Spectrum of Chronic Kidney Disease-Mineral Bone Disorders in Newly Detected Advanced Renal Failure Elderly Patients (CKD Stage 4 and 5)

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ABSTRACT

Introduction*:* CKD MBD remains a complex issue in elderly patients that has yet to be clearly defined. We aimed to evaluate the disturbances in mineral bone disease in newly detected, untreated stage 4 and 5 elderly chronic kidney disease patients.

Material and Methods: A cross-sectional observational study with total of 93 newly detected patients underwent clinical evaluation, biochemical assessment [serum albumin, calcium, intact parathyroid hormone(iPTH), 25- hydroxyvitamin D, phosphorus, alkaline phosphatase(ALP), creatinine], BMD measurement by dual-energy X-ray absorptiometry(DXA) and Lateral Abdominal X ray for aortic calcification(AAC).

Results: Symptoms related to CKD-mineral bone disorder were seen in 33.6% of the study patients. Prevalence of hypocalcemia, hyperphosphatemia, hyperparathyroidism, and hypovitaminosis D were 64.2%, 81.1%, 49.5%, and 89.5%, respectively. Prevalence and severity of hyperphosphatemia, hyperparathyroidism, hypocalcemia and raised ALP increases from stage 4 to stage 5 CKD, while hypovaitaminosis D is equally prevalent in both stages. Secondary hyperparathyroidism is most common form of CKD MBD in untreated elderly CKD population. BMD by DXA showed a low bone mass in 26.81% of our patients at distal forearm. Patients older than 75 years more commonly had osteoporosis, lower ALP, phosphorus and iPTH. AAC was seen in 13.98% of study group. Patients with AAC had higher phosphorus, iPTH and ALP. Compared to non diabetic CKD patients, lower levels of phosphorus, ALP and iPTH were observed in diabetic CKD patients.

Conclusion: Our study shows CKD MBD is prevalent in elderly population where symptoms alone are not enough to diagnose the bone disease.

Keywords: Diabetic Kidney Disease, Secondary Hyperparathyroidism, Predialysis CKD, Bone Mineral Density, Abdominal Aorta Calcification, Hypovitaminosis D, Hypocalcemia, Hyperphosphatemia.

INTRODUCTION

Chronic kidney disease (CKD) is an important public health issue with its incidence varying between 5-10% of population.[1,2] Bone and mineral disorders constitute an important factor in morbidity and mortality of elderly CKD patients[3] Bone and mineral metabolism differ in younger and older individuals due to their differences in dietary habits leading to lower protein, phosphorus and calcium intake in older patients. Elderly patients also have lower physical activity and bone turnover.[4] Evaluation of bone health is required for correctly predicting risk of fracture, for appropriate management of abnormal mineral metabolism, and for making decision regarding treatment of osteoporosis including type of therapy required. Many of the processes involved in the initiation and continuation of the derangements of bone and mineral metabolism have been identified and are being successfully utilized in clinical management of these patients.[5] As elderly patients with CKD have age related bone loss similar to general population and in addition to that they have mineral and bone disorders secondary to reduced renal function resulting in bone disease where traditional approach for management of bone health alone are not sufficient. With the increasing average age of population and ever increasing prevalence of CKD in the elderly, a detailed understanding of these processes is essential for making better treatment choices available for these patients.

CKD related disorders of mineral and bone metabolism are defined by any one or a combination of the following: (1) Abnormalities of metabolism of calcium, phosphorus, parathyroid hormone (PTH), or vitamin D (2) abnormalities of bone turnover, mineralization, volume, linear growth, and strength and (3) any vascular or extraskeletal calcification.[6]

In addition to above factors, other concomitant pathological conditions affecting mineral metabolism or bone health may further complicate the situation such as the adverse effects of medications, postmenopausal osteoporosis etc.

So study aimed to evaluate the disturbances in mineral bone disease in newly detected, untreated stage 4 and 5 elderly chronic kidney disease patients.

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MATERIAL AND METHODS

This was a prospective, observational study carried over a period of 1 year on elderly patients of 60 years and above who had newly detected, untreated, predialysis stable CKD stage 4 and 5 (KDIGO CKD staging[7]) attending the nephrology outpatient department between February 2017 and January 2018.

Exclusion criteria for excluding patients from the study were: (i) CKD Stage 3 and less (ii) Patients on treatment taking medicines containing calcium, oral phosphate binders (calcium or non calcium based), calcitriol, cholecalciferol or Vitamin D analogs; (iii) Patients on medications interfering with bone metabolism including corticosteroids, teriparatide, bisphosphonate, anti cancer drugs, anti seizure drugs etc.; (iv) Patients with rheumatologic diseases involving musculoskeletal system like seronegative spondyloarthritis, rheumatoid arthritis and primary diseases of parathyroid gland; (v) Patients with significant hepatic disorders or recent history of fracture in last six months; and (vi) Age less than 60 years at presentation. Institute ethical committee approved this work.

All patients underwent detailed clinical evaluation which included demographic profile, history of personnel habits of smoking and alcohol consumption, associated co-morbidities including hypertension (HTN), diabetes mellitus (DM), and underlying etiology of kidney disease (proven or presumed). Clinical examination was done and following parameters were noted: Blood pressure by manual sphygmomanometer, anthropometric measurements [height, weight, and body mass index (BMI)], any bone deformity if present, and assessment for any muscle weakness. CKD EPI equation was used for the estimation of glomerular filtration rate.[8]

Biochemistry Markers of CKD-MBD, namely serum total calcium, phosphorus, alkaline phosphatase, intact parathyroid hormone (iPTH), and 25-hydoxyvitamin Vitamin D3 (25OHD) were measured. Routine baseline blood investigations including hemoglobin estimation, serum albumin, serum creatinine, BUN and lipid profile were done. In presence of hypoalbuminemia, corrected calcium (cCa) concentration was calculated as per standard guidelines.

The standard definitions for defining abnormal levels of various biochemical parameters like hypocalcemia (cCa < 8.5 mg/dl), hypercalcemia (cCa >10.5 mg/dl), hyperphosphatemia (phosphorus >4.5 mg/dl), hypophosphatemia (phosphorus <2.5 mg/dl), elevated alkaline phosphatase level (>120 IU/L), hyperparathyroidism (iPTH >65 pg/ml), and Vitamin D insufficiency (25OHD level of <30 nmol/l) were used.

Intact PTH levels falling outside the target range suggested by the KDOQI guidelines were further divided in categories as 65 pg/ml -150 pg/ml,150 pg/ml -300 pg/ml or more than 300 pg/ml.[20] Serum vitamin D levels were further interpret erred, using cut off points of <30, and <15 nmol/l for defining insufficient and deficient levels, respectively.[9,10]

Plasma iPTH was measured using Architect i 1000SR chemiluminescent enzyme labeled immunometric assay and Plasma 25OH Vitamin D (25OHD) assay was done using the chemiluminescence assay.

BMD_was measured by dual-energy X-ray absorptiometry at four sites namely: the distal forearm (distal 1/3rd radius), lumbar spine (L1–L4), hip and neck of femur. The BMD was reported as T-score and Z-scores. Osteoporosis was defined using World Health Organization's (WHO) diagnostic criteria as T-score equal to or less than minus 2.5 either at the lumbar spine (L1–L4), hip, femoral neck, or distal forearm) and osteopenia was defined as T-score between −1 and −2.5 at above sites.[11]

Lateral abdominal X-ray

Lateral abdominal X-ray were done as per KDIGO guidelines

Variable	All (*n* = 93)	CKD stage-4 (*n* = 56)	CKD stage-5 (*n* = 37)	P
Age (years)	69.2±6.8	71.3±7.2	68.4±5.9	0.5
60-75 years	58(62.37%)	35(62.50%)	23(62.16%)	.17
>75 years	35(37.63%)	21(37.50%)	14(37.84%)	.24
Gender – Males	65(69.89%)	39(69.64%)	26(70.27%)	.6
Native kidney disease				.36
Diabetic kidney disease	37(39.78%)	23(41.07%)	14(37.84%)	
CGN	20(21.50%)	12(21.43%)	8(21.62%)	
Hypertensive nephrosclerosis	14(15.05%)	10(17.86%)	4(10.81%)	
CIN	11(11.83%)	7(12.50%)	4(10.81%)	
ADPKD	3(3.23%)	2(3.57%)	1(2.7%)	
Miscellaneous/unknown	8(8.60%)	5(8.93%)	3(8.10%)	
DM	42(45.16%)	25(44.64%)	17(45.74%)	.63
HTN	76(81.72%)	43(76.78%)	33(89.19%)	.59
BMI	21.6±3.2	22.3±3.6	18.4±2.9	.09
Smoking	14(15.05%)	10(17.86%)	4(10.81%)	.34
Alcohol intake	6(6.45%)	4(7.14%)	2(5.45%)	.42
Vegetarian diet	64(68.81%)	38(67.86%)	26(70.27%)	.82

CKD: Chronic kidney disease, n: Number of patients, CGN: Chronic glomerulonephritis, CIN: Chronic interstitial nephritis, ADPKD: Autosomal dominant polycystic kidney disease, DM: Diabetes mellitus, HTN: Hypertension, BMI: Body mass index.

Table-1. Baseline characteristics of the study patients.

Parameters	All N=93	CKD stage 4 N=56	CKD stage 5 N=37	P value
Hb (g/dL)	8.3±1.7	9.1±2.1	7.9±1.6	.07
BUN (mg/dL)	78.4±9.8	64±10.6	94±12.3	.003
S.Cr (mg/dL)	5.2±1.1	4.3±0.9	6.4±1.2	.005
eGFR (mL/min/1.73 m2)	16.9±4.8	22.6±6.4	10.3±2.5	<.001
Symptoms	36(38.70%)	20(35.71%)	16(43.24%)	.09
S. Ca (mg/dL)	8.2±0.9	8.7±1.1	7.5±.89	.001
Range				
<8.5	31(33.33%)	14(25%)	17(45.95%)	
8.5–10.5	62(66.67%)	42(75%)	20(54.05%)	
>10.5	0	0	0	
S. phosphate (mg/dL)	5.3±2.1	5.1±1.9	6.4±2.6	.006
Range				
<2.5	0	0	0	
2.5–4.5	38(40.86%)	30(53.57%)	8(21.62%)	
>4.5	55(59.14%)	26(46.43%)	29(78.38%)	
iPTH (pg/mL)	317±128	231±64	456±208	<.001
Range				
<65	21(22.58%)	15(26.79%)	6(16.22%)	
65-150	39(41.94%)	29(51.79%)	10(27.03%)	
>150	33(35.48%)	12(21.43%)	21(56.76%)	
25(OH)D (ng/mL)	21.6±8.1	24.6±8.6	19.7±10.2	.84
Range				
<15	41(44.09%)	23(41.07%)	18(48.64%)	
15-30	35(37.63%)	22(39.29%)	13(35.14%)	
>30	17(18.28%)	11(19.64%)	6(16.22%)	
S. ALP (IU/L)	179±78	162±39	242±104	.001
Range				
<120	46(49.46%)	34(60.71%)	12(32.43%)	
>120	47(50.53%)	22(39.29%)	25(67.57%)	
S. Chol (mg/dL)	174±44	186±38	164±45.1	.56
S. TG (mg/dL)	216±56	206±48	228±53	.35
S. HDL (mg/dL)	32.4±8.4	34±6.5	30.7±7.7	.17
S. LDL (mg/dL)	124±24	117±45	134±36	.38
S. albumin (g/dL)	2.9±0.8	3.1±1.1	2.8±0.6	.46
BMD (T score≤ -2.5)				.28
Lumbar vertebrae	13(13.98%)	8(14.29%)	5(13.51%)	
Total Hip	8(8.60%)	5(8.77%)	3(8.11%)	
Neck of femur	20(21.51%)	9(16.07%)	11(29.73%)	
Distal forearm	25(26.81%)	13(23.21%)	12(32.43%)	
Abdominal Aorta calcification	13(13.98%)	6(10.71%)	7(18.92%)	

Hb: Hemoglobin, BUN: Blood urea nitrogen, SCr: Serum creatinine, eGFR: Estimated glomerular filtration rate by abbreviated MDRD equation, S. cCa: Serum corrected calcium, iPTH: Intact parathyroid hormone, 25(OH)D: 25 hydroxy Vitamin D, ALP: Alkaline phosphatase, S. Chol: serum cholesterol, S. TG: Serum triglycerides, S. HDL: Serum high-density lipoprotein, S. LDL: Serum low-density lipoprotein.

Table-2: Laboratory parameters

for detection of abdominal aorta calcification (AAC) as a marker of extraskeletal (vascular) calcification. Identified calcific lesions were further graded using the index given by Kauppila et al.[12]

RESULTS

The study population consisted of 93 patients with a mean age of 69.2 ± 6.8 years and male to female ratio of 2.3:1 (Table 1). All of them were Elderly with newly detected CKD in pre dialysis stage 4 and 5. DM and HTN were seen in 45.2% and 81.7% of patients respectively. Symptoms related to CKD-MBD were seen in 38.7% of patients (35.71% in CKD-4 and 43.24% in CKD-5). Bone pains and myalgia were the most common CKD MBD symptoms noted in this study. Symptoms were more commonly observed in CKD stage 5 compared to CKD stage 4 but did not reached significant p value.

Patients were compared in CKD stage 4 with CKD stage 5 (Table 2). Fifty six (60.21%) patients were in CKD stage 4 and 37 (39.79%) patients were in stage 5. The most common etiology for kidney diseases were diabetic kidney disease (39.78%),chronic glomerulonephritis (21.5%), hypertensive

Parameters	All N=93	Age (60-75yrs) N=58	Age (> 75 yrs) N=35	P value
Mean Age	69.2±6.8	63.8±7.2	78.5±5.3	.001
DM	42(45.16%)	28(48.27%)	14(40.0%)	.34
HTN	76(81.72%)	47(81.03%)	29(82.85%)	.58
SYMPTOMS	36(38.70%)	21(36.20%)	15(42.86%)	.12
CKD stage 4	56(60.21%)	34(58.62%)	22(62.86%)	.65
CKD stage 5	37(39.78%)	24(41.38%)	13(37.14%)	.17
BMI (kg/m2)	21.6±3.2	22.8±2.6	20.9±3.1	.09
Smoking	14(15.05%)	8(13.79%)	6(17.14%)	.61
Alcohol intake	6(6.45%)	4(6.89%)	2(5.71%)	.23
Hb (g/dL)	8.3±1.7	8.6±2.1	7.9±2.3	.08
BUN (mg/dL)	78.4±9.8	80.4±12.4	72.5±6.4	.52
S.Cr (mg/dL)	5.2±1.1	5.6±.7	5.1±.89	.74
eGFR (mL/min/1.73 m2)	16.9±4.8	18.2±6.1	15.7±5.4	.49
S. cCa (mg/dL)	8.2±0.9	8.1±1.1	8.3±.74	.22
S. phosphate (mg/dL)	5.3±2.1	5.9±2.4	4.9±1.8	.006
iPTH (pg/mL)	317±128	345.32±94.2	265±78.4	.001
25(OH)D (ng/mL)	21.6±8.1	19.7±7.8	24.5±11.4	
S. ALP (IU/L)	179±78	212.6±56	168±84.2	.005
S. Chol (mg/dL)	174±44	178±34	186±42	.94
S. TG (mg/dL)	216±56	234±53	208±42	.58
S. HDL (mg/dL)	32.4±8.4	30.5±9.4	34.2±7.9	.63
S. LDL (mg/dL)	124±24	114±20	131±29	.27
S. albumin (g/dL)	2.9±0.8	3.0±.9	2.8±.84	.15
BMD (T score≤ -2.5)				
Lumbar vertebrae	13(13.98%)	8(13.79%)	5(14.29%)	.31
Total Hip	8(8.60%)	5(8.62%)	3(8.57%)	.47
Neck of femur	20(21.51%)	10(17.24%)	10(28.57%)	.009
Distal forearm	25(26.81%)	13(22.41%)	12(34.29%)	.003

DM: Diabetes mellitus, HTN: Hypertension, CKD: Chronic kidney disease, BMI: Body mass index, Hb: Hemoglobin, BUN: Blood urea nitrogen, SCr: Serum creatinine, eGFR: Estimated glomerular filtration rate by abbreviated MDRD equation, S. cCa: Serum corrected calcium, iPTH: Intact parathyroid hormone, 25(OH)D: 25 hydroxy Vitamin D, ALP: Alkaline phosphatase, S. Chol: serum cholesterol, S. TG: Serum triglycerides, S. HDL: Serum high-density lipoprotein, S. LDL: Serum low-density lipoprotein, BMD – Bone mass density

Table-3: Laboratory parameters comparing different age groups

nephrosclerosis (15.0%), chronic interstitial nephritis ((11.83%)) and there was no significant differences in baseline characteristics between CKD stage 4 and 5 patients (Table 1).

The most common MBD in CKD stage 4 was secondary hyperparathyroidism (73.21%) followed by hyperphosphatemia (46.43%), raised ALP level (39.29%), and hypocalcemia (25.0%). In CKD stage 5, the most common MBD was secondary hyperparathyroidism (83.78%) followed by hyperphosphatemia (78.38%), elevated ALP level (67.57%), and hypocalcemia (45.95%). CKD biochemical mineral disorder were prevalent in both CKD stages 4 and 5 and prevalence of hyperparathyroidism, hyperphosphatemia, hypocalcemia and elevated ALP increases from CKD stage 4 to stage 5.

Multiple parameters which can affect serum iPTH were assessed. Patients with severe secondary hyperparathyroidism (iPTH >300 pg/mL) were more likely to have lower eGFR, hyperphosphatemia, hypocalcemia and high ALP.

Vitamin D insufficiency was the most common disorder of mineral metabolism seen in overall study group. Vitamin D insufficiency was equally common in CKD stage 4 and 5. Osteoporosis was more common in CKD stage 5 but it did not reached significant p value.

Comparison of patients in age group 60 to 75 years (62.36%) was done with those older than 75 years (37.63%) (Table 3). Both groups were comparable in terms of prevalence of Diabetes, Hypertension, smoking, alcohol intake, CKD stage 4, CKD stage 5, mean Hemoglobin, eGFR, S.creatinine, s.calcium and lipid profile. Patients older than 75yrs had significantly lower levels of serum phosphate (4.9±1.8 vs 5.9±2.4), iPTH (265±78.4 vs 345.32±94.2) and ALP (168±84.2 vs 212.6±56). Osteoporosis (BMD T score less than 2.5) at neck of femur (28.57% vs 17.24%) and distal forearm (34.29% vs 22.41%) was more common in patients older than 75 years while BMD was not significantly different at lumbar spine and hip.

Comparison of demographic and laboratory parameters in diabetic CKD (45.16%) and non-diabetic CKD (54.84%) patients was done (Table 4). Both group were similar in mean age, eGFR, S.creatinine, BUN, Hemoglobin, S.calcium, lipid profile, Hypertension, CKD stage 4 and

Parameters	All N=93	Diabetic N= 42	Non Diabetic N=51	P value
Age	69.2±6.8	68.7±8.2	70.4±5.9	.45
HTN	76(81.72%)	34(80.95%)	42(82.35%)	.92
SYMPTOMS	36(38.70%)	17(40.48%)	19(37.26%)	.64
BMI (kg/m2)	21.6±3.2	22.3±2.8	20.6±3.4	.08
CKD stage 4	56(60.21%)	25(59.52%)	31(60.78%)	.51
CKD stage 5	37(39.78%)	17(40.47%)	20(39.22%)	.37
Smoking	14(15.05%)	7(16.67%)	7(13.73%)	.26
Alcohol intake	6(6.45%)	3(7.14%)	3(5.88%)	.17
Hb (g/dL)	8.3±1.7	8.1±1.9	8.5±1.4	.72
BUN (mg/dL)	78.4±9.8	72.9±7.8	80.4±12.4	.84
S.Cr (mg/dL)	5.2±1.1	5.6±1.3	5.05±.78	.23
eGFR (mL/min/1.73 m2)	16.9±4.8	14.6±5.3	17.4±3.8	.42
S. cCa (mg/dL)	8.2±0.9	8.6±1.3	8.1±1.1	.86
S. phosphate (mg/dL)	5.3±2.1	4.8±1.6	5.6±1.3	.008
iPTH (pg/mL)	317±128	243±89	354±139	.003
25(OH)D (ng/mL)	21.6±8.1	20.9±7.3	22.4±9.2	.55
S. ALP (IU/L)	179±78	145±69	216±86	.001
S. Chol (mg/dL)	174±44	177±39	173±47	.32
S. TG (mg/dL)	216±56	206±52	218±59	.39
S. HDL (mg/dL)	32.4±8.4	30.8±6.1	33.2±8.7	.45
S. LDL (mg/dL)	124±24	129±33	123±21	.28
S. albumin (g/dL)	2.9±0.8	2.8±.74	2.9±.84	.41
Abdominal aorta cacification	13(13.98%)	7(16.67%)	6(11.76%)	.19

HTN: Hypertension, BMI: Body mass index, CKD: Chronic kidney disease, Hb: Hemoglobin, BUN: Blood urea nitrogen, SCr: Serum creatinine, eGFR: Estimated glomerular filtration rate by abbreviated MDRD equation, S. Ca: Serum corrected calcium, iPTH: Intact parathyroid hormone, 25(OH)D: 25 hydroxy Vitamin D, ALP: Alkaline phosphatase, S. Chol: serum cholesterol, S. TG: Serum triglycerides, S. HDL: Serum high-density lipoprotein, S. LDL: Serum low-density lipoprotein, BMD – Bone mass density

Table-4: Laboratory parameters comparing Diabetic pts with Non Diabetic pts.

5, history of smoking and alcohol intake. Diabetic patients had higher BMI (22.3±2.8 vs 20.6±3.4) but it did not reached significant p value. Patients with diabetes mellitus (n=42) had significantly lower serum phosphate (4.8±1.6 vs 5.6±1.3), ALP (145±69 vs 216±86), and iPTH (243±89 vs 354±139) levels as compared with patients without diabetes mellitus (n=51).

Abdominal aorta calcification (AAC) was seen in 13.98% of the total patients. It affected 10.71% and 18.92% of CKD 4 and 5 patients, respectively. Patients with AAC had higher levels of serum phosphorus, iPTH and ALP compared to patients without AAC. There was a non significant trend towards higher prevalence of DM in patients with AAC.

Osteoporosis (BMD T score less than -2.5) was seen in 13.98% at Lumbar vertebrae, 8.60% at total hip, 21.51% at neck of femur, and 26.81% at distal forearm. Patients with lower BMD scores had more severe secondary hyperparathyroidism, higher ALP levels and lower eGFR.

DISCUSSION

Derangements of bone mineral metabolism are frequent in patients with CKD. CKD is becoming increasingly prevalent in elderly population predisposing them to complications of bone mineral disorder resulting in high morbidity. Metabolic bone disease cannot be ruled out only on the absence of clinical signs and symptoms, and correction of underlying derangements is necessary for reduction in disease burden.

As there is scarcity of data in elderly Indian pre dialysis CKD patients on prevalence and characteristics of CKD MBD, our study provides important insight for proper management of these patients.

We observed that in our study male patient's outnumbered female patients as seen in most studies on CKD population in India. Among studies available from India, Praveen et al[13] and Agarwal et al.[14] (community based) have shown a male predominance. One of the main reasons for these differences in the gender may be bias in seeking treatment.[15]

In 61.3% of patients, no symptoms of mineral bone disorders were present; signifying that CKD related mineral bone disorders can be asymptomatic. Hypertension followed by diabetes mellitus is most frequently present co-morbidity. High prevalence of vitamin D insufficiency, hyperphophatemia, hypocalcemia and secondary hyperparathyroidism were observed in this study similar to previous hospital based surveys on CKD-MBD in India.[13,14] In their study Praveen kumar Etta et al reported hypocalcemia, hyperphosphatemia, hyperparathyroidism, and hypovitaminosis D in 64.2%, 81.1%, 49.5%, and 89.5%, of their patients.[13] Similarly high prevalence of CKD MBD was reported by Jabbar et al[16] and they found hyperparathyroidism in 60% of their study population belonging to CKD stage 4 and 5.Agarwal et al in a study of predialysis treatment naïve patients reported prevalence of hypocalcemia in 29.9% and 49.6%; hyperphosphatemia

in 45% and 41.8%; and hyperparathyroidism in 57.8% and 39.4% in CKD stage 4 and 5.

In our study patients with diabetes mellitus (n=42) had significantly lower serum phosphate, ALP, and iPTH levels as compared with patients without diabetes mellitus (n=51). Similar to our study Banerjee et al[17] also observed a higher prevalence of diabetes mellitus in patients with iPTH below range; they inferred that it could be due to underlying adynamic bone disease, which is more prevalent in diabetic patients, especially in the elderly and those on PD. Non diabetic CKD as compared to diabetic CKD had a higher alkaline phosphatase, a higher iPTH and higher proportion of patients with iPTH above KDOQI target range, and an elevated alkaline phosphatase in a study conducted by Sanjay Vikrant et al.[18] Although in a study by Patricia wahl et al unadjusted serum phosphate, PTH, and FGF23 levels were higher and calcium was lower among those with diabetes compared with those without diabetes.[19] This may be due to inclusion of milder CKD stage 3 in this study.

Our study found osteoporosis more frequently in patients older than 75 yrs. These patients also had significantly lower serum phosphorus, iPTH and ALP. A study by Istvan kiss et al also showed inverse relationship between age and iPTH. In their study older patients more frequently had serum calcium, phosphorus and iPTH in target range despite receiving less treatment[20] Similarly a study by Solenne Pelletier et al found that elderly patients (age more than 75 yrs) exhibited lower serum phosphorus and parathyroid hormone concentrations, but slightly higher serum calcium levels compared to patients aged below 75 years.[4]

Presence of Abdominal Aorta calcification is predictor of increased cardiovascular morbidity and mortality in the community[21] and dialysis population.[22] Early identification of AAC in pre dialysis CKD patients may help in identifying patients at high-risk for cardiovascular morbidity and mortality in future, these patients may get benefitted from aggressive treatment of modifiable cardiovascular risk factors. In our study, AAC was noted in 13.98% of patients. In another study from India AAC was identified in only 6.8% of predialysis CKD stages 4 and 5 patients and it was more prevalent in older patients.[23] While study done by Shantha et al reported a prevalence of abdominal aortic calcification in 76.9% of CKD stage 5D patients and they reported that AAC score can predict carotid plaque and cardiac valvular calcification in ESRD patients.[24] Praveen Kumar Etta et al[13] reported AAC in 10.5% of their patients. In their study patients with AAC had higher levels of serum iPTH, phosphorus, and ALP and lower levels of corrected calcium as compared to patients without AAC. In our study, we observed that patients with AAC had more severe derangements of mineral metabolism in terms of higher levels of serum iPTH, phosphorus, and ALP. In our study, serum calcium levels did not correlate with AAC. Available literature is inconsistent regarding interaction of serum levels of calcium, phosphorus, iPTH with vascular calcification. Some cross sectional and observational studies have found a strong correlation between serum levels of calcium, phosphorus, iPTH, and extraskeletal calcification.[25] However other studies have failed to show this correlation[26] and at present reason for this variation among study findings are not clear.

BMD of the hip and radius is reported to be lower in patients with CKD stages 4–5 as compared to general population, while lumbar spine BMD is reported to be similar in both. In patients having CKD-MBD, there is likelihood of coexistence of low BMD with a range of bone abnormalities frequently associated with kidney diseases. Associated abnormalities can vary from high turnover bone lesions secondary to severe hyperparathyroidism to severely reduced bone remodeling as seen in low turnover or adynamic bone disease. These findings are different from common osteoporotic patient where process of bone remodeling is not involved. Various studies have shown that a low BMD can help in predicting fracture risk in non CKD patients. BMD has not been conclusively proven to be useful in patients with CKD stages 4–5 and has limited ability to identify patients at risk of fracture. This finding is linked to inherent problems in measuring BMD in CKD patients as lumbar spine BMD measurements can be inaccurate in presence of anatomic abnormalities in the spine, while BMD measurements at hip are affected by patient positioning. Forearm BMD measurements have not proven reliable in predicting fractures risk in community based population studies, but contrary to findings in general population a meta-analysis by Jamal et al found forearm BMD can prove most sensitive site in patients with CKD stage 5.[27] In our study also, we found a high prevalence of abnormal BMD at the distal forearm, in comparison to that of lumbar spine. Recently many cross-sectional studies have also shown usefulness of DXA based BMD calculation in predicting fracture risk in patients with CKD and BMD has been included by KDIGO for evaluation of CKD MBD in their recent guidelines update although data from randomized controlled trials is lacking[28-31]

Limitations of the study

First, most important is the cross-sectional nature of the study which helps in establishing association but not causal or temporal relationship. In place of one single value, trend of biochemical parameters over a period of time can better help in diagnosing the bone turnover state thus a follow up study is needed for the same set of patients. Detailed dietary history on intake of calcium and phosphorus was not collected. A bone biopsy, which is gold standard for diagnosis of CKD related bone abnormalities, was not carried out. Finally, although study reports a high prevalence of disordered mineral metabolism, only randomized trials could definitively determine whether early screening and treatment of these abnormalities can have a marked effect on CKD, bone, or cardiovascular endpoints.

CONCLUSION

Symptoms of CKD MBD alone are not enough to identify the bone health condition. Bone turnover markers should be done to correctly predict bone health. As in general CKD population CKD MBD is also prevalent in elderly population.

Secondary hyperparathyroidism and high bone turn over disease is most common form of CKD MBD in untreated elderly CKD population. Diabetic CKD patients have lower levels of serum phosphorus, iPTH and ALP. Patients older than 75 years more commonly have osteoporosis, lower levels of serum ALP, phosphorus and iPTH. Prevalence and severity of hyperphosphatemia, hyperparathyroidism, hypocalcemia and raised ALP increases from stage 4 to stage 5 CKD, while hypovaitaminosis D is equally prevalent in both stages. Patients with AAC had higher serum phosphorus, iPTH and ALP.

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