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ASSOCIATION OF MARKERS OF BONE MINERAL DISEASE AND LEFT VENTRICULAR HYPERTROPHY IN PATIENTS OF CHRONIC KIDNEY DISEASE

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Abstract. Background. *Chronic kidney disease (CKD) is an epidemic health problem responsible for an increase in morbidity and mortality secondary to various complications, especially cardiovascular events. Previous studies have suggested that biochemical markers of metabolic bone disease (MBD) are associated with an increase in cardiovascular events by causing left ventricular hypertrophy (LVH). Therefore, the present study aimed to evaluate the association between LVH and CKD-MBD markers as a major predictor for cardiovascular disease (CVD) in CKD patients.* ***Materials and Methods.*** *A single-center, cross-sectional, observational study was carried out at a tertiary care center. A total of 50 CKD patients, stages 3-5, not on dialysis, were included. Demographic details, clinical history, laboratory investigations and echocardiography were obtained. The presence of LVH was determined on the basis of echocardiography, and it was associated with CKD stages and biochemical markers, including CKD-MBD markers.* ***Results.*** *Seventy-two percent of CKD patients had LVH. The proportion of patients with LVH significantly increased with a declining estimated glomerular filtration rate (eGFR). Hypertension was considerably higher in patients with LVH (63.89%). Significant association of LVH was seen with serum creatinine, corrected calcium, phosphorus, total cholesterol, fibroblast growth factor 23 (FGF-23), vitamin D, intact parathyroid hormone (iPTH), eGFR, left ventricular mass index (LVMI) and ejection fraction (p-value < 0.05). On multivariate regression, FGF-23 had a significant positive correlation with LVH (p-value < 0.05, odds ratio > 1). A significant positive correlation was observed between LVMI and systolic blood pressure, serum creatinine, phosphorus, total cholesterol, iPTH, and FGF-23. A significant negative correlation was seen with LVMI and hemoglobin, corrected serum calcium, albumin, eGFR, vitamin D and ejection fraction.* ***Conclusion.*** *The present study shows CKD-MBD markers, including serum calcium, phosphorous, vitamin D, iPTH and FGF-23, are significantly associated with LVH. FGF-23 is an independent predictor of LVH. The present study also demonstrates that CKD-MBD biochemical markers are reliable for screening CVD in CKD patients.*

Key words: *chronic kidney disease-metabolic bone disease, left ventricular hypertrophy, fibroblast growth factor-23.*

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INTRODUCTION

Chronic kidney disease (CKD) is characterized by a progressive and irreversible decline in the glomerular filtration rate. The worldwide estimated prevalence of CKD is 10.4-13.4% [1]. In India, the incidence and prevalence of CKD are approximately 0.16% and 0.76%, respectively [2]. CKD was the 12th leading cause of demise, accounting for 1.1 million fatalities across the globe and the 17th leading cause of disability, according to the 2015 Global Burden of Disease Study. Overall, CKD mortality has progressed by 31.7%, making it one of the fastest-rising causes of death [3].

Cardiovascular diseases (CVD) are the leading cause of morbidity and mortality in CKD patients. In comparison to the normal population, CVD is approximately three times more frequent in patients with CKD, leading to 10 times greater mortality in patients on dialysis as compared to same-age and sex-matched [4]. To explain this, a group of non-traditional factors has also been put forward, including anaemia, abnormalities of bone mineral metabolism, malnutrition, hypoalbuminemia, hyperhomocysteinemia, inflammation, oxidant stress, insulin resistance, altered renin-angiotensin axis and endothelial dysfunction [5].

Coronary artery disease (CAD) and left ventricular hypertrophy (LVH) have been identified as the two most common and important risk factors leading to higher cardiovascular mortality rates in patients with CKD. The prevalence of CAD and LVH in CKD patients is approximately 40% and 75%, respectively [6]. 40% of pre-dialysis patients and 80% of patients undergoing hemodialysis have LVH [7, 8]. This mainly occurs due to left ventricle remodeling in response to various factors that affect the preload and afterload in CKD patients [9, 10, 11]. These changes result in diastolic dysfunction, systolic dysfunction, dilation of chambers and impaired intraventricular conduction, eventually causing heart failure and uremic cardiomyopathy [10].

Multiple studies have proposed numerous factors like hypertension, anemia and deranged bone mineral markers in the development of LVH in CKD [7, 12, 13]. It has been established that there is a role of increased phosphate levels in vascular calcification, which leads to high cardiovascular events and mortality in CKD patients. Some studies have also suggested the connection between hyperphosphatemia and LVH by increasing afterload and other mechanisms [14]. Similarly, fibroblast growth factor 23 (FGF-23), a marker of phosphate load, has been suggested to play a role in the pathophysiology of LVH in CKD patients undergoing hemodialysis [15].

In patients with CKD, the role of deranged bone mineral markers in the pathogenesis of increased cardiovascular events is widely explored. Still, the linkage between these bone mineral biochemical markers and LVH has barely been studied in CKD patients without renal replacement therapy [16]. Therefore, the aim of the present study was to evaluate the association between biochemical markers of bone mineral disease and LVH in non-dialyzed CKD patients.

AIMS AND OBJECTIVES

1. To evaluate markers of bone mineral disease in patients with CKD.

2. To correlate these markers with the development of LVH in pre-dialysis CKD patients.

MATERIALS AND METHODS

Study design

This study was a single-center, cross-sectional, observational study. Participants were recruited from patients attending the outpatient department in the Department of Medicine and Nephrology. A total of 50 patients diagnosed with CKD stage 3-5 were included. The study details were explained to all included patients, and informed written consent was obtained. The Institute Ethics Committee approved the study.

Pre-dialysis CKD patients aged 18-70 years in stages 3 to 5 were included in the study. Patients who were on renal replacement therapy had a history of pre-existing CVD, thyroid dysfunction, parathyroid disease, inflammatory disease, autoimmune disorders, and neoplasms and were on immunosuppressive therapy. Patients who had received treatment with 1-alphacalcidiol, calcitriol or bisphosphonates within 6 months were excluded.

Data collection

In the study, the estimated glomerular filtration rate (eGFR) was calculated using the 2021 CKD-EPI Creatinine equation. Participants were grouped based on eGFR as Group A (n = 15) having eGFR 30-60 ml/min/1.73 m^2 BSA, Group B (n = 23) with eGFR 15-30 ml/min/1.73 m^2 BSA and Group C (n = 12) with eGFR < 15 ml/min/1.73 m^2 BSA.

A thorough physical examination and routine biochemical investigations, including renal function tests, were done for all participants. Specific investigations have been also performed: serum calcium, serum phosphorus, serum intact parathyroid hormone (iPTH), serum vitamin D, and FGF-23.

Corrected calcium equals measured total Ca (mg/dL) + 0.8 (4.0 – serum albumin [g/dL]), where 4.0

represents the average albumin level. Calcium measurement was done by Arsenazo III and Phosphorus by Phosphomolybdate U.V. method. Intact PTH was measured by Chemi-Luminescence Immuno Assay (CLIA) and Vitamin D by Enhanced Chemi-luminescence (Ultra-Sensitive 4th Generation). FGF-23 was measured using an enzyme-linked immunosorbent assay.

All patients were subjected to an M-mode, two-dimensional echocardiography by a single observer at the Department of Cardiology, PGIMS Rohtak. Devereux's equation was used for calculating Left ventricular mass (LVM) = 1.04 x [(LVEDD + IVT + LVPWT)3 – LVEDD3] – 13.6 in which LVEDD was left ventricle end-diastolic diameter, IVT was interventricular septal thickness, LVPWT was left ventricle posterior wall thickness. LVM was divided by body surface area to obtain the LVM index (LVMI) for eliminating the variation due to body constitution. Finally, LVH was defined as LVMI >110 g/m2 in women and LVMI >134 g/m2 in men [17]. Ejection fraction (EF) was calculated using Teicholz's formula = (LV end-diastolic dimension)–(LV end-systolic dimension)/(LV end-diastolic dimension).

STATISTICAL ANALYSIS

The data was analyzed using the Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, Ver 25.0. Categorical variables were done by number and percentage (%). On the other hand, the quantitative data were presented as the means ± S.D. The quantitative variables were compared using the independent t-test (for two groups) and ANOVA test (for more than two groups), and qualitative variables were analyzed using the Chi-Square test. If any cell had an expected value of less than 5, Fisher's exact test was used. Spearman rank correlation coefficient was used to find a correlation between the CKD stage and various parameters, and Pearson's correlation coefficient was used to find the correlation of LVMI with various parameters. Multivariate logistic regression models assessed the association between the FGF-23 and LVH. For statistical significance, a p-value of less than 0.05 was considered statistically significant.

RESULTS

In the present study, 64% of patients aged between 41-60 years (Mean = 51.52 ± 11.1), and 54% were females and 46% – males. Seventy-two percent of CKD patients had LVH. The proportion of patients with LVH was significantly higher in Group C (91.67%) as compared to Group A (46.67%) and Group B (78.26%) (p = 0.33) (Table 1). Baseline characteristics of all patients are summarized in Table 2. LVMI and LVDD significantly increased, while the EF was reduced from group A to group C (p < 0.05).

Hypertension was significantly higher in patients with LVH (63.89%) as compared to patients without LVH (21.43%) (p = 0.011). The distribution of smoking was comparable in patients with and without LVH. Significant association was seen in blood urea, serum creatinine, corrected serum calcium, serum phosphorus, eGFR, serum albumin, total cholesterol, HDL, FGF-23, vitamin D, iPTH, LVMI, EF, LVDD with LVH (p < 0.05) (Table 3). A significant positive correlation was seen between LVMI and systolic blood pressure, diastolic blood pressure, blood urea, serum creatinine, serum phosphorus, serum uric acid, triglyceride, total cholesterol, iPTH, FGF-23, LVDD. A significant negative correlation was seen between LVMI and hemoglobin, corrected serum calcium, serum albumin, HDL, eGFR, vitamin D, and EF (Table 4).

Pearson correlation coefficient

Multivariate regression was performed using three models: Model 1 (including age, + Gender + FGF-23); Model 2 (including Model 1 + Systolic blood pressure + Serum albumin + Total cholesterol + HDL + eGFR); and Model 3 (including Model 2 + Corrected serum calcium + Vitamin D + iPTH + Serum phosphorus). FGF-23 was found to be a significant risk factor of LVH in all 3 models with a p-value <0.05. The higher the FGF-23, the higher the risk of LVH with odds ratio > 1 (Table 5).

Table 1. Association of LVH with CKD stage

	Group A (CKD 3)	Group B (CKD 4)	Group C (CKD 5)	Total	P-value
Without LVH	8 (53.33%)	5 (21.74%)	1 (8.33%)	14 (28%)	0.033*
With LVH	7 (46.67%)	18 (78.26%)	11 (91.67%)	36 (72%)	
Total	15 (100%)	23 (100%)	12 (100%)	50 (100%)	

*Fisher's exact test

Table 2. Hematological and biochemical parameters of study subjects with CKD at different stages

Parameters	Group A (CKD 3)	Group B (CKD 4)	Group C (CKD 5)	Total	P-value
Age (years)	50.67 ± 8.66	53.26 ± 11.54	49.25 ± 13.27	51.52 ± 11.12	0.572§
Systolic blood pressure (mmHg)	128.27 ± 15.96	144.96 ± 13.14	164.83 ± 15.53	144.72 ± 19.66	< 0.0001§
Diastolic blood pressure (mmHg)	79.87 ± 8.70	87.56 ± 5.49	92.83 ± 7.46	86.52 ± 8.45	< 0.0001§
Hemoglobin (g/dL)	12.05 ± 1.34	10.03 ± 0.98	8.12 ± 1.09	10.18 ± 1.82	<0.0001§
Total leukocyte count (cells/mm^3)	8706.67 ± 1812.84	8103.91 ± 1840.92	8141.67 ± 1697.3	8293.8 ± 1783.83	0.572§
Blood urea (mg/dL)	81.54 ± 17.03	96.98 ± 23.78	154.83 ± 61.89	106.23 ± 44.74	< 0.0001§
Serum creatinine (mg/dL)	1.96 ± 0.32	2.91 ± 0.9	6.19 ± 2.86	3.41 ± 2.21	< 0.0001§
Serum sodium (mEq/L)	138.6 ± 3.38	138.48 ± 4.46	141.17 ± 1.47	139.16 ± 3.74	0.101§
Serum potassium (mEq/L)	4.39 ± 0.63	4.25 ± 0.6	4.6 ± 0.47	4.38 ± 0.59	0.246§
Corrected serum calcium (mg/dL)	9.21 ± 0.39	8.26 ± 0.54	7.22 ± 0.73	8.29 ± 0.92	< 0.0001§
Serum phosphorus (mg/dL)	3.84 ± 0.85	5.22 ± 0.79	7.56 ± 1.1	5.37 ± 1.63	< 0.0001§
Serum uric acid (mg/dL)	6.27 ± 2.48	7.22 ± 2.46	8.04 ± 2.85	7.13 ± 2.6	0.211§
eGFR (mL/min/1.73m^2)	36.6 ± 5.94	21.91 ± 6.29	11.17 ± 2.82	23.74 ± 10.98	< 0.0001§
Serum albumin (g/dL)	3.72 ± 0.4	3.35 ± 0.66	2.94 ± 0.36	3.36 ± 0.59	0.002§
Triglyceride (mg/dL)	134.93 ± 27.57	146 ± 27.53	171.75 ± 26.34	148.86 ± 30.08	0.004§
Cholesterol (mg/dL)	206.33 ± 25.59	231.35 ± 23.75	277.42 ± 25.23	234.9 ± 35.80	<0.0001§
HDL (mg/dL)	44.27 ± 5.42	39.96 ± 3.4	35.83 ± 5.41	40.26 ± 5.47	< 0.0001§
LDL (mg/dL)	135.13 ± 26.43	145.74 ± 23.88	169 ± 26.16	148.14 ± 27.75	0.004§
FGF-23 (RU/mL)	326.8 ± 252.78	698.83 ± 249.18	1064.08 ± 366.37	674.88 ± 388.23	< 0.0001§
Vitamin D (ng/mL)	28.6 ± 8.21	23.57 ± 4.15	18.08 ± 2.07	23.76 ± 6.56	< 0.0001§
iPTH (pg/mL)	142.8 ± 74.9	293.61 ± 152.63	632.58 ± 311.87	329.72 ± 260.13	< 0.0001§
LVMI (gm/m^2){Male}	121 ± 27.07	177.2 ± 12.79	208 ± 39.04	156.78 ± 40.43	< 0.0001§
LVMI (gm/m^2){Female}	103.2 ± 27.63	128.46 ± 31.18	170.44 ± 32.41	137.78 ± 39.14	0.001§
Ejection fraction (%)	68.47 ± 2.72	66.09 ± 2.97	62.5 ± 4.19	65.94 ± 3.86	< 0.0001§
LVDD (mm)	44.53 ± 3.93	50.09 ± 4.5	52.33 ± 5.63	48.96 ± 5.48	0.0001§

§ANOVA

Table 3. Association of parameters with LVH

Parameters	Without LVH (n=14)	With LVH (n=36)	Total	P-value
Hypertension				
No	11 (78.57%)	13 (36.11%)	24 (48%)	0.011*
Yes	3 (21.43%)	23 (63.89%)	26 (52%)	
Smoking				
Non-smokers	9 (64.29%)	21 (58.33%)	30 (60%)	0.7
Smokers	5 (35.71%)	15 (41.67%)	20 (40%)	
Age (years)	50 ± 10.47	52.11 ± 11.45	51.52 ± 11.12	0.552†
Hemoglobin (g/dL)	10.91 ± 1.46	9.89 ± 1.89	10.18 ± 1.82	0.075†
Total leukocyte count (cells/mm^3)	8449.29 ± 2373.09	8233.33 ± 1532.88	8293.8 ± 1783.83	0.756†
Blood urea (mg/dL)	83.11 ± 24.23	115.22 ± 47.83	106.23 ± 44.74	0.021†
Serum creatinine (mg/dL)	2.34 ± 0.9	3.83 ± 2.43	3.41 ± 2.21	0.003†
Serum sodium (mEq/L)	139.43 ± 3.65	139.06 ± 3.82	139.16 ± 3.74	0.755†
Serum potassium (mEq/L)	4.2 ± 0.54	4.44 ± 0.6	4.38 ± 0.59	0.189†
Corrected serum calcium (mg/dL)	8.93 ± 0.65	8.05 ± 0.89	8.29 ± 0.92	0.002†
Serum phosphorus (mg/dL)	4.52 ± 1.24	5.7 ± 1.66	5.37 ± 1.63	0.02†
Serum uric acid (mg/dL)	6.19 ± 2.36	7.5 ± 2.62	7.13 ± 2.6	0.111†
eGFR (mL/min/1.73m^2)	30.29 ± 11.59	21.19 ± 9.75	23.74 ± 10.98	0.007†
Serum albumin (g/dL)	3.83 ± 0.38	3.18 ± 0.56	3.36 ± 0.59	0.0002†
Triglyceride (mg/dL)	140.64 ± 26.33	152.06 ± 31.17	148.86 ± 30.08	0.232†
Cholesterol (mg/dL)	199.57 ± 20.60	248.64 ± 30.71	234.9 ± 35.80	< 0.0001†
HDL (mg/dL)	42.86 ± 5.53	39.25 ± 5.17	40.26 ± 5.47	0.035†
LDL (mg/dL)	141.21 ± 26.61	150.83 ± 28.08	148.14 ± 27.75	0.276†
FGF 23 (RU/mL)	293.57 ± 229.45	823.17 ± 332.69	674.88 ± 388.23	<0.0001†
Vitamin D (ng/mL)	29.64 ± 7.88	21.47 ± 4.24	23.76 ± 6.56	0.002†
iPTH (pg/mL)	177.71 ± 87.18	388.83 ± 281.2	329.72 ± 260.13	0.0002†
LVMI (gm/m^2)	93 ± 9.76	167.33 ± 25.82	146.52 ± 40.48	< 0.0001†
Ejection fraction (%)	69.29 ± 1.98	64.64 ± 3.63	65.94 ± 3.86	< 0.0001†
LVDD (mm)	43 ± 3.01	51.28 ± 4.35	48.96 ± 5.48	< 0.0001‡

‡ Independent t-test, * Fisher's exact test, † Chi-square test

Table 4. Correlation of parameters with LVMI

Variables	LVMI gm/m²	
	Correlation coefficient	P-value
Age (years)	0.013	0.928
Systolic blood pressure (mm Hg)	0.533	0.0001
Diastolic blood pressure (mm Hg)	0.501	0.0002
Hemoglobin (g/dL)	-0.419	0.003
Total leukocyte count (cells/mm³)	-0.125	0.387
Blood urea (mg/dL)	0.462	0.0007
Serum creatinine (mg/dL)	0.546	< 0.0001
Serum sodium (mEq/L)	0.082	0.5714
Serum potassium (mEq/L)	0.203	0.1572
Corrected serum calcium (mg/dL)	-0.522	0.0001
Serum phosphorus (mg/dL)	0.535	0.0001
Serum uric acid (mg/dL)	0.35	0.013
Serum albumin (g/dL)	-0.511	0.0001
AST (U/L)	-0.222	0.121
ALT (U/L)	-0.07	0.631
ALP (U/L)	0.056	0.702
Serum bilirubin (mg/dL)	-0.091	0.530
Triglyceride (mg/dL)	0.297	0.037
Cholesterol (mg/dL)	0.661	< 0.0001
HDL (mg/dL)	-0.379	0.007
LDL (mg/dL)	0.27	0.058
eGFR (mL/min/1.73m²)	-0.596	< 0.0001
Vitamin D (ng/mL)	-0.524	0.0001
iPTH (pg/mL)	0.579	< 0.0001
FGF 23 (R.U./mL)	0.742	< 0.0001
Ejection fraction (%)	-0.541	< 0.0001
LVDD (mm)	0.661	< 0.0001

DISCUSSION

CKD is a worldwide health problem and is significantly associated with an increased risk of cardiovascular morbidity, mortality and decreased quality of life. Various cardiovascular complications include CAD, congestive heart failure, arrhythmias, stroke, or peripheral vascular disease. Arterial disease and left ventricular hypertrophy are the two most common

Table 5. Odds ratio for the association between FGF 23 and LVH

Model	LVH (n=50)	
	OR (95% CI)	P-value
Model 1	1.007(1.003 to 1.011)	0.001
Model 2	1.005(1.000 to 1.010)	0.0005
Model 3	1.005(1.002 to 1.009)	0.001

Model 1: Age + Gender + FGF 23, Model 2: Model 1 + Systolic blood pressure + Serum albumin + Cholesterol + HDL + eGFR, Model 3: Model 2+ Corrected serum calcium + Vitamin D + iPTH + Serum phosphorus

and substantial risk factors leading to a high cardiovascular mortality rate in patients with CKD undergoing hemodialysis.

LVH is one of the common manifestations in CKD patients. Many studies showed that the clinical consequences of LVH can vary from heart failure secondary to diastolic and systolic dysfunction with decreased EF to arrhythmias, ischemic heart disease, and sudden cardiac death in CKD [13]. Approximately 40% of patients with pre-dialysis CKD and up to 80% of patients initiating hemodialysis manifest LVH [7, 8].

Mineral bone disorder is one of the common complications in CKD patients and recently gained attention as a critical nontraditional risk factor leading to CVD. In our study, LVH was used as a surrogate marker of CVD, as previous studies have demonstrated that the severity and persistence of LVH are strongly associated with mortality risk and cardiovascular events in CKD patients [18].

In the present study, we observed LVH in 72% of CKD patients, and its prevalence increased progressively in higher stages of CKD. Similar observations were made by Paoletti et al., who found that LVH presented in 74% of patients [19]. Kimura et al. demonstrated in their study that the prevalence of LVH tends to increase as renal function declines: 22.7% in stage 3, 43.6% in stage 4, and 48.3% in stage 5 not on hemodialysis [20].

Markers of metabolic bone disease abnormalities play an important role in the pathogenesis of CVD [21]. PTH can lead to LVH by causing fibroblast activation and myocardial fibrosis, further advancing to irreversible cardiac interstitial fibrosis and collagen deposition. Similarly, VDR BsmI gene polymorphism is involved in the occurrence of LVH in CKD patients by increasing LV mass, inducing renin gene expression and is independently associated with LVH [22,

23]. Hyperphosphatemia can directly affect the cardiovascular system by enhancing vascular calcification, modifying coronary plaque morphology and affecting cardiac microvasculature. It also leads to increased PTH levels, which can further aid in developing LVH.

Our study found a significant association of serum calcium, phosphorous, vitamin D, and iPTH levels (markers of MBD in patients of CKD) with LVH and also observed their positive correlation with LVMI. Similarly, a study by Chu Zhou et al. to evaluate MBD and its association with cardiovascular parameters in CKD found that as the CKD stage advanced from stage 3 to stage 5, the proportion of hyperphosphatemia increased and was associated with increased LVH [24]. Chue CD et al. also observed that higher serum phosphate levels were independently associated with increased LVMI [25].

In this study, we observed that FGF-23 levels (a novel marker of CKD-MB) significantly increased with the progression of CKD from stage 3 to stage 5. FGF-23 concentrations were positively associated with LVH and were an independent risk factor for LVH ($p < 0.05$). This result was supported by many studies that suggest that increased FGF-23 is associated with higher cardiovascular mortality, LVH, endothelial dysfunction and progression of CKD [26, 27, 28]. Gutiérrez et al. did a cross-sectional study on 162 CKD subjects and observed that with an increase in log FGF-23 levels, there was a significant increase in the LVMI (5% increase per 1-SD increase in log FGF-23; $p = 0.01$) and LVH [16]. Faul et al. observed that each unit increase in natural log-transformed FGF-23 (ln FGF-23) was associated with a 5.0 g/m2 greater LVMI. [29]. Nielsen et al. observed that 46% of CKD patients had LVH, and these patients had higher FGF-23 levels, which had a negative correlation with LVEF ($p < 0.01$) [30].

LIMITATIONS OF THE STUDY

There were some limitations of this study. First, the cross-sectional study design does not establish a causal relationship between LVH and CKD, and prospective studies are required for the same. The sample size of our study was small and included only 50 subjects. A larger sample size would have allowed a more accurate justification of the results of our research. Our study population had diabetic patients, too. As diabetic patients frequently have a high prevalence of CVD, this could have been a confounding factor in our study. Patients taking uric acid-lowering agents, phosphate binders or erythropoietin-stimulating agents were also not excluded.

CONCLUSION

As per our study results, biochemical markers of metabolic bone disease increase with the progression of CKD from stage 3 to stage 5. An increase in these markers is associated with LVH, and therefore, an increased risk of cardiovascular events is seen in CKD patients. LVH is affected not only by abnormal mineral metabolism but also by many traditional and non-traditional risk factors, such as dyslipidemia, hypoalbuminemia etc. Although LVH is more pronounced in dialysis patients, it also has prognostic significance in pre-dialysis patients. So, by assessing CKD-MBD, one of the major risk factors, patients can be diagnosed early in the course of the disease, facilitating timely intervention and thereby preventing complications and improving the quality of life in CKD patients. Follow-up and interventional studies are required to further evaluate and establish a strong association between LVH and CKD-MBD markers as major prognostic/predicting factors for CVD in CKD patients.

Several novel therapeutic modalities aiming at CVD risk reduction in CKD are in clinical trials, raising the hope that cardiovascular risk in CKD may be reduced in the future. So, the patients of CKD, at the pre-dialysis stage, can also be screened and treated more aggressively for cardiac disease and associated complications than the normal population.

Conflicts of interest: *None.*

Informed Consent. *Informed consent was taken from all participants. This study was duly approved by the Pt. B. D. Sharma University of Health Sciences Ethics Committee (decision no: BREC/Th/20/Med./02).*

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