fortune Journals

Research Article

ARCHIVES OF NEPHROLOGY AND UROLOGY

ISSN: 2644-2833

Association of Secondary Hyperparathyroidism with Cardiac Structural and Functional Abnormality in Chronic Kidney Disease Stage 4, 5 and Hemodialysis Patients

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Abstract

Background: Kidney disease, particularly chronic kidney disease (CKD), is a global health concern affecting around 10% of adults, leading to 1.2 million deaths annually. By 2040, CKD is projected to be the fifth most common cause of death worldwide. Secondary hyperparathyroidism (SHPT) is a common complication in CKD, associated with cardiovascular risks. Parathyroid hormone (PTH) plays a crucial role in SHPT pathophysiology and is implicated in various long-term complications. Management involves vitamin D analogs, calcimimetics, and, in severe cases, parathyroidectomy.

Aim of the study: The study aims to find out the associations of secondary hyperparathyroidism (SHPT) with left ventricular hypertrophy (LVH), left ventricular diastolic dysfunction (LVDD) and valvular calcification (VC) in chronic kidney disease (CKD) stage 4, 5 and maintenance hemodialysis (MHD) patients.

Methods: The study conducted at the Department of Nephrology in BSMMU, Dhaka, Bangladesh, from November 2022 to September 2023. Participants met specific criteria and provided informed consent. Data collection involved medical and socioeconomic history, physical examinations, anthropometric measurements, and blood tests. Tests included hematological, biochemical, and hormonal analyses, with serum iPTH measured by chemiluminescent assay. Echocardiograms assessed cardiac function and morphology. Inclusion criteria involved age (18-65), CKD stage 4 or 5, and > six months on hemodialysis, while exclusion criteria included certain cardiac, renal, and systemic conditions.

Result: The study examines demographic, clinical, and biochemical aspects of chronic kidney disease (CKD) patients undergoing hemodialysis. Most patients were male (63.7%), with a mean age of 43.1 years. Underlying causes of CKD varied, with glomerulonephritis (GN) being the most common (46.25%). Echocardiographic findings revealed alterations in cardiac parameters, with a majority (86.2%) exhibiting left ventricular hypertrophy (LVH). Correlation analysis showed associations between biochemical parameters and LVH severity, diastolic dysfunction, and valvular calcification. Overall, phosphate levels and parathyroid hormone levels were notably correlated with cardiac parameters.

Conclusion: The study revealed that there is a highly significant association of S. iPTH with left ventricular hypertrophy (LVH), left ventricular diastolic dysfunction (LVDD), and valvular calcification in CKD Stages 4, 5, and maintenance hemodialysis (MHD) patients. It can be inferred that high levels of S. iPTH are an essential predictor of the development of cardiac structural and functional abnormalities in CKD Stages 4 and 5 and maintenance hemodialysis (MHD) patients.

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Citation: Bedar Uddin, Omar Faroque, Muhammad Nazrul Islam, Fakhrul Islam Khaled, Shoriful Islam, F M Monjur Hasan. Association of Secondary Hyperparathyroidism with Cardiac Structural and Functional Abnormality in Chronic Kidney Disease Stage 4, 5 and Hemodialysis Patients. Archives of Nephrology and Urology. 7 (2024): 37-45.

Received: May 05, 2024
Accepted: May 13, 2024
Published: May 20, 2024

Uddin B, et al., Arch Nephrol Urol 2024
DOI:10.26502/anu.2644-2833078

Keywords: Secondary Hyperparathyroidism; Cardiac Abnormality; Chronic Kidney Disease Stage 4, 5; Hemodialysis.

Introduction

Kidney disease is a gradually advancing condition marked by alterations in the structure and function of the kidneys brought about by diverse factors. Chronic kidney disease (CKD) is generally identified by a decline in kidney function, with an estimated glomerular filtration rate lower than 60 mL/min per 1.73 m², or by indicators of kidney impairment, like albuminuria, hematuria, or anomalies identified through laboratory tests or imaging, persisting for a minimum of three months [1]. The significant and increasing global impact of chronic kidney disease is evident, with around 10% of adults globally experiencing some manifestation of the condition. This leads to approximately 1.2 million fatalities and a loss of 28.0 million years of life annually [2,3]. By the year 2040, chronic kidney disease is projected to rise to become the fifth most common cause of death worldwide, showcasing one of the most substantial anticipated increases among all significant causes of mortality [4]. Research indicates that the prevalence of various causes of chronic kidney disease differs significantly across different regions. For instance, in Bangladesh, studies suggest that CKD impacts between 16% and 22% of the population, with 11% of these individuals being in stages III-V [5]. In Bangladesh, the annual incidence of end-stage kidney failure (ESKF) is estimated to be between 200 and 250 people per million [6]. End-stage renal disease (ESRD) notably affects the heart's structure and function. Individuals with ESRD frequently exhibit underlying myocardial pump irregularities, which can be further complicated by frequent fluid shifts [7]. It is the primary cause of mortality in this patient population and accounts for nearly half of all deaths among those undergoing dialysis [8]. Secondary hyperparathyroidism (SHPT) is a frequent complication observed in CKD patients, particularly those in advanced stages and those receiving hemodialysis [9]. SHPT is linked with left ventricular hypertrophy, diastolic dysfunction, and heightened susceptibility to cardiovascular events in individuals with CKD [10]. In CKD, the pathophysiology of SHPT begins with the development of hypocalcemia and hyperphosphatemia resulting from compromised kidney function. This triggers an elevation in parathyroid hormone (PTH) secretion, ultimately culminating in the development of SHPT [11]. In their study, Ahmed et al. (2019) discovered that PTH serves as a significant uremic toxin, potentially leading to long-term complications such as renal osteodystrophy, severe vascular calcifications, changes in cardiovascular structure and function, immune system dysfunction, and anemia [12]. Additionally, Nikodimopoulou and Liakos et al. (2011) found in their study that PTH has been identified as a critical cardiotoxin in ESRD, capable of causing harmful effects in the myocardium [10]. The management of SHPT in CKD patients typically involves using vitamin D analogs, calcimimetics, and, in severe cases, parathyroidectomy [11]. The study aims to find out the associations of secondary hyperparathyroidism (SHPT) with left ventricular hypertrophy (LVH), left ventricular diastolic dysfunction (LVDD) and valvular calcification (VC) in chronic kidney disease (CKD) stage 4, 5 and maintenance hemodialysis (MHD) patients.

Methodology & Materials

This cross-sectional observational study was conducted in the Department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. The study duration was one year, from November 2022 to September 2023. Purposively, 80 patients with CKD Stages 4 and 5 and on maintenance hemodialysis were included as per the selection (inclusion & exclusion) criteria. Before collecting data, informed consent was taken from every participant, and ethical approval was obtained from the institution's ethics committee.

Inclusion criteria:

- Age: 18 to 65 years.
- All predialysis CKD (stage 4, 5) patients.
- All patients on maintenance hemodialysis for > 6 months.
- S. iPTH > 2 times the upper normal limit.

Exclusion criteria:

- All patients with primary cardiac diseases, such as evidence of congenital heart disease or rheumatic heart disease and decompensated cardiac disease (DCM/ICM).
- Renal allograft recipients.
- Severe anemia
- Advanced COPD patients
- Malignancy
- Advanced liver disease.

Operational definitions:

➢ **Chronic Kidney Disease (CKD):**

CKD is defined as kidney structure or function abnormalities that have been present for > three months and have health implications. Criteria for CKD (either of the following present for > three months), stage of CKD down below:

- Stage 4 CKD is defined when GFR is within 15–29 ml/min/1.73 m2 BSA.
- Stage 5 CKD is defined when GFR is less than 15 ml/min/1.73 m2 BSA.

➢ **Secondary hyperparathyroidism:**

Secondary hyperparathyroidism (SHPT) is an increased secretion of PTH due to parathyroid hyperplasia caused by triggers such as hypocalcemia, hyperphosphatemia, or decreased active vitamin D, most commonly associated with chronic kidney disease [13].

➢ **Maintenance Hemodialysis:**

ESRD patients on regular dialysis for 8-12 hours/week for at least three months.

➢ **Cardiac structural and functional abnormality (Left Ventricular Hypertrophy):**

LVH is assessed by calculating- LV Mass (LVM)=0.8{1.04 [LVEDD+IVST+PWT]3–LVEDD3)]}+0.6 in gm. Where LVEDD=Left Ventricular End Diastolic Diameter, IVST = interventricular septal thickness and PWT=posterior wall thickness. LVM index (LVMI) = LVM/Body Surface Area (BSA) in gm/m2 (Devereux RB, 1997). LVH is defined as LV mass index (g/m2) greater than 115 g/m2 in men and greater than 95 g/m2 in women. Mild LVH is defined as LVMI within 116-131 g/m2 in men and 96-108 g/m2 in women. Moderate LVH is defined as LVMI within 132-148 g/m2 in men and 109-121 g/m2 in women. Severe LVH is defined as LVMI, which is ≥149 g/m2 in men and ≥122 g/m2 in women (ASE/EAE guidelines).

➢ **Diastolic Dysfunction:**

Tissue Doppler measurements are obtained at the level of the mitral annulus. Early (e') and late (a") diastolic mitral annular tissue velocities at the septum and lateral walls are measured. Pulsed wave Doppler is used to measure early (E) and late (A) transmitral flow velocities; the ratio of early to late velocities (E/A) is noted. The E/e ratio uses the average of mitral septal and lateral tissue velocities.

➢ **Valvular calcification:**

Cardiac valve calcification is defined as bright echoes of more than 1 mm on one or more cusps of the aortic valve, mitral valve, or mitral annulus. The degree of valvular calcification is graded as Mild (spot-like calcification <3 mm), Moderate (multiple calcium spots >3 mm) and Severe (extensive calcifications of the valvar annulus, the semilunar cusps, or both) [15].

➢ **Data collection procedure:**

After enrollment, a detailed medical and socioeconomic history was recorded in a preformed data sheet. A thorough physical examination was done, and data was documented. Anthropometric measurements, including height and weight, were done, and BMI was calculated from measured height and weight. An estimated glomerular filtration rate (eGFR) was calculated for all serum creatinine values by using the diet modification in renal disease formula (MDRD) to determine the staging of CKD. Blood pressure was measured with a sphygmomanometer in a sitting posture after 5 minutes of rest. With all aseptic precautions, 5 ml of venous blood was collected from the patient's antecubital vein in a vacutainer tube for the required tests. Different Hematological, biochemical and hormonal (Hemoglobin, Serum calcium, Serum inorganic phosphate, S. iPTH, Vitamin D level) tests were done/ recorded among the study population. Serum iPTH was seen by IMMULITE 2000, a solid-phase, two-site chemiluminescent enzyme-labeled immunometric assay. It was performed using Vivid E9 edition (GE Healthcare system), assessing the systolic function, LVH, left ventricular diastolic dysfunction, aortic and mitral calcifications, and hypokinesia. The analysis of systolic function by echocardiogram is usually performed by evaluating the ejection phase, particularly the fractional shortening and the ejection fraction. The diastolic function examination focuses on pulsed Doppler recordings of left-sided mitral inflow E and A waves, pulmonary vein systolic, diastolic, and atrial reversal waves, and the corresponding right-sided tricuspid inflow and hepatic vein flow waves. Left ventricular mass is proportional to the body size. Different cut-off values were used in this study to define the presence of LVH.

➢ **Data processing and analysis:**

All statistical analysis was performed using Windows-based computer software with Statistical Packages for Social Sciences (SPSS-27). Quantitative data were expressed as mean and standard deviation and qualitative data as frequency distribution and percentage. The association between parametric data by Unpaired t-test, one-way ANOVA test, and nonparametric data was analyzed using the chi-square test. Multiple logistics regression analysis/ Multivariate regression analysis was done to see the effect of Serum iPTH on cardiac structural and functional abnormality. Pearson's correlation coefficient test will be used to find out the correlation. For all statistical tests, a p-value of <0.05 will be considered statistically significant at a 95% confidence interval (CI).

Result

Table 1 shows the demographic characteristics of the study patients. It was observed that 25(31.3%) patients were aged>50 years. The mean age was 43.1±12.9 years. 51(63.7%) patients were male and 29(36.3%) were female. Majority 73(91.3%) patients had normal BMI (18.1-25.0 kg/m2). Table 2 shows the distribution of the study patients according to the underlying cause of CKD. It was observed that 37(46.25%) patients had GN; 27(33.75%) had DM; 6(7.5%) had HTN; 3(3.75%) had CPN; 3(3.75%) had unknown cause; 2(2.5%) had ADPKD and 2(2.5%)

had ON. Table 3 shows the comparison of biochemical parameters with the severity of LVH where the mean S. PO4 was 4.8±0.7 (mg/dl) in no LVH, 5.8±1.2 (mg/dl) in mild, 6.3±1.2 (mg/dl) in moderate and 6.8±2.7 (mg/dl) in severe LVH group. The mean iPTH was 193.1±126.5 (pg/ml) in no LVH, 285.3±139.7 (pg/ml) in mild, 506.6±141.2 (pg/ml) in moderate, and 560.6±236.9 (pg/ml) in severe LVH group. The differences were statistically significant ($p<0.05$) among the four groups, but Corrected Ca, Ca XPO4 product, and Vitamin D were statistically not significant ($p>0.05$) among the four groups. Table 4 shows the comparison of clinical and biochemical parameters among the different grades of diastolic dysfunction (DD); the mean S. PO4 was 4.93±0.80 (mg/dl) in no DD, 6.13±1.28 (mg/dl) in G-I DD and 6.93±2.82 (mg/dl) in G-II DD. The mean Ca XPO4 product was 41.29±6.63 (mg2/dl2) in no DD, 51.42±10.58 (mg2/dl2) in G-I DD and 57.46±21.82 (mg2/dl2) in G-II DD. The mean iPTH was 216.8±123.2 (pg/ml) in no DD, 409.4±202.3 (pg/ml) in G-I DD, and 557.3±188.2 (pg/ml) in G-II DD. Table 5 shows the comparison of clinical and biochemical variables among the different valvular calcification; the mean S. PO4 was 6.3±2.9 (mg/dl) in MVC, 5.6±1.5 (mg/dl) in AVC, 6.5±1.3 (mg/dl) in both VC and 5.2±0.8 (mg/dl) in no VC patients. The mean Ca XPO4 product was 50.9±23.1 (mg2/dl2) in MVC, 46.4±9.5 (mg2/dl2) in AVC, 55.2±10.7 (mg2/dl2) in both VC and 43.3±6.1 (mg2/dl2) in no VC patients. The mean iPTH was 461.0±186.4 (pg/ml) in MVC, 386.1±229.4 (pg/ml) AVC, 448.9±224.1 (pg/ml) in both VC and 259.9±146.1 (pg/ml) in no VC patients. Table 6 states that for left ventricular mass index (LVMI), there was a positive correlation with serum phosphate levels (S. PO4) ($r = 0.382$, $p = 0.001$), calcium-phosphate product (Ca x PO4) ($r = 0.429$, $p = 0.001$), and intact parathyroid hormone (iPTH) levels ($r = 0.421$, $p = 0.001$). However, corrected calcium levels did not correlate significantly ($r = 0.172$, $p = 0.128$). Vitamin D levels also did not significantly correlate with LVMI ($r = 0.07$, $p = 0.539$). Regarding the E/A ratio, a marker of diastolic function, significant positive correlations were observed with S. PO4 ($r = 0.300$, $p = 0.007$), Ca x PO4 product ($r = 0.320$, $p = 0.004$), and iPTH levels ($r = 0.358$, $p = 0.001$). However, corrected calcium levels showed only a weak positive correlation that was not statistically significant ($r = 0.075$, $p = 0.509$). Vitamin D levels also exhibited no significant correlation with the E/A ratio ($r = -0.058$, $p = 0.607$). For left atrial diameter (LA diameter), significant positive correlations were found with S. PO4 ($r = 0.346$, $p = 0.002$), Ca x PO4 product ($r = 0.348$, $p = 0.002$), and iPTH levels ($r = 0.276$, $p = 0.013$). However, corrected calcium levels did not exhibit a significant correlation ($r = -0.019$, $p = 0.864$), and there was no significant correlation with vitamin D levels ($r = -0.033$, $p = 0.775$).

Table 1: Demographic characteristics of the study patients (N=80).

Variables	Frequency (n)	Percentage (%)
Age group (years)		
<30	16	20
31-40	21	26.2
41-50	18	22.5
>50	25	31.3
Mean±SD	43.1±12.9	
Sex		
Male	51	63.7
Female	29	36.3
BMI (kg/m^2)		
Underweight (<18.1)	6	7.5
Normal weight (18.1-25.0)	73	91.3
Overweight (25-29.9)	1	1.3

Table 2: Distribution of the study patients according to underlying cause of CKD (N=80).

Underlying cause of CKD	Frequency (n)	Percentage (%)
GN	37	46.25
DM	27	33.75
HTN	6	7.5
CPN	3	3.75
Unknown	3	3.75
ADPKD	2	2.5
ON	2	2.5
Total	80	100

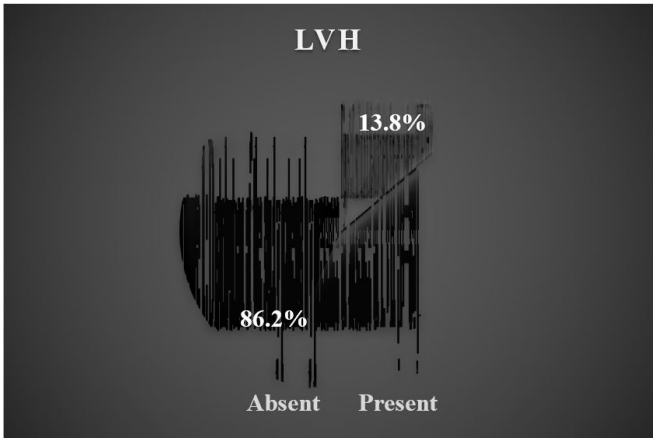

Figure 1: Distribution of the study patients by presence or absence of LVH (N=80)

Citation: Bedar Uddin, Omar Faroque, Muhammad Nazrul Islam, Fakhrul Islam Khaled, Shoriful Islam, F M Monjur Hasan. Association of Secondary Hyperparathyroidism with Cardiac Structural and Functional Abnormality in Chronic Kidney Disease Stage 4, 5 and Hemodialysis Patients. Archives of Nephrology and Urology. 7 (2024): 37-45.

Uddin B, et al., Arch Nephrol Urol 2024
DOI:10.26502/anu.2644-2833078

Table 3: Comparison of biochemical parameters with severity of LVH (N=80).

Variables	LVH severity				p-value
	No LVH (N=11)	Mild (N=30)	Moderate (N=22)	Severe (N=17)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Corrected Ca (mg/dl)	8.4±0.7	8.5±0.8	8.1±1.2	8.7±0.6	0.203
S. PO_4 (mg/dl)	4.8±0.7	5.8±1.2	6.3±1.2	6.8±2.7	<.011*
Ca X PO_4 product	46.9±12.7	48.5±10.0	52.0±9.3	57.3±21.1	0.12
iPTH (pg/ml)	193.1±126.5	285.3±139.7	506.6±141.2	560.6±236.9	<.001*
Vit D (ng/ml)	21.0±6.0	19.5±4.7	22.4±7.6	22.0±7.5	0.393

Table 4: Comparison of clinical and biochemical parameters among the different grade of diastolic dysfunction

Variables	Diastolic dysfunction grading			p-value
	No DD (N=18)	G-I DD (N=48)	G-II DD (N=14)	
	Mean ± SD	Mean ± SD	Mean ± SD	
Corrected Ca(mg/dl)	8.37±0.66	8.38±1.07	8.42±0.36	0.984
S. PO_4 (mg/dl)	4.93±0.80	6.13±1.28	6.93±2.82	.002*
Ca XPO_4 product	41.29±6.63	51.42±10.58	57.46±21.82	.002*
iPTH (pg/ml)	216.8±123.2	409.4±202.3	557.3±188.2	.001*
Vitamin D (ng/ml)	21.71±5.52	20.64±6.89	21.62±6.07	0.784

Table 5: Comparison of clinical and biochemical variables among the different valvular calcification (N=80).

Variables	Valvular calcification				p-value
	Mitral valve (N=14)	Aortic valve (N=9)	Both VC (N=35)	No VC (N=22)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Corrected Ca	8.2±0.3	8.5±0.8	8.4±1.1	8.4±0.8	0.873
S. PO_4 (mg/dl)	6.3±2.9	5.6±1.5	6.5±1.3	5.2±0.8	.020*
Ca XPO_4 product	50.9±23.1	46.4±9.5	55.2±10.7	43.3±6.1	.008*
iPTH (pg/ml)	461.0±186.4	386.1±229.4	448.9±224.1	259.9±146.1	.005*
Vitamin D (ng/ml)	21.4±7.5	21.9±8.5	21.1±6.9	20.4±3.7	0.944

Table 6: Correlation of LVMI and LVDD parameters with biochemical predictors (N=80).

Outcome variable	Predictors	r- value	p-value
LVMI (gm/m2)	Corrected Ca (mg/dl)	0.172	0.128
	S. PO_4 (mg/dl)	.382*	0.001
	Ca xPO_4 product (mg^2/dl^2)	.429*	0.001
	iPTH (pg/ml)	.421*	0.001
	Vitamin D (ng/ml)	0.07	0.539
E/A Ratio	Corrected Ca (mg/dl)	0.075	0.509
	S. PO4 (mg/dl)	0.300*	0.007
	Ca XPO4 product (mg^2/dl^2)	0.320*	0.004
	iPTH (pg/ml)	0.358*	0.001
	Vitamin D (ng/ml)	-0.058	0.607
LA diameter (mm)	Corrected Ca (mg/dl)	-0.019	0.864
	S. PO_4 (mg/dl)	.346*	0.002
	Ca xPO_4 product (mg2/dl2)	.348*	0.002
	iPTH (pg/ml)	.276*	0.013
	Vitamin D (ng/ml)	-0.033	0.775

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Uddin B, et al., Arch Nephrol Urol 2024
DOI:10.26502/anu.2644-2833078

Discussion

Early evaluation and detection of CKD patients' complications, especially focusing on CKD-MBD markers and echocardiographic cardiac structural and functional parameters, is essential for timely management and halting further progression of cardiovascular disease and mineral bone disorders. The purpose of the current study was to find out the association of SHPT with cardiac structural and functional abnormalities in chronic kidney disease (CKD) Stage 4, 5 & hemodialysis (HD) patients to provide substantial elements with this conflicting issue and to help undertake appropriate measures in management and prevention aspects. It was observed that 31.3% of patients belonged to age >50-65 years. The mean age was 43.1±12.9 years, with ranged from 18 to 65 years. In a similar study, Al-Hilali et al. reported that the population's median age was 57, which is higher than our study because more than 65 years of patients were excluded from this study. 51(63.0%) patients were male and 29(36.3%) were female [16]. Bhatti et al. reported that there were 38 (63.33%) male and 22(35.48%) female patients in their study [17]. Globally, CKD is more prevalent among women, but the prevalence of ESRD is higher in men due to certain social, structural, and physical factors [18]. The majority (91.3%) of patients had normal BMI (18.1-25.0 kg/m2) with a mean BMI of (22.1±2.3) Kg/m2. Al Hilali observed a similar range of BMI [16]. BMI at the lower limit of the normal range may be due to inadequate intake, malnutrition, systemic inflammation, the influence of appetite-controlling hormones from the reduction of renal clearance, insulin, insulin-like growth factor resistance, metabolic acidosis, etc. [19]. In this study, concerning the most common etiologies, it was observed that 37(46.25%) patients had GN, 27(33.75%) had DM, and 6(7.5%) had only HTN. For the findings, our study could be correlated with the report of Kapil et al., where the prevalence of HTN and DM was 54.5% and 24.6%, respectively, comparable with our study results [20]. Glomerular disease is the leading cause of end-stage renal disease (ESRD) worldwide [21]. Rashid reported that GN comprises 25-45% of cases of ESRD in developing nations such as Bangladesh, which agrees with our study [22]. Low socioeconomic conditions, malnutrition, inflammation, and highly prevalent infectious diseases are important causes of the predominance of GN as a cause of CKD in our patients. This study showed the comparison of echocardiographic variables with HD patients. As iPTH is considered toxic to the myocardium, it causes myocyte hypertrophy. It increases the interstitial collagen matrix by intracellular calcium deposition due to SHPT, which might increase the risk of HTN in dialysis patients. It also causes coronary artery calcification [16]. The current study observed that the levels of S. iPTH, S. PO4, and Ca, x PO4 product significantly increased with the increasing severity of LVDD, with the highest levels observed in G-II LVDD. This suggests a potential association of elevated S. iPTH, S. PO4, and the Ca XPO4 product level with advanced LVDD ($p<0.05$). Kim et al., Ogawa, and Nitta documented that LVDD commonly occurs earlier than systolic dysfunction in hemodialysis and is observed even in patients with early stages of CKD [23,24]. LVH and LVDD are closely related, and the primary mechanism of LVDD is LVH with myocardial fibrosis, which induces myocardial stiffness and impairs cardiac function during diastole. Kim et al. showed that S. iPTH and S. PO4 are significantly associated with worsening DD [23]. Cicekcioglu et al. demonstrate that high levels of iPTH contribute significantly to LVDD and LVH in hemodialysis patients. However, high PO4 and Ca × PO4 product levels are not related to cardiac complications (LVDD) [25]. Galetta et al. evidenced that uraemic patients on HD have an impairment of the LV function, and in particular, the sub-clinical abnormalities of diastolic function are related to elevated S. PO4 and Ca × PO4 products [26]. Walker et al. explained that patients with biochemically mild PHPT do not have evidence of increased left ventricular mass, diastolic dysfunction, or increased valvular calcifications [27]. Furthermore, the increased serum calcium and PTH levels in those with DD suggest that disease severity may determine the presence of cardiac manifestations in PHPT. This is due to the important role of changes in calcium phosphate homeostasis on cardiovascular damage. This is one more reason for making any effort to achieve optimal control of phosphaturia and calcium phosphate products to reduce the risk of cardiovascular events and heart failure in uremic patients. These study subjects were divided into four groups based on the presence and location of VC. The iPTH levels increased significantly ($p<0.05$) among the groups. Patients with both VC have higher mean iPTH levels than those without VC. This association between SHPT and VC has been explored previously, with studies suggesting that elevated iPTH levels may contribute to developing vascular and valvular calcifications [12]. Increased PO4 levels can promote mineral deposition in the cardiovascular system. The Ca xPO4 product also shows a significant ($p<0.05$) difference among the groups. The group with both VC has the highest mean Ca xPO4 product. This finding reinforces the link between high Ca xPO4 product and VC, a relationship documented in prior studies [16,25]. In a study, Nematullahi et al. showed that serum calcium and parathyroid hormone levels were not significantly associated with the calcification of the heart valves. However, serum phosphorous levels had a significant positive relationship with the calcification of the heart valves [28]. According to some studies, the calcification of heart valves has a significant relationship with calcium, phosphorus, and parathormone levels, while other studies have not reported such a relationship. Raggi et al.'s study found that the severity of calcification of the heart valves was related to the duration of dialysis and serum phosphorus and calcium

[29]. Moreover, it was reported that serum parathyroid hormone level was a major risk factor for the calcification of heart valves and had a direct relationship with valve calcification [30]. The study by Mousavi et al. demonstrated no significant relationship between serum calcium and phosphorus levels with calcification of the heart valves [31]. These differences suggest that VC may be associated with cardiac structure and function alterations, which is consistent with existing research [25]. The above findings suggest statistically significant associations between the presence and location of VC and various parameters related to S. PO4 levels, Ca xPO4 product, iPTH levels, and cardiac structural parameters. There was a significant positive correlation between LVMI and S. PO4, Ca xPO4 product, and iPTH. Strozecki et al. reported that S. PO4 significantly correlates with LVMI and cardiovascular dysfunction [32]. Helvaci et al. reported a significant correlation between LVMI and PTH levels in hypertensive patients [33]. In a similar study, Ali et al. observed a statistically significant positive correlation of LVMI with S. iPTH, S. Ca, and S. PO4 levels [34]. They also concluded that HPT, hyperphosphatemia, and hypertension were significantly associated with DD, while hypovitaminosis D was not significantly associated. Biomarkers of CKD-MBD were significantly associated with LVH and increased LVMI. This study demonstrated a positive significant correlation of E/A Ratio with iPTH, S. PO4, and Ca XPO4 product and also found a positive significant correlation of LA diameter with S. PO4, Ca XPO4 product, and iPTH, which are in agreement with the findings by Kim et al. [23]. Stróżecki et al. showed that S. PO4, Ca XPO4 product, and iPTH significantly correlate with LVMI and E/A Ratio, which corresponds with this study [32]. Similarly, Nasri and Baradaran demonstrated that higher iPTH levels were associated with increased left atrial size and DD in CKD patients on HD [35]. Kim et al. showed that iPTH levels and left atrial volume index levels were independent predictors of LVH and systolic blood pressure, and left atrial volume index levels were independent predictors of LVDD [23].

Limitations of the study: The present study was conducted within a short timeframe and with a limited number of patients. There was an unequal distribution of predialysis stages 4 and 5 and patients undergoing hemodialysis (HD). Patients with intact parathyroid hormone (iPTH) levels below 134 pg/ml were excluded from the predialysis and maintenance hemodialysis (MHD) groups. All participants in the study were sourced from a single dialysis center, where they underwent hemodialysis two to three times weekly using the same dialyzer and dialysis solution. However, the adequacy of dialysis for individual patients was not measured. Unlike the gold standard for assessing Left Ventricular Mass (LVM) and Left Ventricular Hypertrophy (LVH) in adults, which is cardiac MRI, this study did not utilize this imaging technique. Echocardiography was intended to be performed by a single cardiologist, but ultimately, 50% of the echocardiograms were conducted by one cardiologist and the other 50% by different cardiologists.

Conclusion and Recommendations

The research findings indicate a strong correlation between serum intact parathyroid hormone (S. iPTH) levels and various cardiac complications, including left ventricular hypertrophy (LVH), left ventricular diastolic dysfunction (LVDD), and valvular calcification among individuals with chronic kidney disease (CKD) in Stages 4 and 5, as well as those undergoing maintenance hemodialysis (MHD). These results suggest that elevated S. iPTH levels serve as a crucial indicator for the onset of structural and functional heart abnormalities in CKD patients at Stages 4 and 5 and those on MHD treatment.

Funding: No funding sources.

Conflict of interest: None declared.

Ethical approval:

The study was approved by the Institutional Ethics Committee

References

1. Webster AC, Nagler EV, Morton RL, et al. Chronic kidney disease. Lancet 389 (2017): 1238-1252.
2. Bikbov B, Purcell CA, Levey AS, et al. Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 395 (2020): 709-733.
3. Xie Y, Bowe B, Mokdad AH, et al. Analysis of the Global Burden of Disease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016. Kidney Int 94 (2018): 567-581.
4. Foreman KJ, Marquez N, Dolgert A, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016–40 for 195 countries and territories. Lancet 392 (2018): 2052-2090.
5. Kar S, Islam MF. Global dialysis perspective: Bangladesh. Kidney 4 (2023): e1472-1475.
6. Rashid HU. Health delivery system for renal disease care in Bangladesh. Saudi J Kidney Dis Transplan 15 (2004): 185-89.
7. Rangaswami J, McCullough PA. Heart failure in end-stage kidney disease: pathophysiology, diagnosis, and therapeutic strategies. InSeminars in Nephrology 38 (2018): 600-617.

8. Nasri H. Pulmonary artery pressure in association with serum parathormone in maintenance hemodialysis patients. Arch Med Sci 2 (2006): 32-35.

9. Verma A, Anavekar NS, Meris A, et al. The relationship between renal function and cardiac structure, function, and prognosis after myocardial infarction: the VALIANT Echo Study. J Am College of Cardiol 50 (2007): 1238-1245.

10. Nikodimopoulou M, Liakos S. Secondary hyperparathyroidism and target organs in chronic kidney disease. Hippokratia 15 (2011): 33.

11. Habas Sr E, Eledrisi M, Khan F, et al. Secondary hyperparathyroidism in chronic kidney disease: pathophysiology and management. Cureus 14 (2021): 13(7).

12. Ahmed HA, Yassein YS, Elzorkany KM, et al. Influence of secondary hyperparathyroidism on left ventricular function in maintenance hemodialysis patients. Menoufia Med J 32 (2019): 922.

13. Silver J, Levi R. Regulation of PTH synthesis and secretion relevant to the management of secondary hyperparathyroidism in chronic kidney disease. Kidney Int 67 (2005): S8-S12.

14. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 57 (1986): 450-458.

15. Pomerance A. Pathogenesis of aortic stenosis and its relation to age. British Heart J 34 (1972): 569.

16. Al-Hilali N, Hussain N, Ataia AI, et al. Hypertension and hyperparathyroidism are associated with left ventricular hypertrophy in patients on hemodialysis. Indian J Nephrol 19 (2009): 153-157.

17. Bhatti TA, Shah SM, Ashraf W, et al. Correlation of Hypretensive Left Ventricular Hypertrophy with Renal End Organ Damage. Pakistan J Med Health Sci 12 (2018): 291-295.

18. García GG, Iyengar A, Kaze F, et al. Sex and gender differences in chronic kidney disease and access to care around the globe. InSeminars in Nephrol 42 (2022): 101-113.

19. Randon RB, Rohde LE, Comerlato L, et al. The role of secondary hyperparathyroidism in left ventricular hypertrophy of patients under chronic hemodialysis. Brazilian J Med Biol Res 38 (2005): 1409-1416.

20. Kapil U, Khandelwal R, Ramakrishnan L, et al. Prevalence of hypertension, diabetes, and associated risk factors among geriatric population living in a high-altitude region of rural Uttarakhand, India. J Family Med Primary care 7 (2018): 1527-1536.

21. Gupta RD, Mamun AA, Morshed SM, et al. Mon-029 Pattern of Glomerulonephritis in Bangladesh-A Single Center Study at A Tertiary Care Hospital. Kidney Int Rep 4 (2019): S316.

22. Rashid HU. Nephrotic syndrome-evidence based management. Bangladesh Renal J 22 (2003): 1-4.

23. Kim IY, Ye BM, Kim MJ, et al. Association between serum uric acid and left ventricular hypertrophy/left ventricular diastolic dysfunction in patients with chronic kidney disease. PloS one 16 (2021): e0251333.

24. Ogawa T, Nitta K. Clinical impact of left ventricular diastolic dysfunction in chronic kidney disease. Recent Adv Pathogenesis Treatment of Kidney Dis195 (2018): 81-91.

25. Çiçekçioğlu H, Ergün İ, Uçar Ö, et al. Cardiac complications of secondary hyperparathyroidism in chronic hemodialysis patients. Turkish J Med Sci 41 (2011): 789-794.

26. Galetta F, Cupisti A, Franzoni F, et al. Left ventricular function and calcium phosphate plasma levels in uraemic patients. J Int Med 258 (2005): 378-384.

27. Walker MD, Fleischer JB, Di Tullio MR, et al. Cardiac structure and diastolic function in mild primary hyperparathyroidism. J Clin Endocrinol Metabolism 95 (2010): 2172-2179.

28. Nematollahi A, Tamadon MR, Irannejad P, et al. Association of serum phosphorus, calcium and parathyroid hormone with cardiovascular calcification in regular hemodialysis patients. J Parathyroid Dis 6 (2017): 44-49.

29. Raggi P, Boulay A, Chasan-Taber S, et al. Cardiac calcification in adult hemodialysis patients: a link between end-stage renal disease and cardiovascular disease?. J Am College Cardiol 39 (2002): 695-701.

30. Ávila-Díaz M, Mora-Villalpando C, del Carmen Prado-Uribe M, et al. De novo development of heart valve calcification in incident peritoneal dialysis patients. Arch Med Res 44 (2013): 638-644.

31. Mousavi MS, Tabaraei Y, Alipour NK, et al. Relationship between calcium, phosphorous and parathoromone with calcification of heart valves in dialyzed patients in Qom, 2006-2007. Qom Univ Med Sci J 2 (2008).

32. Stróżecki P, Adamowicz A, Nartowicz E, et al. Parathormon, calcium, phosphorus, and left ventricular structure and function in normotensive hemodialysis patients. Renal Failure 23 (2001): 115-126.

Citation: Bedar Uddin, Omar Faroque, Muhammad Nazrul Islam, Fakhrul Islam Khaled, Shoriful Islam, F M Monjur Hasan. Association of Secondary Hyperparathyroidism with Cardiac Structural and Functional Abnormality in Chronic Kidney Disease Stage 4, 5 and Hemodialysis Patients. Archives of Nephrology and Urology. 7 (2024): 37-45.

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DOI:10.26502/anu.2644-2833078

33. Helvaci A, Copur B, Adas M. Correlation between left ventricular mass index and calcium metabolism in patients with essential hypertension. J Am College Cardiol 62 (2013): C98-C110.

34. Ali S, Saber M, Kassem M. The impact of bone mineral biomarkers on cardiac dysfunction in predialysis chronic kidney disease children. Int J Pediatrics 2021 (2021).

35. Nasri H, Baradaran A. Close association between parathyroid hormone and left ventricular function and structure in end-stage renal failure patients under maintenance hemodialysis. J Ayub Med College Abbottabad 16 (2004).

Citation: Bedar Uddin, Omar Faroque, Muhammad Nazrul Islam, Fakhrul Islam Khaled, Shoriful Islam, F M Monjur Hasan. Association of Secondary Hyperparathyroidism with Cardiac Structural and Functional Abnormality in Chronic Kidney Disease Stage 4, 5 and Hemodialysis Patients. Archives of Nephrology and Urology. 7 (2024): 37-45.