Prevalence of Mineral Bone Disease in Dialysis Patients.

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Abstract:

Objective

The objective of the study was to find out the prevalence of bone mineral disease in dialysis patients.

Background

Progressive loss of kidney function in chronic kidney disease (CKD) leads to reduced production of 1- α -(OH) $_2$ -D $_3$ (1,25-dihydroxyvitamin D; calcitriol) and abnormal mineral homeostasis leading to bone mineral disorders. The disorder starts with stage 2 CKD but manifests itself as the disease progresses until stage 3 CKD.

Material and methods

This study was carried out on 61 patients with end-stage renal disease on regular HD at our Centre. After obtaining informed consent, complete blood count, blood urea level, serum creatinine level, albumin level, uric acid level, Ca level, phosphate level, alkaline phosphatase level, and PTH level were done.

Results

Out of 60 patients 41 (68.33%) were high bone turnover, 10 (16.6%) were normal bone turnover whereas 9 (15%) were low bone turnover.

Conclusion

The prevalence of CKD-MBD among dialysis patients is 83.33% at our center and needs proper monitoring by routine investigations including serum phosphate, calcium, vitamin D levels and most importantly i-PTH levels according to guidelines.

Key Words: *Chronic kidney disease, CKD, mineral bone disease, hyperparathyroidism, hemodialysis, parathyroid hormone, calcium, phosphorus.*

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Introduction

The prevalence of chronic kidney disease (CKD) is estimated at 8% to 16% of the total world's population. CKD is associated with numerous morbidities and complications, one of which is mineral and bone disorder (CKD-MBD).¹ CKD-MBD is a complex systemic disease observed in patients with estimated glomerular filtration rates (eGFRs) of 60 mL/min or lower. Alterations in the control mechanisms for calcium and phosphorus homeostasis occur early in the course of CKD and progress as kidney function decreases.²

The disorder has three components:

1. Biochemical abnormalities in concentrations of calcium, phosphorus, parathyroid hormone (PTH), and 1,25-dihydroxyvitamin D $_3$ [1,25(OH) $_2$ D $_3$].
2. Abnormalities in bone, including turnover, mineralization, and volume, and or decreased linear growth and strength.
3. Extra skeletal calcification.³

Pathophysiology

In normally functioning kidneys, about 90% of plasma phosphate is filtered and excreted. However, in patients with CKD, disorders that lead to CKD-MBD (including secondary hyperparathyroidism, hyperphosphatemia, decreased intestinal calcium absorption and

disordered vitamin D metabolism). It begins in stage 2 CKD but does not become clinically detectable until late stage 3 or early stage 4.⁴⁻⁶

Levels of i-PTH are regulated by a negative feedback loop with serum calcium levels. Low serum calcium stimulates the parathyroid glands to secrete i-PTH; high serum calcium inhibits PTH secretion. However, in patients with CKD, low calcium levels stimulate parathyroid gland to secrete PTH and osteocytes and osteoblasts secrete increased levels of fibroblast growth factor 23 (FGF23).⁷ FGF23 maintains normal serum phosphate levels by reducing phosphate reabsorption in the tubules. FGF23 also reduces phosphate absorption in the small intestine through decreased vitamin D (calcitriol) production.⁸ These mechanisms maintain normal serum calcium and phosphorus levels early in CKD, even as the patient's PTH level rises. The patient's serum calcium level generally remains within normal limits until GFR declines to less than 50 mL/min/1.73 m².^{8,9} These changes result into four types of histopathological patterns of bone disease as recognized in CKD 5:

Hyper parathyroid bone disease: High bone turnover disease that is attributed to untreated secondary hyperparathyroidism (SHPT). It is represented by bone anomalies such as cortical bone thinning and increased abnormal trabecular bone.

Adynamic bone disease: Absent or low bone resorption and formation and could be an early finding of CKD. It is often associated with low PTH level and the patients are more vulnerable to develop fractures.

Low turnover of bone with an increased unmineralized osteoid matrix that in turn will lead to decrease bone strength. It is often attributed to deficiency of vitamin D, metabolic acidosis and hypocalcemia.

Mixed renal osteodystrophy Combined mineralization defects and high bone turnover defects.¹⁰

These alterations in bone turnover contribute to decreased skeletal mechanical competence, which can result in fractures and diminished capacity to bear loads. The most common fractures are fragility fractures of the vertebrae, femoral neck of the hip, or the wrist (Colles fractures).¹¹ The other consequence of CKD-BMD is cardiovascular disease which is the leading cause of death in patients with CKD. Hyperphosphatemia has been shown to stimulate osteoblasts and vascular calcification, particularly of arteries and cardiac valves.¹

Monitoring Recommendation

KDOQI recommends beginning to monitor the metabolic abnormalities that accompany CKD-MBD in stage 3. To assess bone health without doing a biopsy, KDIGO recommends measuring serum PTH or bone-specific alkaline phosphatase.¹² Markedly high or low values of these parameters indicate the degree of bone turnover. In addition to evaluating bone with PTH level, clinicians must screen patients for biochemical abnormalities associated with secondary hyperparathyroidism, including hypocalcemia, hyperphosphatemia, and calcitriol level.¹²

The current study was conducted to assess the level and type of BMD at our maintenance hemodialysis unit.

Patients and Methods

This study was carried out on 60 patients with end-stage renal disease (ESRD) on regular HD in our dialysis center at Hijaz hospital. Informed consent was taken from all included patients. This study was done during the period from September to November 2019. The study excludes

patients having acute infections, connective tissue disease, malignancy, thyroid gland dysfunctions, recent myocardial infarction, recent trauma in preceding 6 months.

All studied patients were subjected to full history and laboratory investigations including serum albumin, total Ca level, serum phosphate level, serum alkaline phosphatase level, and serum i-PTH level. The diagnosis of MBD among the studied patients was made according to the following: suggestive MBD-related symptoms (bone pain, muscle weakness, and combination of both symptoms), and pathological fractures), and MBD-related laboratory indicators (serum PTH, serum Ca, serum phosphorus, and serum alkaline phosphatase levels).

The studied patients were divided into three groups according to serum PTH level:

1. **Low bone turnover:** PTH level below 150pg/ml.
2. **Normal bone turnover:**PTH level between 150 and 300 pg/ml.
3. **High bone turnover:** PTH level more than 300 pg/ml.

Results

The study revealed 50 (83.3%) patients with CKD-MBD. Out of total 60 patients 41 (68.33%) were high bone turnover and 10 (16.6%) were normal bone turnover whereas 9 (15%) were low bone turnover as shown in table 1

Table 1: Mineral Bone Disease types in 60 maintenance hemodialysis patients.

	Number of patients	Percentage
Total patients	60	100%
High bone turnover	41	68.33%
Normal bone turnover	10	16.6%
Low bone turnover	9	15%

The pattern of calcium and phosphate levels in three different patterns of bone disease is expressed in table 2.

Figure 1: Bar diagram showing the percentage of patients with different types of bone mineral disease

Discussion

The study revealed majority, 41(68.33%) patients with high bone turnover and 41 patients there were 29 (70.7%) who had hypocalcemia, 11 (26.8%) had normal calcium levels whereas only

one patient (2.4%) had borderline high calcium level. Phosphate levels in 35 (85.3%) of these 41 patients were high whereas 6 (14.7%) had normal levels. The reason for this can be that therapy with vitamin D was ineffective, and evaluation for the use of other vitamin D analogues and the possible need of surgical intervention of the parathyroid glands for tertiary hyperparathyroidism has to be considered. In the other group with high PTH and low serum Ca levels, the lack of vitamin D effectiveness could be either undertreatment with vitamin D or poor patient compliance.¹³

Table 2: serum calcium and phosphorus levels and type of mineral bone disease in 60 hemodialysis patients.

	Low bone turnover	High bone turnover	Normal bone turnover
Ca <8.5 8.5-9.5 >9.5	1	29	4
	6	11	6
	1	1	
PO4 <2.5 2.5-4.5 >4.5			1
	5	6	2
	4	35	1

The other group of low bone turnover had 6 patients (66.6%) had borderline high, 1 (16.6%) had high and (16.6%) had low serum calcium levels whereas phosphate in 4 patients (44.4%) was high n= 5 (66.6%) had normal levels. In this study, patients with low bone turnover disease had higher mean serum Ca level compared with the mean serum Ca levels in both the hyperparathyroid bone disease group and the patients with no laboratory evidence of bone disease. Most of these patients are using calcium supplements and high doses of vitamin D analogues without prescription (personal experience).

The nature and type of renal bone disease vary from one patient to another, and is multifactorial and the gold standard for diagnosis of renal bone disease is bone biopsy but its invasive nature as well as its cost and overall complexity has withdrawn it from the clinical practice.¹⁴ Hence, serum markers of bone turnover have been used to evaluate bone turnover in patients with CKD.¹⁵ Consequently, serum PTH level has taken the leading position among the noninvasive tools for assessing renal bone disease.¹⁶

Conclusion

The prevalence of CKD-BMD among dialysis patients was high in our study, majority being high turnover. Proper monitoring and management of BMD will lead to avoidance of complications associated with it.

Conflict of interest: None declared

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