

Fibroblast Growth Factor 23 in Pre-Dialysis Chronic Kidney Disease Patients and its Comparison with Left Ventricular Hypertrophy

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Abstract

Background: An emerging global burden is Chronic kidney disease (CKD) which is characterized by progressive kidney damage. CKD is highly correlated with cardiovascular complications, notably left ventricular hypertrophy (LVH). With advancement in medical technologies, Fibroblast growth factor-23 (FGF-23), a hormone regulating phosphate metabolism, has emerged as a potential, non-invasive biomarker linked to cardiovascular abnormalities in CKD. Thus, the present study was designed to understand the relative changes in serum FGF-23 levels and its relation with cardiac changes in non-dialysis CKD patients. **Material and Methods:** A prospective observational analytical study was conducted at Sharda Hospital, Greater Noida, over 18 months (May 2023 – November 2024). Sixty-eight adult CKD patients not on dialysis were enrolled based on KDIGO criteria. The FGF-23 levels measured via ELISA. Cardiac evaluations included electrocardiography (ECG) and 2D echocardiography (2D Echo) to detect LVH and related abnormalities. **Results:** The most affected age group was 51–60 years (30.88%). A majority were male (76.47%) and from urban areas (73.53%). Most patients (63.24%) were in CKD Stage V, and 55.88% had abnormal ECG findings, with LVH being the most prevalent (39.71%). 2D Echo showed concentric LVH in 58.82% and diastolic dysfunction in 19.12% of patients. Elevated FGF-23 levels (>400 pg/ml) were found in 63.24% of participants, with a mean level of 427.10 ± 59.41 pg/ml. A strong association was observed between elevated FGF-23 levels and the presence of LVH. **Conclusion:** The study concluded that elevated FGF-23 levels in non-dialysis CKD patients are significantly associated with LVH and diastolic dysfunction. Thus, with further studies FGF-23 may be established as a valuable biomarker for early cardiovascular risk assessment in CKD. Further studies are needed to explore FGF-23-targeted therapies to mitigate CKD-related cardiac complications.

Keywords: Diabetes, Hypertension, Proteinuria, Renal Failure, Non-Dialysis CKD Patients, Cardiovascular Complications, Diastolic Dysfunction, Left Ventricular Hypertrophy (LVH), Fibroblast Growth Factor 23 (FGF-23), Chronic Kidney Disease (CKD).

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INTRODUCTION

Chronic Kidney Disease (CKD) represents a major global health burden characterized by the progressive decline of kidney function over a prolonged period. It is typically classified based on the estimated glomerular filtration rate (eGFR) and the presence of kidney damage markers, such as albuminuria. CKD frequently remains clinically silent in its early stages, with symptoms often manifesting only in advanced phases, which complicates early diagnosis and timely intervention. As the disease advances to Stage 5, patients usually require renal replacement therapies such as dialysis or kidney transplantation to sustain life.^[1]

One of the most significant complications associated with CKD is cardiovascular disease, which greatly contributes to patient morbidity and mortality. Among cardiovascular manifestations, left ventricular hypertrophy (LVH) and systolic dysfunction are particularly prevalent in CKD patients. These cardiac abnormalities are known to exacerbate the risk of adverse outcomes, highlighting the interplay between renal impairment and cardiovascular health. Despite considerable progress in understanding the pathophysiology of CKD-associated cardiovascular disease,

the underlying molecular and biochemical factors driving this association require further elucidation.^[2]

Fibroblast Growth Factor 23 (FGF-23) has emerged as a critical biomarker and potential pathogenic mediator in CKD. It is a hormone primarily involved in phosphate homeostasis and vitamin D metabolism, produced by osteocytes and osteoblasts in bone. Elevated circulating levels of FGF-23 have been consistently observed in CKD patients and correlate with declining kidney function. Beyond its role in mineral metabolism, growing evidence links high FGF-23 concentrations to cardiovascular abnormalities, notably LVH, and increased risk of heart failure and mortality. This dual relationship positions

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FGF-23 as a promising target for understanding and potentially mitigating cardiovascular complications in CKD.^[3]

Epidemiology of chronic kidney disease: an update 2022 summarizes how CKD is extremely common also highlights a large burden in low- and middle-income countries, including Singapore, Greece, and Israel [Figure 1].^[4]

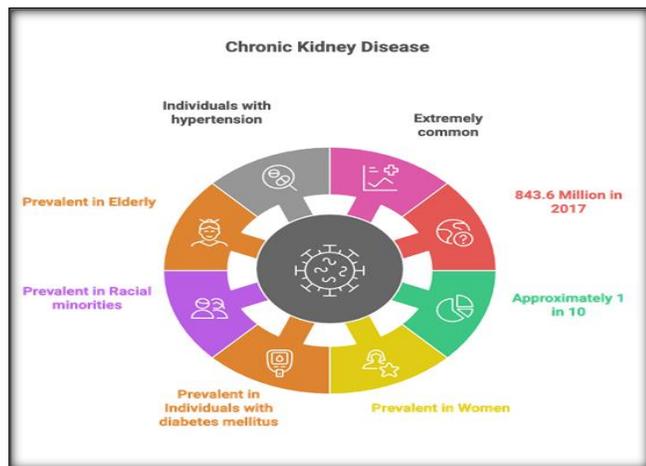


Figure 1: Causes and epidemiology of Chronic Kidney Disease

Chronic kidney disease (CKD) occurs frequently and has devastating consequences. This should prompt major efforts to develop preventative and therapeutic measures that are effective. The aim of these measures should be lowering the incidence of CKD and slowing its progression.

The present study aims to explore the association of serum FGF-23 levels with renal function and cardiovascular abnormalities, specifically focusing on pre-dialysis CKD patients. By examining the prevalence and extent of LVH and systolic dysfunction relative to FGF-23 concentrations, this research seeks to better define the pathophysiological role of FGF-23 in CKD progression and cardiovascular risk. Understanding these relationships may contribute to improved risk stratification, earlier intervention strategies, and the development of novel therapeutic targets aimed at reducing the cardiovascular burden in CKD patients.

MATERIALS AND METHODS

Study Design: The study design was prospective observational analytical, conducted in the Department of Medicine at SMS&R, Sharda Hospital, Greater Noida. The research was carried out over a period of 18 months, from May 2023 to November 2024.

Study Population: The study included adult patients aged over 18 years of both genders who were diagnosed with chronic kidney disease (CKD) and were not yet on dialysis. Patients were excluded if they were already taking phosphate binders or active vitamin D supplements, or if they had pre-existing conditions known to elevate fibroblast growth factor-23 (FGF-23) levels, such as autosomal dominant hypophosphatemic rickets or X-linked hypophosphatemic rickets. CKD was diagnosed and staged in accordance with the National Kidney Foundation–Kidney Disease Outcomes

Quality Initiative (NKF/KDOQI, 2022) and KDIGO criteria. CKD was defined as kidney damage lasting more than three months, or a glomerular filtration rate (GFR) less than 60 mL/min/1.73 m² for over three months. Classification followed the CGA (Cause, GFR, Albuminuria) system. GFR was categorized from G1 (≥ 90 mL/min/1.73 m²) to G5 (< 15 mL/min/1.73 m²), and albuminuria from A1 (< 30 mg/g) to A3 (> 300 mg/g). Investigations included complete blood count (CBC), serum creatinine (SCr), fasting plasma glucose (FPG), hemoglobin (Hb), and serum corrected calcium and phosphorus levels. FGF-23 levels were measured in serum samples using an enzyme-linked immunosorbent assay (ELISA) kit.

RESULTS

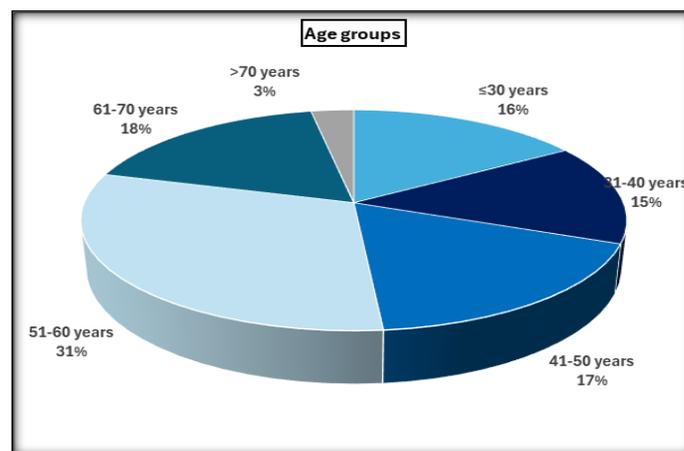


Figure 2: Pie chart representing age distribution. (n = 68, data is represented as percentage)

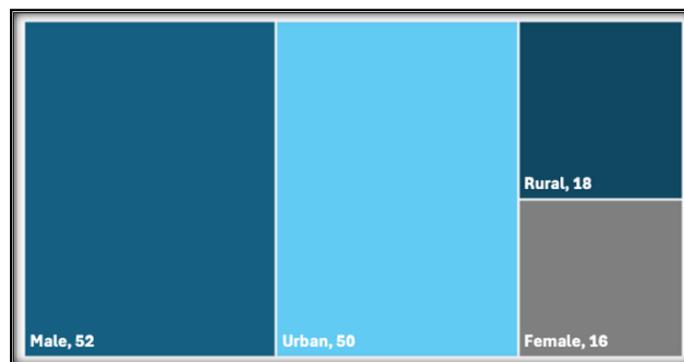


Figure 3: Tree map representing the demographics of study population (n = 68)

In this study, 51-60 years (30.88%) was the most common age group and rest of the distribution is presented in [Figure 2]. Majority of patients belonged to urban areas and were male [Figure 3]

The duration of chronic kidney disease (CKD) among the 68 individuals in the sample shows a distribution where the majority have been living with the condition for more than a year [Table 1].

In the present study, 52.94% population was suffering from diabetes while 83.82% were suffering from hypertension. The duration of CKD in maximum patients was more than 2 years [Table 1]

Table 1: Distribution of patients according to the duration of CKD.

Duration of CKD	Frequency (n=68)	Percentage (%)
<1 year	11	16.18%
1-2 years	27	39.71%
>2 years	30	44.12%

The eGFR stages indicate how well the kidneys are functioning and filtering the blood, lower values might indicate loss of function. Maximum patients in the current study belonged to the fifth stage of eGFR [Table 2].

Table 2: Distribution of patients according to eGFR Stages

eGFR Stage	Frequency (n=68)	Percentage (%)
Stage I (>90 ml/min)	0	0%
Stage II (60-89)	1	1.47%
Stage III (30-59)	7	10.29%
Stage IV (15-29)	17	25.00%
Stage V (<15)	43	63.24%

Presence of excess proteins in urine is a significant indicator for chronic kidney disease. Thus patients were tested for the level of proteins in urine and 60 patients (88.24%) were suffering from proteinuria.

The pulse rate of the patients were slightly elevated along with the systolic and diastolic blood pressure, indicating the severity of hypertension and increased heart rate whereas the respiratory rate was within the normal range [Figure 4].

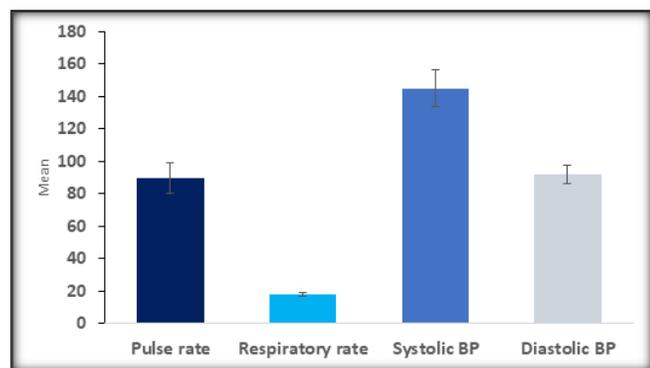


Figure 4: Bar graphs representing mean values of vital parameters (n = 68 and data is represented by mean ± SD.

Laboratory analyses of the cohort (n=68) demonstrated multiple clinically significant abnormalities. The mean hemoglobin concentration was 8.68 ± 1.54 g/dL, consistent with anemia frequently observed in chronic kidney disease (CKD) and related comorbidities. Total leukocyte count

($8.46 \pm 4.99 \times 10^3/\mu\text{L}$) remained within reference limits, indicating the absence of overt infection or acute inflammatory response. However, elevated mean random blood glucose levels (189.32 ± 52.61 mg/dL) suggest suboptimal glycemic control or potential undiagnosed diabetes mellitus. Renal impairment was evident with markedly increased serum creatinine (6.04 ± 2.79 mg/dL) and blood urea nitrogen (117.83 ± 54.72 mg/dL), indicative of reduced glomerular filtration and compromised renal clearance. Hypoalbuminemia was present with a mean serum albumin of 3.39 ± 0.61 g/dL, possibly reflecting malnutrition or diminished renal synthetic function impacting protein homeostasis. Lipid profile revealed normal total cholesterol levels, while hypertriglyceridemia (199.99 ± 83.32 mg/dL) coupled with decreased HDL cholesterol (40.16 ± 10.10 mg/dL) denotes dyslipidemia associated with increased cardiovascular risk in CKD populations. Mild elevations in hepatic transaminases—SGOT (41.65 ± 52.70 U/L) and SGPT (39.22 ± 33.85 U/L)—may indicate subclinical hepatic dysfunction or muscle injury.

The ECG report was normal for 44.12% patients while 55.88% patients had abnormal ECG reports. The abnormal findings majorly included Left ventricular hypertrophy (LVH) [Table 3].

Only 10.29% of patients were detected with systolic dysfunction, ruling out other heart conditions such as pumping impairment heart failure etc. These results pointed out towards the loss in function of heart due to CKD [Figure 5].

Table 3: Type of ECG changes

ECG Change	Frequency (n=68)	Percentage (%)
Left ventricular hypertrophy (LVH)	27	39.71%
Left axis deviation (LAD)	3	4.41%
Poor R wave progression	3	4.41%
Sinus tachycardia	4	5.88%

Table 4: Fibroblast growth factor 23 (FGF-23) Levels (pg/ml) in the current study

FGF-23 Level (pg/ml)	Frequency (n=68)	Percentage (%)
150-400	25	36.76%
>400	43	63.24%

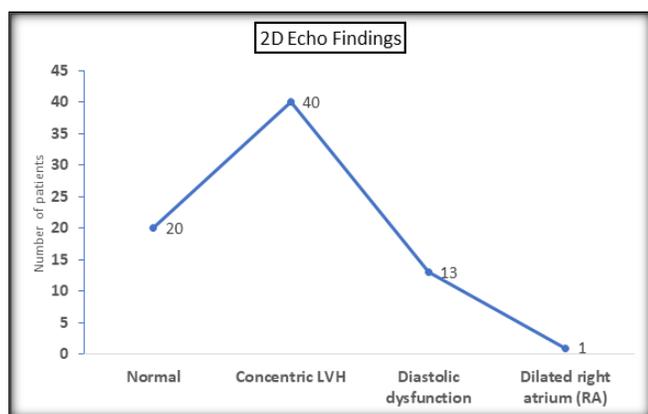


Figure 5: Line charts depicting 2D echo findings

[Table 4] represents the FGF-23 levels in the present study. The mean FGF-23 level for the sample is 427.10 ± 59.41 pg/ml, indicating a generally elevated level of this biomarker. FGF-23 is a hormone involved in phosphate regulation and is often elevated in conditions such as chronic kidney disease (CKD), where phosphate retention can lead to disturbances in mineral metabolism. The higher percentage of individuals with elevated FGF-23 levels suggests that this sample may have a high prevalence of kidney dysfunction or related metabolic disturbances. Elevated FGF-23 levels may indicate a need for closer monitoring of mineral and bone health in these individuals.

DISCUSSION

Analysis of the data reveals a pronounced trend linking higher FGF-23 concentrations with worsening stages of chronic kidney disease among the individuals studied. In this group, most participants were already at advanced stages of CKD, with the majority showing estimated glomerular

filtration rates well below 15 ml/min. Such levels are typically associated with significant phosphate retention, which in turn is known to stimulate increased secretion of fibroblast growth factor 23 by osteocytes.

This observation is closely reflected in the laboratory findings, with around two-thirds of the patients exhibiting FGF-23 levels that surpassed the 400 pg/ml threshold. The relationship likely stems from the progressive decline in kidney function: as the kidneys lose their ability to excrete phosphate efficiently, FGF-23 rises in an effort to maintain mineral balance. However, these sustained elevations in FGF-23 have broader implications beyond mineral metabolism.

A notable proportion of the cohort also showed evidence of left ventricular hypertrophy and other forms of cardiac involvement. Recent research has pointed towards a role for excess FGF-23 in contributing directly to structural and functional cardiac changes, independent of traditional risk factors such as hypertension and diabetes, both of which remained prevalent in the group. This supports the growing body of evidence suggesting that FGF-23 is not merely a biomarker of kidney dysfunction but may actively contribute to the cardiovascular complications so often seen in CKD.

Additionally, a cluster of other adverse findings—including anemia, reduced serum albumin, and metabolic derangements—further illustrates the complexity of advanced kidney disease and its systemic effects. When piecing together these clinical, biochemical, and cardiac findings, the interplay between reduced renal clearance, secondary increases in FGF-23, and multi-organ impact becomes apparent.

To sum up, these tables underscore a strong correlation between higher FGF-23 levels and more severe kidney dysfunction. This hormone’s elevation is both a reflection of declining renal filtration and potentially a driver of cardiovascular abnormalities, reinforcing the value of close monitoring and further investigation into targeted interventions in CKD populations.

Study (Author, Year)	Population/Setting	Main Focus	Key Findings
Gutiérrez et al, ^[5] 2009	CKD patients, echocardiography & CT	FGF-23, LVH, coronary calcification	Higher FGF-23 linked to increased LV mass & risk of LVH
Hidaka et al, ^[6] 2024	CKD stages 2–4 (n > 2,300), CRIC cohort	FGF-23, LVH, long-term outcomes	LVH mediates effect of FGF-23 on mortality and AF/CHF
Karim et al, ^[7] 2024	74 CKD patients, multi-stage	FGF-23, LVH incidence & risk factors	Elevated FGF-23 = greater risk of LVH; conventional factors NS
Kumar et al, ^[8] 2022	Pre-dialysis CKD & controls, India	FGF-23, carotid artery calcification	Higher FGF-23 correlates with more frequent vascular calcification
Takashi et al, ^[9] 2022	118 T1D patients with normal/mildly impaired kidneys	FGF-23, phosphate, kidney function	FGF-23 inversely associated with eGFR

CONCLUSION

Diastolic dysfunction and left ventricular hypertrophy (LVH), common side effects of chronic kidney disease (CKD), are found in non-dialysis individuals in this study. The majority of the research group exhibited increased FGF-23 levels, which may indicate renal failure and cardiovascular stress. Diabetes, hypertension, and proteinuria are common in this group, highlighting CKD’s severity. The data suggest that elevated FGF-23 levels may cause circulatory abnormalities such as systolic dysfunction and LVH in CKD patients. These findings underline the need for early cardiovascular and kidney disease detection and therapy to improve patient outcomes. Since most participants

had severe CKD, urgent care is needed to stop renal and cardiovascular deterioration. To manage these coexisting diseases, more study is needed to understand the causal association between FGF-23 levels and CKD’s cardiovascular effects. Additionally, FGF-23-targeting drugs must be researched.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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