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CORRELATION BETWEEN PARATHYROID HORMONE AND LEFT VENTRICULAR FUNCTION IN CHRONIC KIDNEY DISEASE PATIENTS

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ABSTRACT

Cardiovascular risk factors are a significant burden in chronic kidney disease (CKD). Abnormalities of left ventricle (LV) structure and function are present in 70-80% of patients with CKD and more than half of them die of cardiovascular diseases. In this study we aimed to correlate, parathyroid hormone (PTH) levels with left ventricular hypertrophy (LVH) and LV ejection fraction by 2D-Echo-CD in patients with CKD. One hundred and twenty patients with clinical evidence of CKD were enrolled for the present study. The 120 patients were stratified into three stages based eGFR. Significant correlation of serum PTH with ejection fraction were observed in group 3 (P=<0.0001) than groups 1&2 (P=0.2621; P=0.0024 respectively). Abnormal high PTH >250 pg/ml significantly correlates with low EF and significant LVH. There is a role for high PTH in the development of the LVH as well as LV ejection fraction in CKD patients.

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KEYWORDS; **Left ventricular hypertrophy, ejection fraction, PTH, CKD, 2D-Echo-CD.**

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INTRODUCTION

Chronic kidney disease (CKD) causes complicated changes in calcium and phosphorus metabolism[1]. Some observational studies suggest CKD is well established as a risk state that results in greater rates of prevalent and incident cardiovascular disease (CVD)[2,3] and CVD is the most common cause of death in patients with CKD. As estimated glomerular filtration rate (eGFR) decreases to less than 60 ml/min/1.73 m^2 in populations, CVD prevalence and future mortality increase[4].

Increased attention has been focused on endocrine abnormalities in patients with CKD to explain this association[5]. Parathyroid hormone (PTH) having a mechanism to maintain calcium and phosphorus levels within physiological ranges. Clinical studies indicate that PTH may contribute to development of left ventricular hypertropy[6,7]. Despite the commonly seen abnormalities in serum calcium and phosphate in chronic kidney disease (CKD), only a few studies exist regarding the association between high serum PTH levels and left ventricular function in CKD patients. We therefore aimed to consider the evidence regarding the role of high PTH in the development of left ventricular hypertrophy as well as left ventricle (LV) ejection fraction as marker of LV function in patients with CKD.

MATERIALS AND METHODS

Subjects

A total of one hundred and twenty patients with clinical evidence of CKD patients and age and sex matched thirty control population were enrolled in this prospective study. The age of the subjects ranged from 28 to 76 years, had blood samples taken for serum PTH measurement in addition to general examination. Those on renal bone disease were excluded, leaving 86 males and 34 females for the present study. 120 patients were stratified in to three stages based on calculation of eGFR by MDRD formula **(**eGFR (ml/min/1.73 m^2) = 186 (S.Cr) $^{-1.154}$ × (age) $^{-0.203}$) namely group 1 (eGFR 30-59 ml/min, n=26), group 2 (e GFR 16-29 ml/min, n=30) and group 3 (<15 ml/min, n=64) (Table1).

Methods

All patients underwent routine biochemistry tests including S.Calcium, S.Phosphorus, high sensitive C-reactive protein (HSCRP), S.Creatinine, Bl.urea, Hemoglobin (Hb) and eGFR based on MDRD formula which was measured by standard methods. 2D-Echo-CD was done by a single operator for all cases. Intact PTH was measured using Immulite (Diagnostic Products Corporation, Los Angles, CA, USA) based on a two-site chemiluminescent immunometric assay. The percentage of LVH is calculated in the abnormal PTH patient group i.e. number of LVH patients with abnormal PTH (>200 pg /ml) divided by total number of abnormal PTH patients in a group. The reference range for PTH in the present study is 10-69 pg/ml. written informed consent was obtained from all the participants.

Statistical Analyses

Statistical analyses were performed using medcalc statistical software. Values are given as mean ± standard deviation. The significance between PTH and ejection fraction were analyzed by Pearson correlation. $P<0.05$ was taken as a significant value.

Table 1
Laboratory data among the groups [a]

	Control (n=30)	Group1 (n=26)	Group2 (n=30)	Group3 (n=64)
Age years	53.45±18.55	58±8.76	55.6±11.38	48.40±11.66
Hb gms/dl	13.22±1.89	10.44±1.34	8.99±2.40	7.92±2.17
S.HSCRP mg/l	2.67±1.10	5.21±2.38	6.98±2.51	6.77±3.00
Bl.Urea mg/dl	32.03±3.49	58±17.97	77.88±24.02	117.37 ±46.67
S.Creatinine mg/dl	1.1±0.78	2.67±0.36	4.39±0.41	8.63±3.73
S.Phosphorus mg/dl	3.01±0.26	3.60±0.62	4.76±0.92	6.41±1.47
S.Calcium mg/dl	9.42±0.81	10.16±1.74	10.40±2.37	9.70±2.73
S.iPTH pg/ml	45.64±5.14	143±89.80	207.68±98.05	254.95±101.37
e GFR ml/min/1.73m^2	75.41±12.71	52.13±7.89	25.32±4.61	11.2±3.48

[a] ***Values given are mean ± standard deviation ;***

RESULTS

Commonest cause of CKD in this study was diabetes mellitus. Abnormal PTH was found in patients with low ejection fraction and LVH in high percentage (60.80%) in group 3 than in group 1 (14.28%) and group 2 (23%) (*Table 2*). Significant correlation of serum PTH with ejection fraction were observed in group 3 (r=-0.5777, *P*=<0.0001) than groups 1&2 (r=0.2282, *P*=0.2621; r=-0.5338, *P*=0.0024 respectively). No association was observed between serum phosphorus or calcium level and CVD events

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Table 2
Correlation between iPTH Vs EF among groups [a]

	iPTH(pg/ml)	LVH [b]	EF	*P* value
Group 1	143±89.80	14.28	68.30±12.54	0.2621
Group 2	207.68±98.05	23	56.73±15.06	0.0024
Group 3	254.95±101.37	60.86	25.78±14.34	<0.0001

[a] ***Values given are mean ± standard deviation***
[b] ***Values in mean percentage***

DISCUSSIONS

Previous investigations have demonstrated a relationship between elevated PTH and cardiovascular disease in animal models[8]. Rostand and Drueke[9] reviewed the link between elevated PTH and cardiovascular disease in CRF patients. Among the correlation, they found that the elevated PTH was associated with left ventricular hypertrophy and increased left ventricular mass[10,11]. PTH level greater than 70 pg/ml is independently associated with CVD events in patients with CKD stages 3 and 4[12]. Also in the present investigation, the association between PTH and LVH was stronger when PTH≥250 pg/ml. Literature survey[11] has revealed that there is an association between excess PTH and a decrease in the left ventricular ejection fraction in uremic patients. In short, a chronic excess of PTH may impair LV passive compliance by inducing myocardial calcification and by causing LVH either directly[13-16] or indirectly[17-24]. Foley et al[25] and Levin et al[26] in separate cohort studies, identified not only that the majority of patients displayed LVH by the time they require dialysis, but also that there was a progressive increase in its prevalence as renal function fell below a creatinine clearance of 50

ml/min. In the present study also, the same findings observed but instead of creatinine clearance, we used the calculated eGFR using MDRD formula. PTH level increase is in response to decreases in the renal production of 1,25dihydroxyvitamin D, and hypovitaminosis D itself has been implicated in CVD[27-30].

CONCLUSION

Abnormal PTH (>250 pg/ml) is a good cardiac marker in CKD patients in our study. There is a role for high PTH levels in the development of the LVH as well as reduced LV ejection fraction in CKD patients. This factor needs more attention to reduce the risk of cardiovascular morbidity and mortality.

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