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The Frequency of Serum Bone Biomarkers, Biochemical Parameters, Bone Mineral Density and Osteoporosis with Bone Mineral Disease in Chronic Renal Failure Along with Factors Affecting Osteoporosis Development.

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KEYWORDS
Bone biomarkers, Osteoporosis, Bone mineral disease and chronic kidney disease.

ABSTRACT:

Introduction: Chronic kidney disease (CKD) is associated with the development of mineral bone disorder (MBD), osteoporosis, and fragility fractures. Among CKD patients, adynamic bone disease or low bone turnover is the most common type of renal osteodystrophy. Changes in mineral and humoral metabolism as well as bone structure develop early in the course of CKD. CKD-MBD includes abnormalities of calcium, phosphorus, PTH and vitamin D abnormalities in bone turnover, mineralization, volume, linear growth, strength, vascular and other soft tissue calcification. Biomarkers such as bALP and iPTH may assist to assess bone turnover. The consequences of CKD-MBD include increased fracture risk, greater morbidity, and mortality. Thus, the goal is to prevent the occurrences of fractures by means of alleviating CKD-induced MBD and treating subsequent osteoporosis. There is no consensus on the optimal diagnostic method of compromised bone assessment in patients with CKD. Bone quantity and mass can be assessed by dual-energy x-ray absorptiometry (DXA) or quantitative computed tomography (QCT). Bone quality on the other side can be assessed by non-invasive methods such as trabecular bone score (TBS), high-resolution bone imaging methods, and invasive bone biopsy. Bone turnover markers can reflect bone remodelling, but some of them are retained by kidneys. Understanding the mechanism of bone loss is pivotal in preventing fracture in patients with CKD. Several non-pharmacological and therapeutic interventions have been reported to improve bone health. Controlling laboratory abnormalities of CKD-MBD is crucial. Anti-resorptive therapies are effective in improving BMD and reducing fracture risk, but there are uncertainties about safety and efficacy especially in advanced CKD patients. Accepting the prevalent of low bone turnover in patients with advanced CKD, the osteo-anabolics are possibly promising. Parathyroidectomy should be considered a last resort for intractable cases of renal hyperparathyroidism. There is a wide unacceptable gap in osteoporosis management in patients with CKD.

Objectives: We wanted to evaluate of Serum Bone biomarkers and Biochemical parameters and

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Bone mineral density levels with Osteoporosisand bone mineral disease in CKD patients as a potential biomarker.

Methods: This study was conducted in 300 subjects out of which 150 were CKD patients (cases) and 150 were healthy subjects (controls). 3 ml peripheral venous blood was collected and supernatant serum as used for the analysis of Serum iPTH, Serum Osteocalcin and Serum TRACP5b by (ELISA) method. We found significantly increased levels of Serum iPTH (OR-3.07, P < 0.0001***), Serum Osteocalcin (OR-7.12, P < 0.001**), Serum (TRACP) 5b (OR-5.62, P < 0.0001***) Serum Glomerular Filtration Rate (eGFR), Serum Urea, Serum Creatinine, Serum Uric Acid, Serum Sodium, Serum Potassium, and Serum Chloride were measured on the Serum supernatant from 3 millilitres of peripheral venous blood using Diacetyl monoxime, Jaffe's method, Caraway's method, Cockcroft-Gault method, Colorimetric method and Mercuric thiocyanate method. We discovered that the serum glomerular filtration rate (eGFR) was considerably elevated (OR-7.67, P < 0.0001***). The following serum levels were measured Serum Urea (OR-5.85, P < 0.0001***), Serum Creatinine (OR-7.59, P < 0.001**) and Serum Uric acid (OR-5.83, P < 0.0001***). In Osteoporosisand bone mineral disease in CKD patients, serum levels of Serum Sodium (OR-5.77, P < 0.0565*), Serum Potassium (OR-5.83, P < 0.0005***), Serum Chloride (OR-7.87, P < 0.03*), Serum vitamin D (OR-9.95, P < 0.19), Serum Calcium (OR-7.85, P < 0.17) and Serum Phosphorus (OR-3.85, P < 0.15) were lower than those in controls. This study functioned effectively for post-dialysis patients with low sodium and potassium levels but high Serum glomerular filtration rate (eGFR), Serum Urea, Serum Creatinine, Serum Uric acid and Serum Chloride levels. 3 ml peripheral venous blood was collected and supernatant serum as used for the analysis of Serum iPTH, Serum Osteocalcin and Serum TRACP5b by (ELISA) method.

Results: We found significantly increased levels of Serum iPTH (OR-3.07, P < 0.0001***), Serum Osteocalcin (OR-7.12, P < 0.001**), Serum (TRACP) 5b (OR-5.62, P < 0.0001***), Serum Glomerular filtration rate (OR-7.67, P < 0.0001***), Serum Urea (OR-5.85, P < 0.0001***), Serum Creatinine (OR-7.59, P < 0.001**) and Serum Uric acid (OR-5.83, P < 0.0001***) with Osteoporosisand bone mineral disease in CKD patients as compared to controls.

Conclusions: Treatment strategies for CKD associated osteoporosis should be patients cantered to determine the type of renal osteodystrophy. This review focuses on the mechanism, evaluation and management of patients with CKD-MBD.Bone mineral disease in chronic kidney disease patients can be detected at early stage by the use of noninvasive methods of estimation of Serum iPTH, Serum Osteocalcin and (TRACP)5b levels and can be used as prognostic (biomarker).

Introduction: Chronic kidney disease (CKD) is associated with the development of mineral bone disorder (MBD), osteoporosis and fragility fractures [1]. The grade or severity of CKD can be classified based on glomerular filtration rate (GFR) category ranging from stage G1 to G5 [2]. In stage G1 and G2, the GFRs are normal (more than 90 mL/min/1.73 m2) and slightly decreased (60–89 mL/min/1.73 m2), respectively [3]. For patients with CKD stage G3a and G3b, the GFRs decrease from mild to moderate (40–59 mL/min/1.73 m2) and moderate to severe (30–44 mL/min/1.73 m2) [4]. The renal function is severely impaired in patients with CKD stage 4 (15–29 mL/min/1.73 m2) and CKD stage 5 (add D if treated by dialysis) referring to kidney failure (less than 15 mL/min/1.73 m2) [5]. By definition, CKD-MBD is a systemic disorder of mineral and bone metabolism, which is manifested by either one or a combination of the following: abnormalities of calcium, phosphorus, parathyroid hormone (PTH) or vitamin D metabolism abnormalities in bone turnover, mineralization, volume, linear growth, strength vascular or other soft tissue calcification [6]. The consequences of CKD-MBD include increased fracture risk, greater morbidity and mortality [7]. Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture [8]. The world health organization defines osteoporosis as a T score ≤ - 2.5. CKD is an independent risk factor of

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osteoporosis [9]. The prevalence of osteoporosis was 31.8% among CKD G3–5 patients [10]. The osteoporosis was twice more common in those with eGFR < 60 mL/min than those with eGFR > 60 mL/min [11]. As CKD makes progress, decreased bone mineral density (BMD) mostly involves hip, but not spine [12]. CKD is a risk factor for fragility (low trauma) fractures [13]. The study found in early decreased renal function (eGFR< 60 mL/min/1.73 m2) was related to increase incident fracture risk, but not with increased prevalence of vertebral fracture or falls [14]. In a prospective cohort study in veterans with CKD G3–5, CKD is related to a moderately greater fracture risk after adjusting age, and BMD patients with CKD G5D and kidney transplant the incidence of hip fracture in haemodialysis groups [15]. Chronic kidney disease (CKD) is associated with the development of mineral bone disorder (MBD), osteoporosis and fragility fractures [16]. Among chronic kidney disease patients, adynamic bone disease or low bone turnover is the most common type of renal osteodystrophy [17]. Changes in mineral and humoral metabolism as well as bone structure develop early in the course of CKD [18]. CKD-MBD includes abnormalities of calcium, phosphorus, PTH and vitamin D abnormalities in bone turnover, mineralization, volume, linear growth, strength, vascular and other soft tissue calcification [19]. Biomarkers such as bALP and iPTH may assist to assess bone turnover. The consequences of CKD-MBD include increased fracture risk, greater morbidity, and mortality [20]. Thus, the goal is to prevent the occurrences of fractures by means of alleviating CKD-induced MBD and treating subsequent osteoporosis [21]. There is no consensus on the optimal diagnostic method of compromised bone assessment in patients with CKD [22]. Bone quantity and mass can be assessed by dual-energy x-ray absorptiometry (DXA) or quantitative computed tomography (QCT) [23]. Bone quality on the other side can be assessed by non-invasive methods such as trabecular bone score (TBS), high-resolution bone imaging methods and invasive bone biopsy [24]. Bone turnover markers can reflect bone remodelling, but some of them are retained by kidneys [25]. Understanding the mechanism of bone loss is pivotal in preventing fracture in patients with CKD [26]. Several non-pharmacological and therapeutic interventions have been reported to improve bone health [27]. Controlling laboratory abnormalities of CKD-MBD is crucial anti-resorptive therapies are effective in improving BMD and reducing fracture risk, but there are uncertainties about safety and efficacy especially in advanced CKD patients [28]. Accepting the prevalent of low bone turnover in patients with advanced CKD, the osteo-anabolics are possibly promising [29]. Parathyroidectomy should be considered a last resort for intractable cases of renal hyperparathyroidism. There is a wide unacceptable gap in osteoporosis management in patients with CKD [30].

Objectives: We wanted to evaluate of Serum Bone biomarkers and Biochemical parameters and Bone mineral density levels with Osteoporosisand bone mineral disease in CKD patients as a potential biomarker.

Methods: This study was a case control study conducted in Department of Biochemistry, Pacific Medical College and Hospital, Udaipur, (Rajasthan) India. Study was carried out after obtaining ethical clearance from Institutional Ethics committee, Pacific Medical College and Hospital, Pacific Medical University, Udaipur, (Rajasthan) India. Study involved 300 subjects, 150 healthy subjects and 150 chronic kidney disease patients attending the Dialysis Unit, Nephrology OPD/IPD and Department of Medicine in Pacific Medical College and Hospital, Udaipur, Rajasthan.

Inclusion criteria:

- Osteoporosis with Bone mineral disease in chronic kidney disease patients grades wise distribution (G1, G2, G3a, G3b, G4 and G5) before starting renal replacement therapy.
- Subjects between 18–65 years age group were considered.

Exclusion criteria:

- Acute infections
- Malignancy
- Chronic liver disease
- Thyroid gland dysfunctions
- Myocardial infarction

Method of Analysis: 3 ml peripheral blood samples were collected from all participants both patients and controls. The blood samples were centrifuged at 4000 rpm for 15 minutes. The 50µl of centrifuge serum was used in a fully auto-analyzer Roche cobase 801 to measure the serum parathyroid hormone, which was estimated by Chemiluminescence Immunoassay (CLIA).

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The Bone biomarkers and Biochemical parameters were estimated by Enzyme-linked immunosorbent assay (ELISA)semi auto-analyzer ELISA Reader Bio-Red PR 4100, Beckman coulter AU 5800, Elbscience kit and lot no. E-EL-H1347. The serum was stored at -70°C until assayed. **Statistical Analysis:** All the parameter of case and control were analyzed for mean and standard deviation. The results were expressed as Mean ± standard deviation. The student t-test was used and a p-value < 0.05 was considered statistically significant. Pearson correlation coefficient was used to find the correlation between the level of Serum Bone biomarkers and Biochemical parameters and Bone mineral density levels with Osteoporosisand Bone mineral disease in CKD patientsas compared to controls as well as pre and post dialysis of patients. Data was analyzed using Statistical software i.e. Statistical Package for Social Sciences (SPSS) version 21.0. After analysis of data distribution patterns appropriate statistical tests was utilized for analysing measures of central tendency, dispersion and odds ratio.

Results: The study included subjects 300 participants among them 150 were Pre dialysis patients with chronic kidney disease with ages ranged from 18 to 65 years with a mean of 48.26±10.49 years and 150 were controls. There were 150 Case groups (male 77% and female 73 %) and 150 Control groups (male 93% and female 53%). Older age osteoporosisand bone mineral disease with CKD patientswere more common i.e. in the 50–60-year age group. The p-value of 0.05 was considered significant to compare the pattern of renal profile between the two groups [Table 1].

Figure 1: Study design:

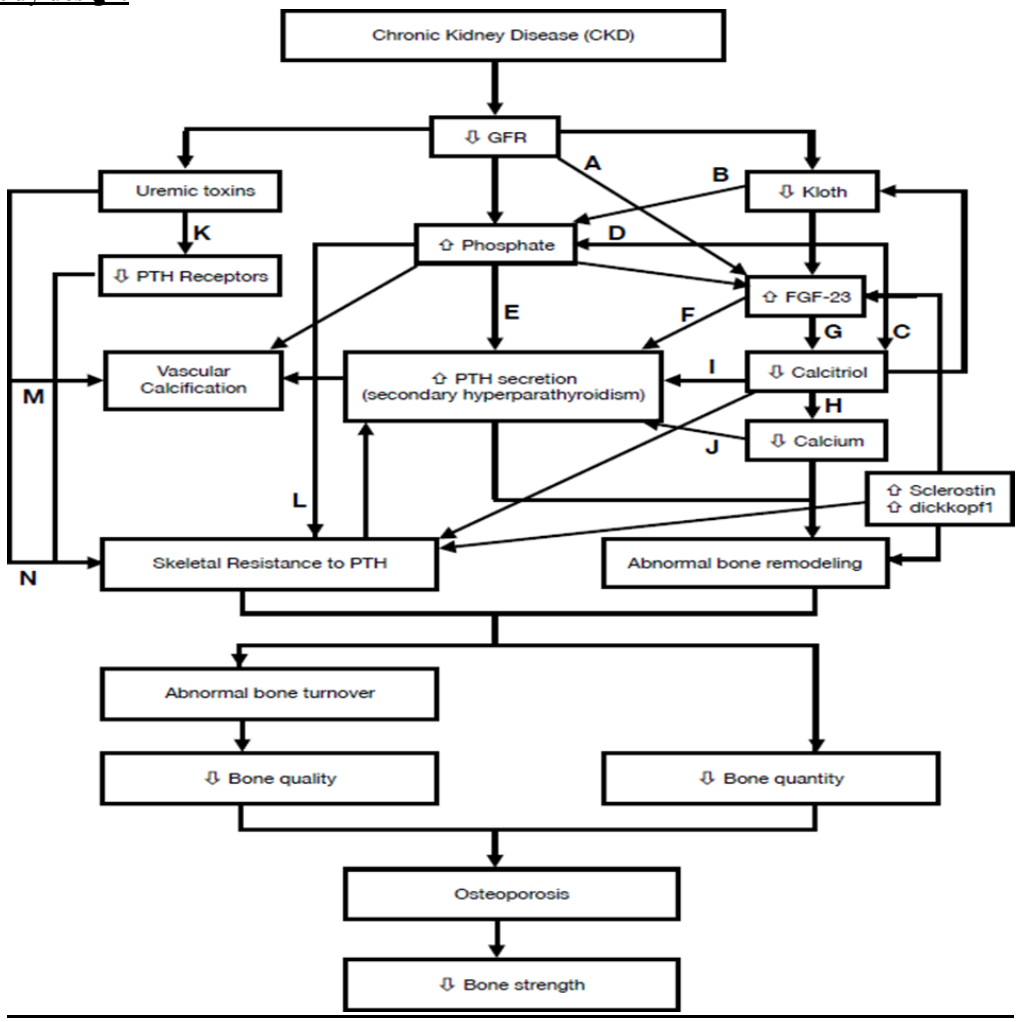

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Table No 01: Comparison between control groups (Pre dialysis values and Post dialysis values) of chronic kidney disease (CKD) patients.

S. No.	Parameters	Pre dialysis Groups (Mean ± SD) (399)	Post dialysis Groups (Mean ± SD) (399)	Control Groups (Mean ± SD) (399)	Odds Ratio (OR)	(P) Value
01.	S. Osteocalcin (ng/mL)	17.55±1.33	13.19±1.37	9.99±1.29	9.17	0.0013(**)
02.	S. TRCAP 5b (ng/mL)	15.87±1.48	11.65±1.67	9.03±1.70	7.73	0.001(**)
03.	S. iPTH (pg/mL)	33.79±6.07	35.71±5.21	37.83±5.25	5.17	0.81
04.	S. Vitamin D (ng/mL)	19.85±2.58	15.47±7.31	37.95±5.15	7.59	0.65
05.	S. ALP (IU/L)	155.87±11.65	165.81±11.37	147.93±1.30	9.85	0.001(**)
06.	S. Calcium (mg/dl)	8.91±3.33	7.81±3.27	9.93±5.73	9.37	0.29
07.	S. Magnesium (mg/dl)	1.95±1.21	2.27±1.30	2.95±1.53	5.27	0.27
08.	S. GFR (mL/min)	70.15±5.33	65.71±40.42	55.87±7.31	9.65	0.97
09.	S. Urea (mg/dl)	90.95±5.83	71.83±3.71	39.72±5.59	7.97	0.001(**)
10.	S. Creatinine (mg/dl)	9.97±1.77	7.93±0.97	0.97±1.37	7.95	0.001(**)
11.	S. Uric Acid (mg/dl)	11.73±5.89	9.51±5.51	5.65±1.29	5.83	0.001(**)
12.	S. Sodium (mEq/L)	131.91±8.55	133.39±7.71	135.87±3.33	7.91	0.65
13.	S. Potassium (mEq/L)	9.71±1.27	33.75±1.38	35.0±1.77	9.93	0.001(**)
14.	S. Chloride (mEq/L)	113.75±7.85	119.95±7.81	105.99±9.97	9.65	0.001(**)
15.	S. Phosphorus (mg/dl)	7.51±1.55	5.31±1.87	3.97±1.75	3.99	0.77

*P value<0.05, **P value <0.005, ***P value <0.0005 as considered significant.

Compares the markers of bone formation (serum osteocalcin) and resorption (serum tartrate-resistant acid phosphatase 5b) with biochemical parameters between cases groups and controls groups using mean ± SD, odds ratio (OR) and P-values. We found significantly increased levels of Serum osteocalcin (OR-9.17, P < 0.0013**), Serum tartrate-resistant acid phosphates' 5b (OR-5.62, P < 0.001**), Serum iPTH (OR-3.07, P < 0.001**), Serum alkaline phosphates (OR- 9.85, P < 0.001**), Serum glomerular filtration rate (OR-9.65, P < 0.001**). Serum urea (OR-7.97, P < 0.001**), Serum creatinine (OR-7.95, P < 0.001**), Serum uric acid (OR-5.83, P < 0.001**), Serum potassium (OR-9.83, P < 0.001**) and Serum chloride (OR-9.65, P < 0.001**). The following serum levels were measured Serum vitamin D (OR-9.59, P < 0.65), Serum calcium (OR-9.37, P < 0.29), Serum magnesium (OR-5.27, P < 0.27), Serum Sodium (OR-5.90, P < 0.65) and Serum phosphorus (OR-3.99, P < 0.77) levels were significantly lower cases groups, pre dialysis groups and post dialysis groups in chronic kidney disease patients. We observed significantly increased levels of Serum Osteocalcin (15.03±1.31), TRAPCP 5b (11.75±1.44) and S iPTH (65.77±6.06) in CKD patients as compared to control.

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Urea, Creatinine, Uric acid, eGFR, Potassium and Chloride were also significantly elevated in CKD patients as compared to controls [Table 1]. All these observations were statistically significant (P <0.05). Serum Sodium was however elevated in CKD patients but was non-significant [Figure 1].

Figure 1: Comparison between control groups of Pre dialysis values and Post dialysis values in chronic kidney disease (CKD) patients.

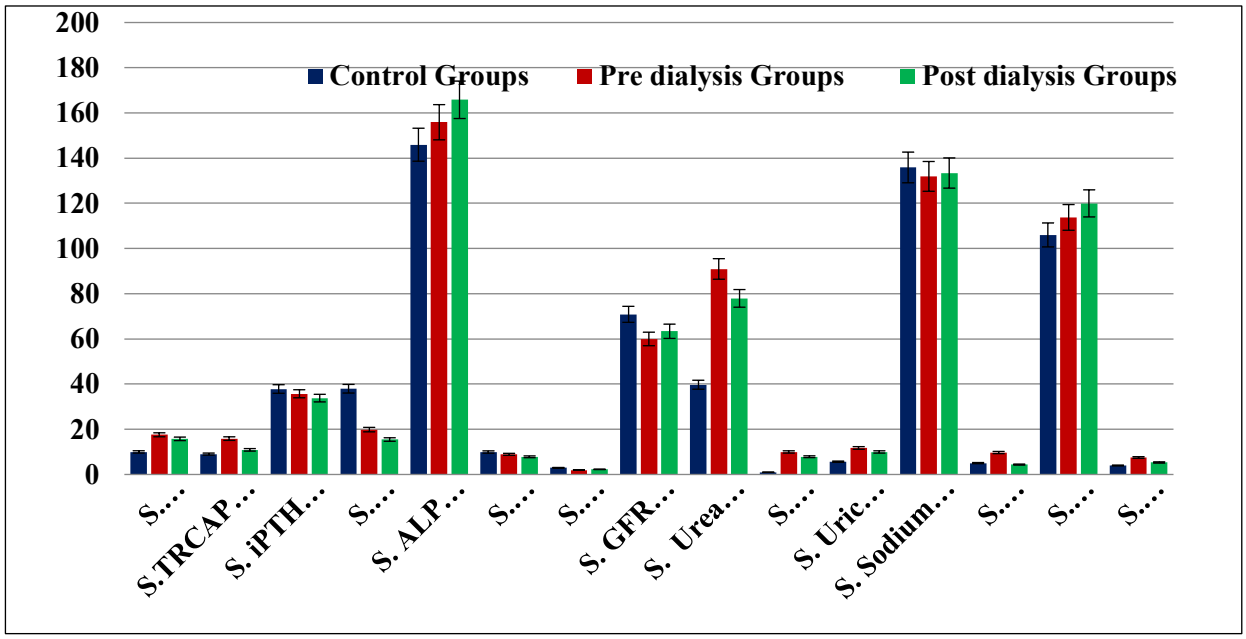

Table No 02: Comparison between control groups of Serum Bone biomarkers and Bone mineral density levels with Osteoporosis and Bone mineral disease in CKD patients.

S. No.	Parameters	Osteoporosis (BMD) Case Groups (T- Score Test) (Mean ± SD) (150)	Osteoporosis (BMD) Controls Groups (T- Score Test) (Mean ± SD) (150)	Odds Ratio (OR)	(P) Value
01.	Skull	2.9±0.81	2.3±0.73	9.17	0.001(**)
02.	Cranium	2.8±0.83	2.1±0.85	7.73	0.001(**)
03.	Mandible	2.9±0.73	2.3±0.71	5.17	0.001(**)
04.	Vertebrates	1.9±0.71	2.4±0.65	7.59	0.57
05.	Sternum	2.7±0.65	2.5±0.55	9.85	0.001(**)
06.	Ribs	2.8±0.85	2.3±0.65	9.37	0.001(**)
07.	Clavicle	1.9±0.91	2.4±0.51	5.27	0.59
08.	Scapula	2.8±0.73	2.5±0.73	9.65	0.001(**)
09.	Humerus	1.8±0.65	2.3±0.63	7.97	0.51
10.	Ulna	1.7±0.77	2.4±0.71	7.95	0.53
11.	Radius	1.9±0.87	2.5±0.81	5.83	0.49
12.	Carpals	2.7±0.55	2.4±0.51	7.91	0.001(**)
13.	Metacarpals	1.7±0.47	2.5±0.49	9.93	0.65

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14.	Phalanges	1.9±0.85	2.3±0.83	9.65	0.77
15.	Pelvis	1.7±0.55	2.4±0.59	3.99	0.65
16.	Hip bone	1.8±0.73	2.5±0.71	9.17	0.71
17.	Femur	1.9±0.78	2.3±0.81	7.73	0.81
18.	Patella	2.7±0.77	2.4±0.75	5.17	0.001(**)
19.	Tibia	1.8±0.57	2.5±0.51	7.59	0.73
20.	Fabula	1.9±0.65	2.3±0.67	9.85	0.77
21.	Calcaneus	2.7±0.31	2.4±0.39	9.37	0.001(**)
22.	Talus	2.7±0.21	2.5±1.27	5.27	0.001(**)
23.	Tarsals	2.7±0.33	2.3±0.33	9.65	0.001(**)
24.	Metatarsals	1.8±0.83	2.4±0.73	7.97	0.67
25.	Phalanges	1.9±0.35	2.3±0.31	9.17	0.85

*P value<0.05, **P value <0.005, ***P value <0.0005 as considered significant.

Comparison between control groups of Serum Bone biomarkers and Bone mineral density between cases groups and controls groups using mean ± SD, odds ratio (OR) and P-values. We found significantly increase levels of Skull (OR-5.81, P <0.001**), Cranium (OR-7.83, P <0.001**),Mandible (OR-9.73, P <0.001**), Sternum (OR-3.97, P <0.001**), Ribs (OR-9.17, P <0.001**),Scapula (OR-5.17, P <0.001**), Carpals (OR-7.91, P <0.001**), Patella (OR-5.17, P <0.001**), Calcaneus (OR-9.37, P <0.001**),(OR-5.27, P <0.001**) and Tarsals (OR- 9.65, P <0.001**),The following decrease levels of Vertebraes (OR- 9.65, P < 0.57), Clavicle (OR-7.73, P < 0.59), Humerus (OR-7.59, P < 0.51) Ulna (OR-9.85, P < 0.53), Radius (OR-9.17, P < 0.49), Metacarpals (OR-9.93, P < 0.65), Phalanges (OR-9.65, P < 0.77), Pelvis (OR-3.99, P < 0.65), Hip bone (OR-7.73, P < 0.71), Femur (OR-5.17, P < 0.81), Tibia (OR-7.59, P < 0.73), Fabula (OR-9.85, P < 0.77), Talus Metatarsals (OR-7.97, P < 0.67) and Phalanges(OR-9.17, P < 0.85).All these observations were statistically non-significant (P <0.05). The following Serum Bone biomarkers and Bone mineral density levels were measured significantly lower cases groups, Osteoporosis with Bone mineral disease (BMD) in chronic kidney disease (CKD) patients.

Figure No 02: Comparison between control groups of Serum Bone biomarkers and Bone mineral density levels with Osteoporosis and Bone mineral disease in CKD patients.

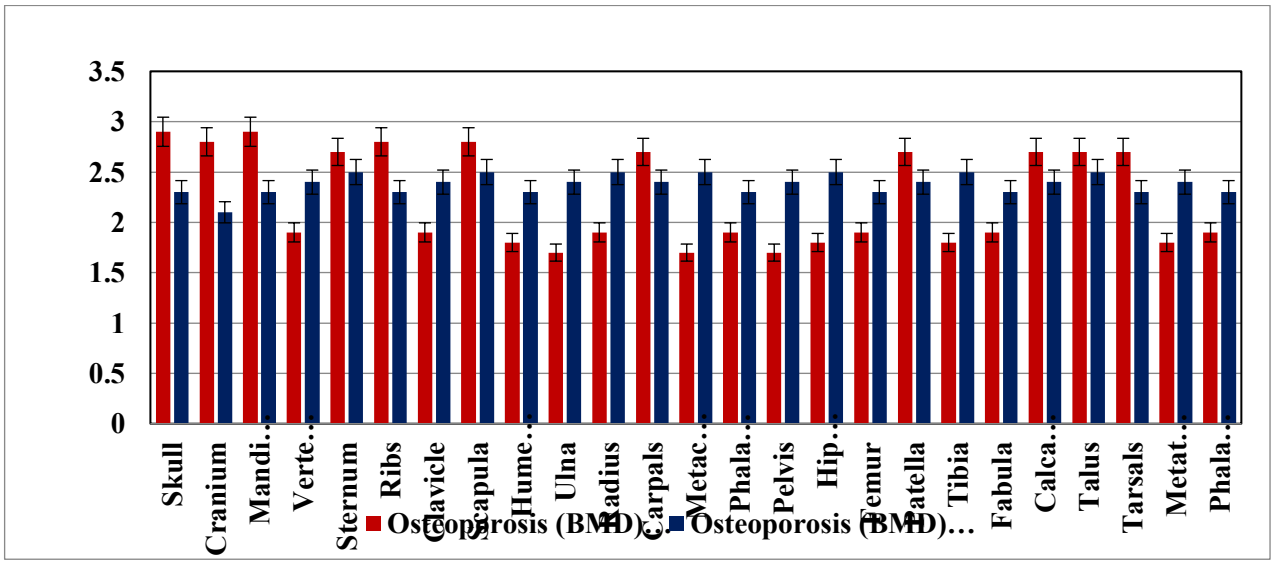

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Table No 03: Comparison between control groups of Serum Bone biomarkers and Bone mineral density levels with Osteoporosis and Bone mineral disease in CKD patients.

S.No.	Parameters	Osteoporosis (BMD) Case Groups (Z- Score Test) (Mean ± SD) (150)	Osteoporosis (BMD) Controls Groups (Z- Score Test) (Mean ± SD) (150)	Odds Ratio (OR)	(P) Value
01.	Skull	2.9±0.81	2.3±0.73	5.81	0.001(**)
02.	Cranium	2.8±0.83	2.1±0.85	7.83	0.001(**)
03.	Mandible	2.9±0.73	2.3±0.71	9.73	0.001(**)
04.	Vertebraes	1.9±0.71	2.4±0.65	9.65	0.65
05.	Sternum	2.7±0.65	2.5±0.55	3.97	0.001(**)
06.	Ribs	2.8±0.85	2.3±0.65	9.17	0.001(**)
07.	Clavicle	1.9±0.91	2.4±0.51	7.73	0.67
08.	Scapula	2.8±0.73	2.5±0.73	5.17	0.001(**)
09.	Humerus	1.8±0.65	2.3±0.63	7.59	0.77
10.	Ulna	1.7±0.77	2.4±0.71	9.85	0.65
11.	Radius	1.9±0.87	2.5±0.81	9.17	0.71
12.	Carpals	2.7±0.55	2.4±0.51	7.91	0.001(**)
13.	Metacarpals	1.7±0.47	2.5±0.49	9.93	0.65
14.	Phalanges	1.9±0.85	2.3±0.83	9.65	0.47
15.	Pelvis	1.7±0.55	2.4±0.59	3.99	0.57
16.	Hip bone	1.8±0.73	2.5±0.71	9.17	0.75
17.	Femur	1.9±0.78	2.3±0.81	7.73	0.49
18.	Patella	2.7±0.77	2.4±0.75	5.17	0.001(**)
19.	Tibia	1.8±0.57	2.5±0.51	7.59	0.57
20.	Fabula	1.9±0.65	2.3±0.67	9.85	0.51
21.	Calcaneus	2.7±0.31	2.4±0.39	9.37	0.001(**)
22.	Talus	2.7±0.21	2.5±1.27	5.27	0.001(**)
23.	Tarsals	2.7±0.33	2.3±0.33	9.65	0.001(**)
24.	Metatarsals	1.8±0.83	2.4±0.73	7.97	0.65
25.	Phalanges	1.9±0.35	2.3±0.31	9.17	0.47

*P value<0.05, **P value <0.005, ***P value <0.0005 as considered significant.

Comparison between control groups of Serum Bone biomarkers and Bone mineral density between cases groups and controls groups using mean ± SD, odds ratio (OR) and P-values. We found significantly increase levels of Skull (OR-5.81, P <0.001**), Cranium (OR-7.83, P <0.001**),Mandible (OR-9.73, P <0.001**), Sternum (OR-3.97, P <0.001**), Ribs (OR-9.17, P <0.001**), Scapula (OR-5.17, P <0.001**), Carpals (OR-7.91, P <0.001**),Patella (OR-5.17, P <0.001**), Calcaneus (OR-9.37, P <0.001**),Talus (OR-5.27, P <0.001**) and Tarsals (OR- 9.65, P <0.001**),The following decrease levels of Vertebrates (OR- 9.65, P < 0.65), Clavicle (OR-7.73, P < 0.67), Humerus (OR-7.59, P < 0.77) Ulna (OR-9.85, P < 0.65), Radius (OR-9.17, P < 0.71), Metacarpals (OR-9.93, P < 0.65), Phalanges (OR- 9.65, P < 0.47), Pelvis (OR-3.99, P < 0.57), Hip bone (OR-7.75, P < 0.71), Femur (OR-5.17, P < 0.49), Tibia (OR-7.59, P < 0.57), Fabula (OR-9.85, P < 0.51), Metatarsals (OR-7.97, P < 0.65) and Phalanges (OR-9.17, P < 0.47). All these observations were statistically

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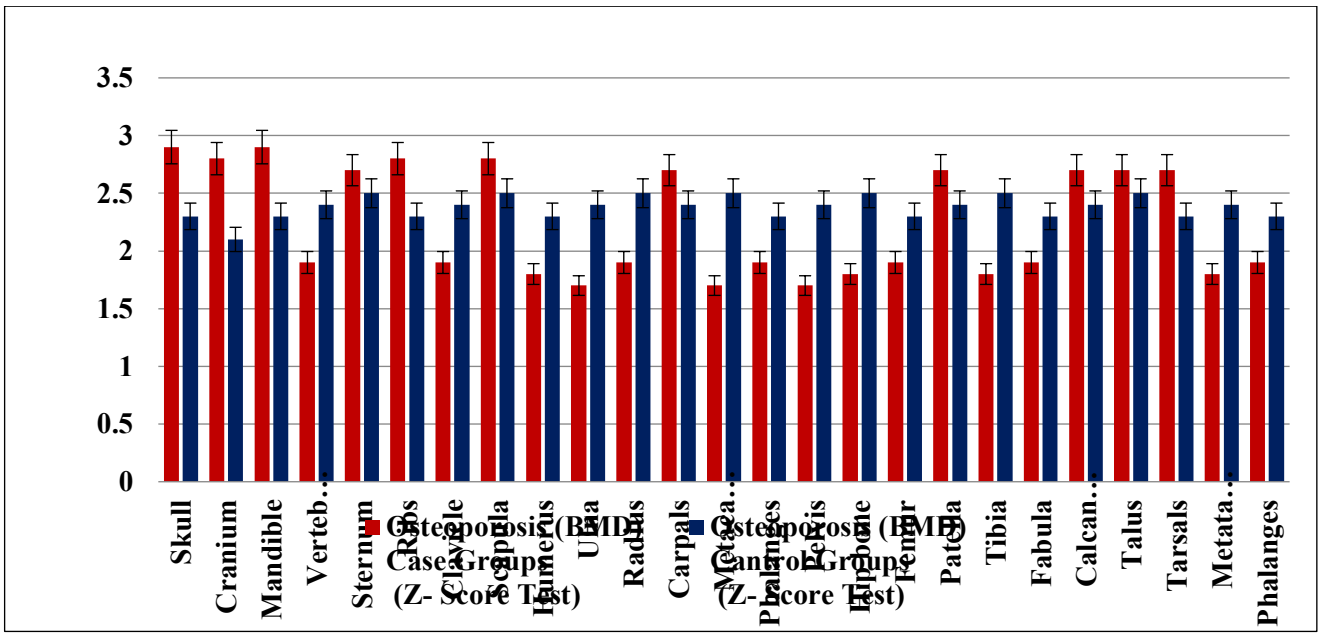
non-significant (P <0.05). The following Serum Bone biomarkers and Bone mineral density levels were measured significantly lower cases groups, Osteoporosis with Bone mineral disease in CKD patients.

Figure No 03: Comparison between control groups of Serum Bone biomarkers and Bone mineral density levels with Osteoporosis and Bone mineral disease in CKD patients.



Pathophysiology: Synthesis of vitamin D is mainly reduced in CKD-MBD. Both 25(OH)D (calcitriol) and 1,25$(OH)_2$D (calcitriol) play a crucial role on bone metabolism [31]. Through vitamin D receptor (VDR) on bone cells, vitamin D stimulates calcium resorption and osteoclast differentiation via induction of Receptor activator of nuclear factor kappa B ligand (RANK-L) synthesis [32]. Cholecalciferol (Vitamin D3) 800 IU/day is recommended for the treatment and prevention of vitamin D deficiency in CKD and dialysis patients [33]. The effects of vitamin D supplementation on CKD and dialysis patients include decreased serum PTH level, increased serum calcitriol level, reduced proteinuria, endothelial cardiovascular markers improvement and decreased inflammation markers [34]. The increases the sensitivity of CaSR and vitamin D receptor (VDR) expression decreases PTH gene expression and PTH secretion of the parathyroid gland [35]. Additional calcium supplements or calcium-containing medications should be avoided for patients with adequate daily calcium intakes of 800–1000 mg per day [36]. Phosphate load from phosphate-rich sources should be avoided [37]. CKD-MBD suggest limiting calcium-based phosphate binders for all patients with CKD G3a–5D. Daily dietary calcium intake with 1000 mg/day is recommended for achieving neutral calcium balance [38].

Discussion: Changes in mineral and humoral metabolism as well as bone structure develop early in the course of CKD [39]. CKD and MBD included abnormalities of calcium, phosphorus, PTH and vitamin D abnormalities in bone turnover, mineralization, volume, linear growth, or strength and vascular or other soft tissue calcification [40]. In patients with CKD and MBD, using DXA or FRAX to screen fracture risk should be considered [41]. Biomarkers such as bALP and iPTH may assist to assess bone turnover, except for bone biopsy [42]. Among CKD patients, adynamic bone disease or low bone turnover is the most common type of renal osteodystrophy [43]. Before initiating an anti-resorptive or anabolic agent to treat osteoporosis in CKD patients, lifestyle modifications, such as exercise, calcium, vitamin D supplementation [44]. Managing hyperphosphatemia and SHPT are also crucial because non-calcium-based phosphate binders, such as sevelamer

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are superior to calcium-based binder in increasing the bone formation rate and improving trabecular architecture [45]. In patients with CKD G1–3, physicians should use bisphosphonates and other osteoporosis treatments the same as for patients without CKD [46]. Bisphosphonates are generally not recommended in patients with eGFR <35 mL/min or evidence of adynamic bone disease due to avoiding over suppression of bone remodelling [47]. In KT recipients, bisphosphonates have efficiency in improving femoral neck and lumbar spine BMD [48]. Data concerning using anabolic agents in patients with CKD MBD are limited larger studies are needed to assess the role of teriparatide or abaloparatide in adynamic bone disease [49].

Conclusion: Treatment strategies for CKD associated osteoporosis should be patients cantered to determine the type of renal osteodystrophy. This review focuses on the mechanism, evaluation and management of patients with CKD-MBD.Bone mineral disease in chronic kidney disease patients can be detected at early stage by the use of noninvasive methods of estimation of Serum iPTH, Serum Osteocalcin and Serum (TRACP) 5b levels and can be used as prognostic (biomarker).

Additional Information:

Disclosures:

Human subjects: Consent for treatment and open access publication was obtained or waived by all participants in this study. **Ethics statement:** Institutional ethics committee was convened in Pacific Medical College and Hospital, Udaipur, (Rajasthan) India. Ethical approval for the project was approved by Institutional ethics committee, Pacific Medical College and Hospital, Udaipur, Rajasthan India. Informed written patient consent form for treatment and publication in open access journal has been obtained from each study participant prior to enrollment in study and sample collection. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relatioships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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