Original Article

Pattern of Renal Osteo Dystrophy in Chronic Renal Disease Patients

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ABSTRACT

Objective: To study the Pattern of Renal Osteo dystrophy in chronic renal Disease patients.
Study Design: Observational study
Place and Duration of Study: This study was conducted at the Rawal Teaching Hospital Institute of Health Sciences, Rawalpindi and Idris Teaching Hospital Sialkot during Feb 2018 to Feb 2020.
Materials and Methods: This study conducted on 100 patients The Demography data and laboratory finding was recorded on designed Performa. The informed consent was taken before taking the sample and clinical examination. The permission of Ethical Committee was considered before collection of data and get publishing in medical journal. The results were analysis by SPSS version 10.
Results: The maximum incidence was diabetes mellitus patients 42(42%), minimum PCKD2(2%) and Undiagnosed patients 2(2%). In moderate renal disease Muscle pain was 14(53.83%) in male 12(46.15%) in female, Severe Renal disease 22(55%) male 18(45%) female were having muscle pain. Serum Calcium was normal 9.49±0.545, low 8.30 ± 0.1732, high 11.32 ± 0.487, Inorganic Phosphate the normal value 3.68 ± 0.565, in high 6.83 ± 1.66, Alkaline phosphatase normal value 216.66 ± 51.86, High value 727.11 ± 405.03, Intact Parathormone normal value 5.45 ± 1.806, high value 25.09 ± 16.338. Para thyroid hormone was normal to slightly elevated in low turnover, in high turnover it was Markedly Elevated.
Conclusion: The most common histological type of renal Osteo dystrophy among dialysis and chronic kidney disease sick persons not on dialysis was hyperparathyroid bone disease; however, the presence of a dynamic bone disease was significant in both groups.

Key Words: Pattern, chronic renal disease, Osteo dystrophy

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INTRODUCTION

Constant renal malady is related with explicit irregularities of skeletal the tendency towards a relatively stable equilibrium between interdependent elements, normally called renal defective ossification of bone (ROD), which if not rewarded properly during the basic periods of skeletal development can bring about bone disfigurements and an upset development design. The fundamental variables for the improvement of ROD are unsettling influences in the calcium phosphate the tendency towards a relatively stable equilibrium between interdependent elements, in nutrient D and hormone of parathyroid digestion just as changes in the hormone-secreting cell in the anterior pituitary hub, i.e., on secreting internally and relating to a hormone whose release only affects tissue surrounding the gland levels. As of late it has been perceived that the range of kidney bone illness covers 'high-' just as 'low-turnover' conditions. As a result of incessant kidney ailment itself and of the treatment of kidney bone illness, high plasma phosphate levels and a raised calcium phosphorus item are normal. These are significant hazard factors for the advancement of blood vessel calcification and vessel of the heart dreariness and mostly in youthful grown-ups who have been on kidney substitution treatment since adolescence[1,2]. Since aluminum-containing phosphate folios are no longer shown in kids, aluminum- related with pathology of bone isn't considered in these proposals.

The European Pediatric Peritoneal Working Group (EPPWG) was built up in 1999 by children nephrologists with a significant enthusiasm for abdominal dialysis and has, between others, distributed rules on interminable and intense abdominal dialysis[3-6]. The gathering consolidates expert of children nephrology from 12 European nations. One of the elements of the gathering is to build up master direction in significant clinical territories related with constant renal disappointment and dialysis [now the European children Dialysis Working Group (EPDWG) related to different individuals from the multidisciplinary group.

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These rules were started and talked about at gatherings of the gathering and created by email conversation to create accord dependent on combined clinical experience and announced studies.

MATERIALS AND METHODS

This observational study of 100 patients has been conducted during Feb 2018 to Feb 2020 in the department nephrology Rawal teaching hospital institute of health sciences Rawalpindi and Idris teaching hospital Sialkot. The Demography data and laboratory finding were recorded on designed Performa. The informed consent was taken before taking the sample and clinical examination. The permission of Ethical Committee was considered before collection of data and get publishing in medical journal. The results were analysis by SPSS version 10.

RESULTS

The maximum incidence was diabetes mellitus patients 42(42%), minimum PCKD2 (2%) and Undiagnosed patients 2(2%) as shown in table 1.

The Diabetes M patients were 2 (5%) in mild renal disease, they were 6 (27%) male and 7 (33%) female in moderate renal disease and 5 (24%) male, 2(10%) female patients. In chronic GN 4 (18%) male 2(9%) female in moderate renal disease. In female 4(36%), in HTN only 4(18%) female and no male in moderate renal disease, 12(54%) male 6(27%) female patients in Severe Renal disease in TIN 2(33%) male 4(66%) female patients Severe Renal disease were found, OBS Uropathy 2(50%) male and no female in moderate renal disease 2(50%) male and no female were found in Severe Renal disease. In PCKD only 2(100%) female were found in Severe Renal disease, In case of undiagnosed patients only 2(100%) female were found (Table 2). In moderate renal disease Muscle pain was 14(53.83%) in male 12(46.15%) in female, Severe Renal disease 22(55%) male 18(45%) female were having muscle pain. Bone pain was 8(57.14%) male 6(42.85%) female in moderate renal disease and 22(52.38%) male 20(47.61%) female were having bone pain Severe Renal disease patients. Bone tenderness was 10(62.50%) male 6(37.50%) in female in moderate renal disease patients and 18(50%) in male and 18(50%) in female was seen in Severe Renal disease patients. The Itching was 4(33.33%) in male 8(66.66%) in female of Severe Renal disease patients was observe (Table 3).

Serum Calcium was normal 9.49±0.545, low 8.30 ± 0.1732, high 11.32 ± 0.487, Inorganic Phosphate the normal value 3.68 ± 0.565, in high 6.83 ± 1.66, Alkaline phosphatase normal value 216.66 ± 51.86, High value 727.11 ± 405.03, Intact Parathormone normal value 5.45 ± 1.806, high value 25.09 ± 16.338 was seen in table 4.

Para thyroid hormone was normal to slightly elevated in low turnover, in high turnover it was Markedly Elevated. In mixed Combined Picture of low And high turnover, Alkaline Phosphatatase was Normal to low in low turnover in case of high turnover it was Elevated in case of mixed there was Combined Picture of low And high turnover. The phosphate was normal to Elevated in low turnover and was elevated in high turnover and in mixed it was Combined Picture of low and high turnover. The calcium was variable to elevate in low turnover bone disease and was variable in high turnover bone disease and Combined Picture of low And high turnover in mixed bone lesions of osteodystrophy. The radiograph was normal to osteopenia in low turnover osteodystrophy and erosion + sclerosis was seen in high turnover lesions of osteodystrophy (table 5).

In case of PTH there was 20.9 +_ 12.140, in normal bone in low turnover it was 13.76 +_ 5.53, in high turnover it was 58.55 +_ 10.33, in mixed picture it was 15.45 ± 4.31.

Table No. 1: Diagnosis Distribution

Diagnosis	Percentage% of patients
Diabetes M	24 Male & 18 Female (42%)
Chronic GN	12 Male & 10 female (22%)
HTN	12 Male & 10 Female (22%)
TIN	2 Male & 4 Female (6%)
OBS Uropathy	4 Male (4%)
PCKD	2 Female (2%)
Undiagnosised	2 Female (2%)

Table No 2: Demographic and etiology and severity of renal disease distribution

Etiology	Mild Renal disease			Moderate Renal disease			Severe Renal disease		
	Male (Mean age)	Female (Mean age)	Total (Mean age)	Male (Mean age)	Female (Mean age)	Total (Mean age)	Male (Mean age)	Female (Mean age)	Total (Mean age)
Diabetes M	2/42 (5%)	----	2/42 (5%)	6/42 (27%)	7/21 (33%)	13/42 (60%)	5/21 (24%)	2/21 (10%)	7/42 (34%)
Chronic GN	----	----	----	4(18%)	2 (9%)	6 (27%)	8 (36%)	4 (36%)	8 (72%)
HTN	----	----	----	----	4 (18%)	4 (18%)	12(54%)	6 (27%)	18(81%)
TIN	----	----	----	----	----	----	2 (33%)	4 (66%)	6(100%)
OBS Uropathy	----	----	----	2 (50%)	----	2 (50%)	2 (50%)	----	2 (50%)
PCKD	----	----	----	----	----	----	----	2(100%)	2(100%)
Undiagnosed	----	----	----	----	----	----	----	2(100%)	2(100%)

Table No 3: Signs and symptoms distribution

Signs & symptoms	Moderate renal disease			Severe Renal disease		
	Male	Female	Total	Male	Female	Total
Muscle pain	14 53.83%)	12(46.15%)	26 (100%)	22 (55%)	18 (45%)	40 (100%)
Bone pain	8 (57.14%)	6 (42.85%)	14 (100%)	22(52.38%)	20(47.61%)	42 (100%)
Bone tenderness	10 62.50%)	6 (37.50%)	16 (100%)	18 (50%)	18 (50%)	36 (100%)
Itching	----	----	----	4 (33.33%)	8 (66.66%)	12 (100%)

Table No. 4: Serum calcium, phosphate, alkaline phosphates and intact parathormone* levels

Parameters		Normal	Low	High
Serum Calcium (mg/dl)	Number Range Mean± SD	80 (80%) 8.5-10.5 9.49± 0.545	10 (10%) 8.00-8.40 8.30± 0.1732	10 (10%) 10.80-12.00 11.32± 0.487
Inorganic Phosphate (mg/dl)	Number Range Mean± SD	32 (32%) 2.4-4.5 3.68± 0.565	-	68 (68%) 4.6-10.90 6.83± 1.66
Alkaline phosphatase (U/L)	Number Range Mean± SD	64 (64%) 60-306 216.66± 51.86	-	36 (36%) 318-.1412 727.11± 405.03
Intact Parathormone (Pmol/L)	Number Range Mean± SD	16 (16%) 1.7-7.8 5.45± 1.806	-	84 (84%) 8.80-74.00 25.09± 16.338

Table No. 5: The probability of various lesions of osteodystrophy

Parameter	**Low turnover**	**High turnover**	**Mixed**	**Normal**
PTH	Normal to Slightly elevated	Markedly Elevated	Combined Picture of low And high turnover	Normal
Alkaline Phosphatatase	Normal to low	Elevated	=	=
Calcium	Variable to elevated	Variable	=	=
Phosphate	Normal to elevated	Elevated	=	=
Radiograph	Normal to osteopenia	Erosion + Sclerosis	=	=

Table No. 6: Correlation between biochemical data of various renal osteodystrophy lesions

Parameter	Normal values	Normal bone Means + SD	Low turnover Mean + SD	High turnover Mean + SD	Mixed Mean + SD
PTH	1.7-7.8 Pmol/L	20.9+12.140 (2.4-48)	13.76+5.53 (4.60-22.80) P<0.014	58.55+10.33 (42.60-74.0) P<0.0001	15.45+4.31 (12.40-18.50)
Alkaline Phosphatatase	60-306 U/L	324.57+106.34 (179.489)	211.13+55.57 (106-294) P<0.0001	1238+167.2 (961-1412) P<0.0001	783.5+146.37 (680-887)
Calcium	8.5-10.5 Mg/dl	9+0.483 (8.0-9.80)	10.14+0.76 (9.20-12.00) P<0.0001	8.95+0.797 (8.40-10.50) Not significant	9.85+0.212 (9.70-10.00)
Phosphate	2.4-4.5 Mg/dl	5.92+1.842 (3.0-10.90)	4.71+1.22 (2.70-7) P<0.015	9.23+1.01 (82.0-10.70) P<0.0001	7.35+1.485 (6.30-8.40)
Radiograph	NAD	NAd (17) Dec. Density (2)	NAD (12) Dec. Density (6) Osteopenia (5)	Erosions+ (5) NAD (1)	Erosions + Dec. Density (1) Erosions + (1)

Alkaline Phosphatatase it was 324.57 ± 106.34 in normal bone, in loe turnover it was 211.13 ± 55.57, in high turnover it was 1238 ± 176.2. Calcium was 9 ± 0.483 in normal bone in low turnover, it was 10.14 ± 0.76, in high turnover it was 8.95 +_ 0.797, in mixed puicture it was 9.85 +_ 0.212 mg/dl. Phosphate it was 5.93 ± 1.842 in normal bone, it was 4.71 ± 1.22 in low turnover but it was 9.23 ± 1.01, but in mixed oicture

7.35 ± 1.485 mg/dl. Radiograph NAD (17) Decreased Density (2) in low turnover NAD (12) decreased. Density (6) and Osteopenia (5) in low turnover bone osteodystrophy. In high turnover NAD (1) and erosions (5) and mixed picture erosions decreased density (1) erosions (1) (table 6).

DISCUSSION

Renal Osteodystrophy (ROD) involves a wide range of signs that incorporates a high-turnover state, for example, hyper parathyroid bone illness and a low-turnover state, for example, OM and ABD.[7] ROD happens from the get-go throughout ceaseless kidney disease (chronic kidney disease) and exacerbates as renal work decays. Bone illness is basic between sick persons with (chronic kidney disease) stage 5 and when dialysis is started, practically all patients are affected.[8]

Our objective was to assess the predominance of renal Osteo dystrophy and set up a relationship between serum biochemical markers related with the pace of bone turnover, for example, Para thyroid hormone, alkaline phosphatase, basic alkaline phosphatase, or OC, with hidden bone the study of the microscopic structure of tissues, so as to build up a precise conclusion of ROD, which is basic to dole out treatment. We found a general high predominance of dynamic bone sickness—33% and 8% among CKD patients on dialysis and CKD patients not on dialysis, individually. Be that as it may, singular investigations have discovered a commonness of a unique ailment as high as fifty eight percent & fifty two percent between dialysis sick persons & chronic kidney disease sick persons not on dialysis, separately. We discovered hyper parathyroid bone infection was the most widely recognized kind of renal Osteo dystrophy in both chronic kidney disease sick persons on dialysis and those not on dialysis. In the dialysis gathering, Para thyroid hormone, alkaline phosphatase, basic alkaline phosphatase and OC were fundamentally higher in those with high turnover (HTO) bone ailment than in those with low turnover (LTO) bone infection. Thus, in interminable kidney ailment (chronic kidney disease) sick persons not on dialysis, Para thyroid hormone, basic alkaline phosphatase, and OC were essentially higher in those with high turnover of bone infection than in those with low turnover of bone malady.

Different techniques, for example, serum biochemical markers, imaging examines, and the tissue changes that affect a part or accompany a disease considers are right now used to analyze renal Osteo dystrophy. Calcium, Phosphorus, para thyroid hormone, alkaline phosphatase, & basic alkaline phosphatase are between the most regularly utilized serum biochemical markers. Like past examinations, we found no huge relationship between Calcium or Phosphorus with pace of bone turnover in ROD.[9, 10].

Serum levels of PTH can foresee the nearness and seriousness of SHPT without corresponding with the basic bone disease.[11,12] Levels of iPTH in dialysis patients multiple occasions ordinary and under multiple times typical are related with a more noteworthy recurrence of high turnover & low turnover of bone sickness, respectively.[13] Although Para thyroid hormone is a decent pointer of bone digestion, the affectability and particularity to determine high turnover of bone illness to have less than five hundred ng/mL and ABD ailment with levels <100 ng/mL are lacking. 28 Bone biopsy concentrates among dialysis patients uncovered that bone rebuilding and reaction to Para thyroid hormone differs between different racial groups.[14.15] In an investigation of 76 ESKD patients, most of African American patients with low turnover of bone malady had higher serum Para thyroid hormone levels than those of whites with low turnover of bone disease[16]. In our precise survey, albeit singular sick persons had varieties in the connection of Para thyroid hormone with basic bone turnover, at a total level there was a decent relationship between's the degree of PTH and bone turnover between both dialysis and non-dialysis patients.

Radiographic assessment of bone can give significant data with respect to the nearness of hyperparathyroidism, for example, osteopenia, sub Periosteal resorption, and blisters. Be that as it may, related with X-Ray finding are less touchy and don't decide kidney osteodystrophy. Between sick persons with advance bone illness, plain movies may uncover subperiosteal resorption in extreme OF or looser zones in serious OM.[17] The significance of bone mineral thickness (BMD) estimation is indistinct in sick persons with renal Osteo dystrophy; be that as it may, a lower BMD has appeared to foresee crack hazard in dialysis patients.[18,19] In chronic kidney disease sick persons, distal span is the favored site for BMD estimation, as BMD of the spine might be deceiving a direct result of aortic calcifications.

The commonness of weaker bone or potentially bone weakening increases the risk of a broken bone additionally increments with a diminishing kidney filtration rate.[20-22] In an investigation of patients with CKD, the most significant levels of BMD in the lumbar spine, hip, and distal lower arm were found in those with a glomerular filtration rate somewhere in the range of 70 and 110 mL/min/1.73 m2 (stages 1 and 2 CKD), while those with a glomerular filtration rate somewhere in the range of 6 and 26 mL/min/1.73 m2 (stage 4 CKD) had the least BMD levels. The variations from the norm in bone digestion that may be answerable for the diminished BMD were not portrayed in these studies.[23-26]

A blend of serum biochemical markers can foresee the hidden pace of bone turnover with more precision. An investigation of 30 constant hemodialysis sick persons

in whom a bone biopsy was acted related to appraisal of biochemical markers indicated that if just PTH was thought about, 36.6% of patients were accurately grouped by their finding. Be that as it may, if both Para thyroid hormone & bone thickness were thought about, forty six point six percent were arranged accurately. Considering Para thyroid hormone & related with x-Ray changes in clavicular and metacarpal bones, for example, Periosteal, endosteal, and intracortical resorption, sixty percent of sick persons were ordered correctly.[21]

Taking everything into account, we found that on an aggregate premise serum levels of Para thyroid hormone, alkaline phosphatase, basic alkaline phosphatase, & osteocalcin are high in highturnover bone sickness and low in low-turnover bone infection. Utilization of a blend of at least 3 markers may decide basic kidney osteodystrophy with more precision than individual biochemical markers. Be that as it may, a bone biopsy ought to be supported in more youthful patients with ESKD, with PTH levels somewhere in the range of two hundred & five hundred pg/dl. Where other biochemical markers are not very much characterized.

CONCLUSION

The most common histological type of renal Osteo dystrophy among dialysis and chronic kidney disease sick persons not on dialysis was hyperparathyroid bone disease; however, the presence of a dynamic bone disease was significant in both groups. A combination of two or three serum biochemical markers such as Para thyroid hormone, alkaline phosphatase, basic alkaline phosphatase, and OC might help clinicians to more accurately diagnose renal Osteo dystrophy in order to assign treatment with vitamin D.

Author's Contribution:

Concept & Design of Study:	Mohammad Husain Bloch
Drafting:	Faisal Iqbal, Nadeem Shafiq
Data Analysis:	Kamran Hamid
Revisiting Critically:	Mohammad Husain Bloch, Faisal Iqbal
Final Approval of version:	Mohammad Husain Bloch

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REFERENCES

1. Prevalence of chronic kidney disease and associated risk factors—United States, 1999–2004. MMWR Morb Mortal Wkly Rep 2007; 56:161-165.
2. Thomas R, Kanso A, Sedor JR. Chronic kidney disease and its complications. Prim Care 2008; 35: 329– 344.
3. Andress DL. Vitamin D treatment in chronic kidney disease. Semin Dial 2005;18: 315– 321.
4. González EA, Sachdeva A, Oliver DA, Martin KJ. Vitamin D insufficiency and deficiency in chronic kidney disease. A single center observational study. Am J Nephrol 2004; 24:
5. Mittalhenkle A, Gillen DL, Stehman-Breen CO. Increased risk of mortality associated with hip fracture in the dialysis population. Am J Kidney Dis 2004;44: 672– 679.
6. Nickolas TL, Leonard MB, Shane E. Chronic kidney disease and bone fracture: a growing concern. Kidney Int 2008;74:721.
7. Alem AM, Sherrard DJ, Gillen DL, et al. Increased risk of hip fracture among patients with end-stage renal disease. Kidney Int 2000;58: 396– 399.
8. Ball AM, Gilllen DL, Sherrard DJ, et al. Risk of hip fracture among dialysis and renal transplant recipients. JAMA 2002;288: 3014– 3018.
9. Kanis JA, Johnell O, De Laet C, et al. International variations in hip fracture probabilities: implications for risk assessment. J Bone Miner Res 2002; 17:1237– 1244.
10. Stehman-Breen CO, Sherrard DJ, Alem AM, et al. Risk factors for hip fracture among patients with end-stage renal disease. Kidney Int 2000;58: 2200– 2205.
11. Tejwani NC, Schachter AK, Immerman I, Achan P. Renal osteodystrophy. J Am Acad Orthop Surg 2006;14: 303.
12. Moe S, Drüeke T, Cunningham J, et al. Definition, evaluation, and classification of renal osteodystrophy: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2006; 69: 1945– 1953.
13. Coco M, Rush H. Increased incidence of hip fractures in dialysis patients with low serum parathyroid hormone. Am J Kidney Dis 2000;36: 1115.
14. Jüppner H, Potts Jr JT. Immunoassays for the detection of parathyroid hormone. J Bone Miner Res 2002;17(Suppl 2): N81– N86.
15. Friedman PA. PTH revisited. Kidney Int Suppl 2004;91: S13– S19.
16. Martin KJ, Olgaard K, Coburn JW, et al. Diagnosis, assessment, and treatment of bone turnover abnormalities in renal osteodystrophy. Am J Kidney Dis 2004; 43: 558– 565.
17. Souberbielle JC, Friedlander G, Cormier C. Practical considerations in PTH testing. Clin Chim Acta 2006;366: 81– 89.
18. Negri AL, Alvarez Quiroga M, Bravo M, et al. Whole PTH and 1-84/84 PTH ratio for the non

invasive determination of low bone turnover renal osteodysthrophy. Nefrologia 2003;23:327– 332.
19. Gal-Moscovici A, Popovtzer MM. New worldwide trends in presentation of renal osteodystrophy and its relationship to parathyroid hormone levels. Clin Nephrol 2005; 63: 284– 2.
20. Ureã P, Bernard-Poenaru O, Ostertag A, et al. Bone mineral density, biochemical markers and skeletal fractures in haemodialysis patients. Nephrol Dial Transplant 2003;18: 2325– 2.
21. Coen G, Mantella D, Manni M, et al. 25-Hydroxyvitamin D levels and bone histomorphometry in hemodialysis renal osteodystrophy. Kidney Int 2005;68:1840– 1848.
22. Coen G, Ballanti P, Balducci A, et al. Renal osteodystrophy: alpha-Heremans Schmid glycoprotein/ fetuin-A, matrix GLA protein serum levels, and bone histomorphometry. Am J Kidney Dis 2006;48: 106– 113.
23. Coen G, Ballanti P, Bonucci E, et al. Renal osteodystrophy in predialysis and hemodialysis patients: comparison of histologic patterns and diagnostic predictivity of intact PTH. Nephron 2002;91:103– 111.
24. Douthat WG, Garay G, de Arteaga J, et al. [Biochemical and histological spectrum of renal osteodystrophy in Argentina]. Nefrologia. 2003; 23(Suppl 2): 47– 5.
25. Bervoets AR, Spasovski GB, Behets GJ, et al. Useful biochemical markers for diagnosing renal osteodystrophy in predialysis end-stage renal failure patients. Am J Kidney Dis 2003; 41: 997
26. Lehmann G, Stein G, Hüller M, et al. Specific measurement of PTH (1-84) in various forms of renal osteodystrophy (ROD) as assessed by bone histomorphometry. Kidney Int 2005;68: 1206– 1214.