 (60.0)	0.050
Diabetes, *n* (%)	5 (31.2)	3 (20.0)	4 (25.0)	5 (33.3)	0.839
Smoking, *n* (%)	3 (18.7)	2 (13.3)	3 (18.7)	3 (20.0)	0.965
Dyslipidemia, *n* (%)	1 (6.2)	-	-	1 (6.7)	0.558
Biochemical profile					
Hemoglobin (g/dL)	9.4 (1.6)	9.5 (2.0)	8.9 (2.1)	9.9 (2.0)	0.612
eGFR (mL/min/1.73 m^2), median (IQR)	14.9 (8.0-21.3)	21.4 (7.9-26.5)	12.0 (7.3-21.0)	15.1 (10.6-30.9)	0.805
Serum corrected calcium (mg/dL)	8.8 (0.9)	8.7 (0.9)	8.9 (1.2)	8.4 (1.3)	0.765
Phosphorus (mg/dL)	5.1 (1.5)	4.9 (2.1)	5.6 (1.8)	6.3 (2.5)	0.153
Ca-P product (mg^2/dL^2), median (IQR)	41.7 (34.8-52.1)	37.8 (32.6-42.7)	44.9 (38.2-54.9)	48.8 (36.0-62.2)	0.187
iPTH (pg/mL), median (IQR)	227.8 (86.6-1270.6)	178.7 (104.9-221.1)	194.0 (73.3-994.2)	181.3 (101.8-283.1)	0.936
1,25(OH) 2D (ng/mL), median (IQR)	21.6 (2.8-31.8)	8.3 (3.3-35.1)	25.5 (15.5-34.7)	13.5 (2.1-20.5)	0.278
CAAC, *n* (%)	1 (6.2)	3 (20.0)	5 (31.2)	6 (40.0)	0.143

1,25(OH) D=1,25-dihydroxyvitamin D, BMI=body mass index, CAAC=carotid artery calcification, Ca-P=calcium-phosphorus, CKD=chronic kidney disease, eGFR=estimated glomerular filtration rate, FGF=fibroblast growth factor, IQR=interquartile range, iPTH=parathyroid hormone, SD=standard deviation. Data shown as mean (SD), unless otherwise specified

mean serum phosphorus and median calcium–phosphorus product.

The median serum FGF-23 level was found to be higher in patients with CAAC compared to those

without CAAC, which is in accordance with previous reports.[5,22] The median eGFR, Ca–P product, $1,25(OH)_2D$, and serum intact iPTH level in patients with CAAC were higher compared to those in patients without CAAC. CAAC was associated with both early and late stages of CKD. Other biochemical variables (Hb, corrected calcium, serum phosphorus, calcium–phosphorus product, eGFR, iPTH, 25-OH vitamin D) were found to be diffusely distributed along with ascending order of FGF-23 quartiles but proved to be statistically insignificant. Univariate and multivariate logistic regression was applied to find out the risk factors for CAAC. On age–sex matched univariate logistic regression analysis, log FGF-23, log iPTH, and mean corrected calcium were significant risk factors for CAAC. On multivariate logistic regression, only log FGF-23 and mean corrected calcium were found to be independent determinants of CAAC.

The mortality rate in patients with CKD who are initiating hemodialysis treatment was found to be independently associated with increased levels of FGF-23.[18] As cardiovascular disorders are a major cause of mortality in patients with CKD, targeting nontraditional risk factors such as FGF-23 may decrease the mortality in these patients. However, more studies are warranted with large sample size to determine the role of anti-FGF-23 therapy to curtail the incidence of cardiovascular and cerebrovascular events in pre-dialysis patients with CKD.

Limitations

The major limitation of this study was the small sample size, thus limiting the generalizability of the results to overall population. Secondly, intake of dietary phosphorus in patients and healthy adults that could alter the serum FGF-23 levels was not evaluated. This might be responsible for not finding any statistically significant difference in median FGF-23 levels between the patients and healthy adults.

Conclusion

In conclusion, the prevalence of CAAC increases with the progression of CKD. The results demonstrate a significant association between FGF-23 and CAAC, indicating that it is an independent determinant of CAAC in patients with CKD. Therefore, it can serve as a promising parameter other than the traditional risk factors for atherosclerosis to be focused on, to prevent CAAC and predict better clinical outcomes in CKD.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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