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Evaluation of Vitamin D And Parathryoid Hormone in Chronic Kidney Disease

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Abstract: *Chronic kidney disease is a common clinical condition and is associated with various complication and alteration in hormone homeostasis. Secondary hyperparathyroidism(SHPT) is a known complication which results in alteration in bone and mineral metabolism that occurs as a direct result of CKD. SHPT causes primarily cardiovascular calcification and is responsible for increase in morbidity and mortality. Identifying patients at risk and evaluating for SHPT is important because early intervention slows or arrests the progression of bone and cardiac disease in CKD patients. The aim is to evaluate the variation between iPTH and vitamin-D in various stages of CKD. A total of 154 CKD patients which are divided into stage I(n=13), stage II(n=18), stage III (n=19), stage IV (n=27), stage V(n=77) are included in the study. Serum urea, creatinine, albumin, iPTH, 25(OH) D3, calcium and phosphorus are estimated. eGFR calculated by MDRD 6-variable equation. Pearson's correlation and ANOVA test are used to assess the relation between the parameters. In CKD values of serum iPTH levels are higher in stage V compared to other stages, Vit D levels are sufficient in all stages. Statistical significant difference is found with iPTH and phosphorus among different stages of CKD. iPTH (r=-0.33), phosphorus(r=-0.28) are negatively correlated and 25(OH)D3(r=0.035) positively correlated with eGFR. Statistically significant correlation was found between PTH and eGFR with p-value 0.02. Our study shows importance of the determination of iPTH and phosphorus for early detection of SHPT. iPTH level are increased earlier than other bone markers. So early screening of CKD patients with serum iPTH levels helps in early detection and intervention of SHPT which reduces considerable mortality and morbidity.*

Keywords: *Secondary Hyperparathyroidism, CKD, iPTH, Vitamin D*

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I. Introduction

There is an increase surge in non communicable disease as compared to communicable disease as the most common cause of mortality and morbidity which causes considerable financial burden on the society. Chronic Kidney disease(CKD) is one such condition which has shown an increase incidence owing to increase incidence of Diabetes and Hypertension [1].Screening program have documented that in the adult US population the estimated prevalence of CKD stage 1 – 4 is 11.6% (~ 26 million people), a figure similar to that reported in other high income countries, such as Norway (10.2%), Japan (12.7%), Taiwan (11.8%), China (10.7%), and South Korea (13.7%) [2]. In India data on the incidence of chronic kidney disease are sparse. The prevalence of CKD and albuminuria as estimated by shuchi et al are 8.7 and 7.1% respectively in two major cities [3].Chronic kidney disease can result due to cardiovascular disease and diabetes, many possible explanation has been proposed. However a reduced estimated GFR was independent and strong risk factor for adverse CVD outcome, reduced kidney function, abnormal apolipopritein level, elevated plasma homocystein , enhanced coagulability, anaemia , left ventriclular hypertrophy, increased calcification, endothelial dysfunction and arterial stiffness are other causes. Whether and how these factor interact remain unclear [4].The CKD is also associated with Metabolic Bone Diseases, a systemic disorder of mineral and bone metabolism characterized by abnormalities of calcium, phosphorus, PTH, or vitamin D and abnormalities in bone histology, linear growth, or strength, or Vascular or other soft tissue calcification**.** Traditionally, such lesions have been defined according to alterations in bone turnover, ranging from high bone turnover (secondary hyperparathyroidism, osteitisfibrosa) to lesions of low bone turnover (adynamic bone disease and osteomalacia) [5].1,25-dihydroxyvitamin D (1,25 OH2 D3) deficiency is known to occur during the progression of CKD because the final hydroxylation step of 25-hydroxyvitamin D (25(OH)D3) to 1,25 OH2 D3 (calcitriol) is mediated by kidney 1a´-hydroxylase.[8] Calcitriol

deficiency plays a major role in the development of secondary hyperparathyroidism (HPTH), as 1,25 OH2 D3 deficiency promotes parathyroid gland growth (hyperplasia) and increased parathyroid hormone (PTH) synthesis through loss of the ability to up regulate vitamin D receptor expression within parathyroid cells[9]. The end result is elevated serum iPTH and abnormal calcium (Ca) and phosphorus (P) balance. The goal of our study is to assess the variation in PTH levels and vitamine D in various stages of CKD.

II. Material And Methods

A total of 158 Chronic Kidney Disease patients who were admitted in Nephrology department in the month January were recruited after taking informed consent. Patients with malignancy, chronic liver disease and infection were excluded. These cases were divided into 5 stages depending on eGFR value as stage I (n=13), stage II(n=18), stage III (n=17), stage IV (n=31), and stage V(n=79).The following investigations were done. Serum urea, creatinine, albumin, iPTH, 25(OH) D3, calcium and phosphorus are estimated. Serum creatinine was estimated by Jaffe's kinetic method on Siemens Dade Dimension analyzer. Serum urea was estimated by enzymatic kinetic UV assay. Calcium, phosphorus was estimated by Colorimetric assay with endpoint determination. iPTH, VITAMIN-D were determined by electrochemilumniscent immunoassay. eGFR calculated by MDRD 6-variable equation.

MDRD (6-variable): GFR (mL/min/1.73 m2) = 170X(S.Cr / 88.4) albumin0.318X (0.762,if F) (1.18, if African American) - 0.999X age- 0.176X (SU X 2.78) - 0.17 X.

III. Results

The study comprises of 158 CKD cases which are divided into 5 groups based on eGFR. The study population comprised 93 men and 65 women with a mean age of 68 years. Table 1 depict the demographics of patients population with mean and standard deviation in different stages of CKD.

Table 1 : Baseline demographic according to stages

Variables	Group I Stage I	Group II Stage II	Group III Stage III	Group IV Stage IV	Group V Stage V	P-Value
Number of patients	13	18	17	31	79	-
Age(years)	40.53±10.3	41.23±9.23	44.12±15.12	53.96±13.48	47.79±15.18	-
Male	8	11	13	18	43	-
Female	5	7	4	13	36	-
Blood Urea(mg/dl)	38.12±14.1	39.63±11.2	40.12±18.16	89.41±54.28	128.62±62.55	<0.001
Creatinine(mg/dl)	1.23±0.12	1.53±0.24	1.67±0.35	3.07±0.66	8.29±3.79	<0.08
Calcium(mg/dl)	8.76±0.76	8.67±0.56	8.56±0.85	7.89±0.77	8.86±9.22	0.8
Phosphorus(mg/dl)	2.67±0.91	3.08±1.2	3.89±1.51	5.08±2.06	5.8±2.4	<0.006
Albumin(gm/dl)	3.75±0.23	3.66±0.9	3.62±0.53	3.17±0.62	3.21±0.88	0.7
Vitamin D(ng/ml)	18±13.45	23± 18.97	30.98±26.45	31.86±22.87	32.2±29.29	0.9
iPTH(pg/ml)	14.3±7.8	13.87±9.87	10.3±11.67	20.56±25.36	111.8±182.2	<0.002
eGFR	90±7.8	56.8±6.7	42.71±7.65	18.56±3.66	7.5±3.18	<0.001

CKD classification based on eGFR according to guidelines of the National Kidney Foundation

In CKD stages I, II, III, IV and V Mean±SD values of serum iPTH(pg/ml) levels are14.3±7.8, 13.87±9.87, 10.3±11.6, 20.5±25.4, 111.8±182.3 (P=0.002), Calcium(mg/dl) levels are 8.8±0.7, 8.6±0.5,8.6±0.8, 7.9±0.8, 8.9±9.2 (P=0.8), Phosphorus(mg/dl) levels are2.67±0.91, 3.08±1.2, 3.8±1.5, 5.0±2.0, 5.8±2.4 (P=0.006), 25(OH)D3(ng/ml) levels are18±13.45, 23± 18.97, 40±26.4, 31.9±22.9, 32.2±29.3 (P=0.9) respectively. Statistical significant difference is found with urea, creatinine, eGFR, phosphorus and iPTH but not with VIT-D, calcium among different stages of CKD.

Data was analysed on Medcal using ANOVA, student 't' test and pearson's correlation. On pearson's correlation, the concentrations of phosphorus(r=-0.28) is negatively correlated where asiPTH (r=0.33), and 25(OH)D3(r=0.035) are positively correlated with eGFR. Statistically significant correlation was found with iPTH (p=0.014) and phosphorus (p=<0.001)

(Fig 1and 2) .

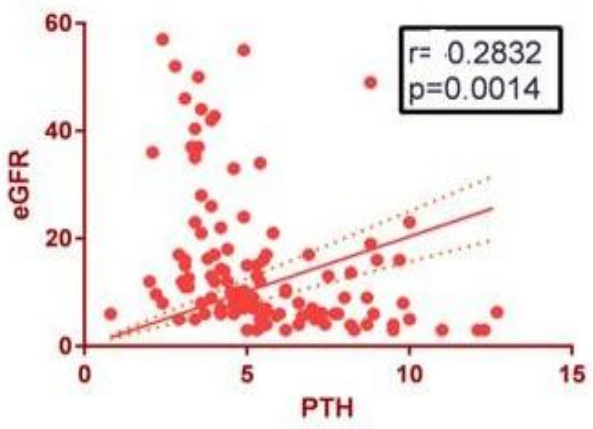

Figure 1 : Correlation between eGFR and PTH

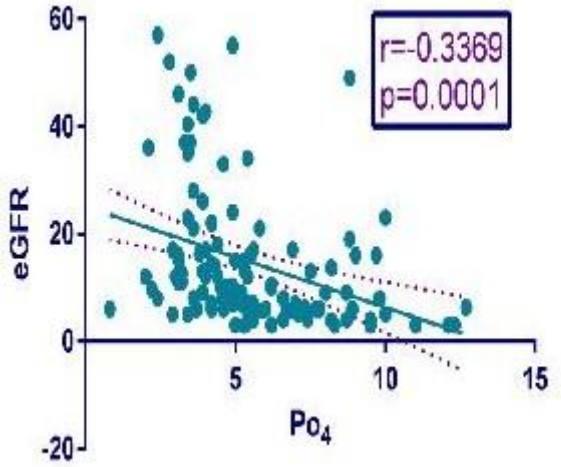

Figure 2 : Correlation between Phosphorus and eGFR

IV. Discussion

In this study a total of 158 cases of CKD were and classified into 5 groups based on eGFR values. Males are found to be more effected than females.No statistical significance was found between total calcium, Albumin and Vitamin D between different groups. This is in accordance with the results shown by Kavan et al, and schiefka et al The mean Vitamin D levels in all groups are above 30, which are above the deficiency levels this can be explained as all the patients are under treatment and are receiving vitamin D supplementation. Statistically significant difference was found between phosphorous and PTH among different groups these results are in agreement with SriharshaDamera, Kalani L. Raphael 2011[9] 6 . In this study, Serum phosphorus showed a statistically significant correlation with eGFR. When GFR falls, the phosphorus clearance decreases significantly, leading to phosphorus retention. Phosphorus induces PTH secretion by 3 mechanisms

1.**Direct stimulatory effect**
2.Induction of mild hypocalcemia by precipitation with calcium ions CaHPO4
3.Stimulation of FGF 23 which leads to sever inhibition of 1 α hydroxylase and depressed level of 1,25dihydroxyvitamin D, the down regulation of the vitamin D receptors on the PTH gland leads to Vitamin D resistance [7]. Elevated PTH is known to cause cardiomyocyte damage in animals with CKD and

parathyroidectomy in dialysis patients is associated with reductions in left ventricular hypertrophy and in cardiovascular mortality. Thus, taken together we may speculate that low 1,25 OH2 D3 and elevated iPTH levels in CKD stage 3 and 4 may contribute to the high prevalence of cardiovascular and advanced renal disease seen in these populations[8,9,10].Secondary hyperparathyroidism is a very early disease and its diagnosis and treatment is crucial in the management of patients with CKD. Levin et al demonstrated that the PTH starts to increase as early as the beginning of CKD stage III (estimated GFR, _60 mL/min), along with normal levels of serum calcium and phosphorus [11].CKD-MBD refers to the changes in bone, and it is a multifactorial disorder resulting from abnormalities in mineral metabolism, which include vitamin and calcitriol deficiency, hyperparathyroidism, disordered phosphate and calcium metabolism ,and elevated fibroblastic growth factor 23 (FGF23) [12]**.** Historically, the four major types of bone disease that occur in CKD are osteitisfibrosacystica, low turnover or adynamic bone disease, mixed uremic osteodystrophy(MUO), and osteomalacia [13]. Hyperparathyroidism that develops relatively early in CKD is the major driving force in the development of osteitisfibrosa [14].Early intervention and supplementation of Vit D is helpful in mitigating the harmful effect of Increased PTH. Our study shows importance of the determination of PTH and phosphorus for early detection of SecandaryHyperParathyroidism(SHPT) [15].

V. Conclusion

iPTH level are increased earlier than other bone markers. So early screening of CKD patients with serum iIPTHlevels helps in early detection and intervention of SHPT which reduces considerable mortality and morbidity.

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