



Original Research Article

Prevalence and Pattern of Mineral Bone Disorder in Chronic Kidney Disease Patients Using Serum Levels of Alkaline Phosphatase, 25-Hydroxy Vitamin D and Parathormone

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ABSTRACT

Background: Chronic kidney disease (CKD) is a global health problem affecting 5-10% of the world population. Changes occur in serum and tissue concentrations of alkaline phosphatase, 25-hydroxy vitamin D and parathormone levels in CKD, leading to pathological changes in bones.

Objectives: To study the prevalence of mineral bone disorder (MBD) in CKD stage 3 to stage 5D patients using alkaline phosphatase, 25-hydroxy vitamin D & parathormone (PTH) levels as parameters; & to correlate the biochemical abnormalities with clinical disease.

Methods: Study was conducted between May 2011 to Dec 2012 at IPGMER & SSKM hospital, Kolkata in 190 patients with CKD stages 3-5D. In all patients, serum levels of alkaline phosphatase, 25-hydroxy vitamin D & parathormone levels were estimated and correlated clinically.

Results: 70% patients had abnormal levels of parathormone and vitamin D deficiency. 56% patients had elevated alkaline phosphatase levels. Parathormone and alkaline phosphatase levels correlated with each other.

Keywords: Chronic kidney disease, Alkaline phosphatase, Parathormone, 25-hydroxy vitamin D.

INTRODUCTION

Chronic kidney disease (CKD) is an international public health problem affecting 5-10% of the world population.^[1] As renal function declines, there is a progressive deterioration in mineral homeostasis, with a disruption of normal serum and tissue concentrations of phosphorus and calcium, and changes in circulating levels of parathyroid hormone (PTH), 25-hydroxyvitamin D (25(OH)D), 1,25-

dihydroxyvitamin D (1,25(OH)₂D) and other vitamin D metabolites, fibroblast growth factor-23 (FGF-23), and growth hormone.

In addition, there is evidence at the tissue level of a downregulation of vitamin D receptor and of resistance to the actions of PTH. The mineral and endocrine functions disrupted in CKD are critically important in the regulation of both initial bone formation (bone modelling), and bone structure and function during adulthood (bone

remodelling). As a result, bone abnormalities are found almost universally in patients with CKD requiring dialysis (stage 5D), and in the majority of patients with CKD stages 3-5. More recently, there has been an increasing concern of extraskeletal calcification that may result from the deranged mineral and bone metabolism of CKD and from the therapies used to correct these abnormalities.

All three of these processes i.e., abnormal mineral metabolism, abnormal bone, and extraskeletal calcification, are closely interrelated and together make a major contribution to the morbidity and mortality of patients with CKD.

Therapy is generally focused on correcting biochemical and hormonal abnormalities in an effort to limit their consequences.

Hence, this study was undertaken to study the prevalence & pattern of Parathormone (PTH), alkaline phosphatase(ALP) & vitamin-D(vit-D) in CKD stages 3to 5D.

MATERIALS AND METHODS

This study is a Prospective single centre study conducted in the department of nephrology, I.P.G.M.E.R & S.S.K.M Hospital, Kolkata.

Study period-May 2011 to Dec 2012.

All patients with CKD stage 3 to stage 5D attending OPD / admitted in nephrology ward were included in study.

Detailed history and physical examination was done with reference to bone pain, fractures, cardiovascular disease, and patients were subjected to following investigations:

- Intact Parathyroid hormone assay(Ipth)
- Total alkaline phosphatase
- 25-hydroxy vitamin-D levels

- Other routine investigations for kidney disease

Investigations:

1. iPTH-measured by 2site immunoradiometric assay (2nd generation assay).
Ckd3-5-normal range = reference limits of particular assay
Ckd5d-normal range =2 to 9times upper reference limit for assay
2. 25(OH)vitD-measured by radio immunoassay
Normal range >30ng/ml
3. Total alkaline phosphatase - Normal level \leq 250IU/L.

Inclusion criteria: All patients with proven CKD stage 3- stage 5D.

Exclusion criteria:

1. Patients suffering from systemic diseases like SLE/RA,
2. Patients on steroids and other drugs which have effect on bone
3. Patients with primary bone disease.

Statistical method:

Categorical variables are presented as distributions (i.e., frequencies and percentages).

RESULTS

190 patients with chronic kidney disease stage 3 to stage 5D were tested for evidence of mineral bone disorder. Out of these, two thirds were males and one third was females. Majority of patients were middle aged. 47% patients were diabetic and 84% patients had hypertension.

CKD Stage 3:

In this stage, 53.3% patients had normal iPTH levels whereas; in significant number (46.7%) of patients ipth was elevated above range. Total alkaline phosphatase levels were within normal range in all patients. 25 hydroxy vitamin-D levels were below normal in 60% patients.

Table 1: Baseline characteristics.

Parameters		Number(n=190)	Percent(%)
Age(years)	20-40years	42	22.1
	41-60years	95	50.5
	61-80years	53	27.9
Sex	Male	128	67.4
	Female	62	32.6

Table 2 : Distribution of cases according to serum ipth levels in CKD stages 3 to 5D.

CKD stages		Intact PTH levels			Total
		Below normal	Normal	Above normal	
CKD stage 3	No.	0	16	14	30
	%	0%	53.3%	46.7%	100%
CKD stage 4	No.	0	18	40	58
	%	0%	31.0%	69.0%	100%
CKD stage 5	No.	3	3	64	70
	%	4.3%	4.3%	91.4%	100%
CKDstage 5D	No.	12	6	14	32
	%	37.5%	18.8%	43.8%	100%
Total	No.	15	43	132	190
	%	7.9%	22.6%	69.5%	100%

Table 3 : Distribution of cases according to serum alkaline phosphatase levels in CKD stages 3 to 5D.

CKD stages		Alkaline phosphatase levels(IU/L)		Total
		≤250	>250	
CKD stage 3	No.	30	0	30
	%	100%	0%	100%
CKD stage 4	No.	52	6	58
	%	89.7%	10.3%	100%
CKD stage 5	No.	42	28	70
	%	60.0%	40.0%	100%
CKDstage 5D	No.	14	18	32
	%	43.8%	56.3%	100%
Total	No.	138	52	190
	%	72.6%	27.4%	100%

Table 4 : Distribution of cases according to serum 25-hydroxy vitamin-D levels in CKD stages 3 to 5D.

CKD stages		25-hydroxy vitamin-D (ng/ml)			Total
		<15	15-30	>30	
CKD stage 3	No.	6	12	12	30
	%	20.0%	40.0%	40.0%	100%
CKD stage 4	No.	15	25	18	58
	%	25.9%	43.1%	31.0%	100%
CKD stage 5	No.	28	28	14	70
	%	40.0%	40.0%	20.0%	100%
CKDstage 5D	No.	8	17	7	32
	%	25.0%	53.1%	21.9%	100%
Total	No.	57	82	51	190
	%	30.0%	43.2%	26.8%	100%

CKD Stage 4: Out of 190 patients, 69% patients had ipth above normal range and in only 31% patients ipth was normal. Total alkaline phosphatase was within normal range in 90% patients and remaining 10% had high levels. 70% patients had low levels

of 25 hydroxyvitamin-D and rest had normal levels.

CKD Stage 5: ipth was normal in only 4.3% patients. 91% had high levels of ipth and in 4.3% patients it was below normal range. 40% patients had alkaline phosphatase above normal and in 60% it was normal. 25

hydroxy vitamin-D was low in 80% patients and in rest it was normal.

CKD Stage 5D: ipth was elevated in 44% patients and below normal in 37% patients. Only 19% patients had ipth in normal range. Total alkaline phosphatase was elevated in 56% patients and normal in 44% patients. 25-hydroxy vitamin-D was low in 78% patients.

DISCUSSION

It is now accepted that the presence of chronic kidney disease (CKD) is associated with poor outcomes.^[2-5] Recently, increased attention has been focused on endocrine abnormalities in patients with CKD as a way to explain some of these associations.^[6] Mineral bone disorder was common in our patients with CKD. Beginning in CKD stage 3, secondary hyperparathyroidism was the earliest change noted which was present in nearly half of patients. As CKD stage progressed, prevalence of hyperparathyroidism increased to involve more than 90% patients in CKD stage 5. Also the severity of hyperparathyroidism was more as CKD stage progressed. A dynamic bone disease as evident by low ipth levels was uncommon in nondialytic population but affected more than one third of patients on dialysis..

Total alkaline phosphatase levels correlated with serum ipth levels. In patients with normal or mildly elevated ipth levels, alkaline phosphatase remained normal. But in patients with very high ipth(>300pg/ml), alkaline phosphatase was uniformly elevated. Also the titre correlated with that of ipth.

VitaminD abnormalities were common in all CKD stages. 60-80% patients had low levels of 25 hydroxy vitaminD. 1,25-dihydroxyvitamin D deficiency is known to occur during the progression of CKD, because the final hydroxylation step of 25-hydroxyvitamin D to 25(OH)₂D to

1,25(OH)₂D is mediated by kidney 1 α -hydroxylase.^[7] Severity of deficiency did not correlate with CKD stage or other mineral abnormalities.

The prevalence of deficiency of 25(OH)D₃ remained stable until stage 5 & appears to be dissociated from the HPTH prevalence. Levin A et al. found that 49% patients with low 1,25 (OH)D₃ levels had high iPTH, irrespective of 25(OH)D₃ levels; whereas, only 35% of those with low 25(OH)D₃ levels had high iPTH.^[2]

PTH testing is clearly more practical. These findings have implications for 1,25(OH)D₃ testing of individuals, given the biological relevance of that deficiency to HPTH, & the demonstration that low levels of 1,25(OH)D₃ occur earlier than does elevations in iPTH levels.^[2]

Although decreased renal 1 α -hydroxylase in CKD is largely responsible for reduced circulating levels of 1,25(OH)D₃, other potential factors may exist, which also suppress this hydroxylating enzyme.^[2,8] In addition, low levels of 25(OH)D₃ substrate may contribute to decreased levels of 1,25(OH)D₃ particularly in CKD patients with nephrotic range Proteinuria.^[2,9] One recent survey noted that 86% CKD patients had inadequate 25(OH)D₃ levels, which has been previously defined by others.^[2,10,11]

Interventional studies are needed to define the serum levels of 1,25(OH)D₃ that would provide adequate suppression of iPTH and subsequent potential untoward effects of mineral imbalances.^[2]

Literature on the prevalence of these multi center study found that, hyperparathyroidism presents early in CKD & worsens with progression of CKD stages. There is an increase in the prevalence of hyperparathyroidism from CKD stage 4. Hyperparathyroidism was present in 69% patients in CKD stage 4 & 91.4% patients in CKD stage 5 which was similar to Levin A et

al. study ^[2] in which 56% patients in CKD stage 4 had hyperparathyroidism.

Vitamin-D abnormalities were common in all stages of CKD. Additional data indicate that vitamin D treatment is an important factor that may mitigate the effects of HPTH & hyperphosphatemia on cardiovascular mortality.^[2,6]

CONCLUSION

Abnormalities of mineral bone metabolism are common in CKD patients. These abnormalities start in early CKD stages & worsen with disease progression. Hence, this shows the importance of early recognition, understanding of their pathophysiological consequences, & planning management strategies to prevent their progression. Thus, reducing the cardiovascular morbidity & mortality.

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