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Original Research Article

"Clinical pattern of bone mineral derangements, if any (High bone turnover disease/ Low bone turnover disease) in CKD Patients undergoing Haemodialysis"

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Abstract: Chronic kidney disease related mineral and bone disease (CKD-MBD) is a worldwide challenge in haemodialysis patients associated with high morbidity and mortality. CKD-MBD, the new terminology used for Renal Osteodystrophy and Renal bone disease (KDIGO).In clinical practice, bone biopsy is used infrequently to detect MBD in CKD, because it is an invasive and often expensive procedure and the samples obtained require specialized processing that is not widely available. Instead iPTH levels can be highly sensitive and it is one of the useful noninvasive biochemical parameters to detect MBD in CKD. Therefore, the present study was carried out to detect Pattern of CKD-MBD by non-invasive biochemical method of serum intact parathyroid hormone (iPTH) estimation in CKD patients who have been on haemodialysis for ≥ 5 months. This study was a cross-sectional observational study. The study population of 330 patients (>18 years) on maintenance haemodialysis coming to Dialysis Unit of Department of Medicine over a period of three years were enrolled in the study. Each patient was considered only once for the study. Also biochemical analysis of serum iPTH, corrected calcium, phosphorus and tALP, of all cases were done using fully automated equipments.Patients were divided into three groups ie. High Bone Turn Over (PTH value > 300pg/ml), Low Bone Turn Over (PTH value < 100pg/ml) and a group with apparently Normal Bone (based on 100-300 pg/ml intact PTH values). All statistical analyses were performed using SPSS statistical software, version 17. Chi square, ANOVA with Post-Hoc Tukey HSD and Coefficient tests were used. The control of CKD-MBD was assessed in the backdrop of the KDIGO guidelines. In the present study Nineteen patients were complained with bone pain and almost five patients were had bone fracture. MBD presents itself in three forms in CKD patients undergoing Haemodialysis in the present study. In clinical pattern most common MBD was found in the present study High bone turn over (40.3%) followed by low bone turn over (33.5 %, iPTH<100 pg/mL) and normal bone turn over (26.2%).There were statistically significant association of serum iPTH, with Corrected Ca and P ($p = 0.032$ and $p = 0.035$, respectively) observed. The results of the present study revealed that bone pain was significantly associated with iPTH levels.(χ^2 =6.631 and P=0.036). The pattern of CKD-MBD is dominated by high bone turn-over disease in our centre. We have also demonstrated that disorders of mineral metabolism are associated with short-term effects, such as hospital admissions and muscle- and skin and bone complaints. Short of a bone biopsy, biochemical tests such as an intact PTH can be used to evaluate bone disease because markedly high or low values do predict underlying bone turnover. Controlling PTH levels prevents damage to bones. PTH levels should be evaluated regularly in haemodialysis patients and awareness regarding PTH abnormalities should be there among the treating physicians also.
Keywords: Haemodialysis, High bone turn over, Low bone turn over, Parathyroid hormone, Bone-Mineral disorders.

INTRODUCTION:

Chronic kidney disorders have a progressive course in most cases, and finally result in end-stage renal disease (ESRD) [1]. End-stage renal disease (ESRD) is reached as soon as the renal function drops below 10 to 15 percent of the normal function [2]. Many people who have severe chronic kidney disease (CKD) will eventually develop kidney failure and will require dialysis. Despite remarkable advances in the technical ability to provide maintenance dialysis, the mortality rate of patients on long-term dialysis has remained unacceptably high and not significantly improved over the past decade.

Chronic kidney disease related mineral and bone disease (CKD-MBD) is a worldwide challenge in haemodialysis patients[3]. With chronic reduction in kidney function, there is an increase in the levels of PTH and eventually a decrease in levels of 1,25 vitamin D, both these processes obviously affect the bones. Increased PTH level and decreased 1, 25 vitamin D both affect bone turnover associated with abnormal bone mineralization [4]. The disorders of bone have to be considered not only with regard to the bone itself but also with regard to the consequences of disturbed mineral metabolism at extra skeletal sites, including the vasculature [5].

CKD-MBD, the new terminology given by KDIGO(Kidney Disease: Improving Global Outcomes)[5], is an international initiative with a key mission of developing evidence-based clinical practice guidelines used for Renal Osteodystrophy and Renal bone disease, is essentially a broad clinical disorder which is a manifestation of any one or combination of various abnormalities in clinical setting like[6]:

- Abnormalities of biochemical parameters (calcium, phosphorus, parathyroid hormone (PTH) and Vitamin D metabolism).
- Abnormalities in bone turn over, mineralization, volume, linear growth or strength.
- Calcification of the vasculature or other soft tissues (KDIGO 2009)[5].

These are closely inter-related and together MBD in CKD has high morbidity and mortality in patients receiving dialysis [7].

In clinical practice, bone biopsy is used infrequently to detect MBD in CKD, because it is an invasive and often expensive procedure and the samples obtained require specialized processing that is not widely available [8,9]. Instead iPTH levels can be highly sensitive and it is one of the useful noninvasive biochemical parameters to detect MBD in CKD. In India, number of dialysis patients is growing but few data are available about their bone mineral derangements or bone disorders in variance with studies carried out in the west.

Therefore, the present study was carried out to detect Pattern of CKD-MBD by non-invasive biochemical method of serum intact parathyroid hormone (iPTH) estimation in CKD patients who have been on haemodialysis for ≥ 5 months in the dialysis unit at Gian Sagar hospital, Punjab.

MATERIALS AND METHODS:

SOURCE OF DATA

This study was a hospital- based cross-sectional observational study.The study was conducted under the Department of Physiology of Gian Sagar Medical College and Hospital, in close collaboration with Dialysis Unit-Department of Medicine and Department of Biochemistry. The study was based on data collected on patients coming to dialysis unit of department of Medicine, Gian Sagar Medical Hospital, Ramnagar, and Patiala. All the Chronic Kidney Disease Patients on maintenance haemodialysis coming to Dialysis Unit of Department of Medicine of Gian Sagar Medical College & Hospital, Ramnagar (Patiala) over a period of three years from December,2012 till December,2015. Each patient was considered only once for the study.

Sampling method – Non Random sampling method
Sample (enrolled patients during a period of three years) –Three hundred thirty (330) CKD patients on maintenance haemodialysis .

Ethical approval and informed consent: - This study was approved by ethical committee of Gian Sagar medical College and Hospital. An informed consent was taken from all the subjects before the initiation the study. All the subjects were duly informed about the purpose of asking questions as per Performa attached with consent form, details of blood sample collection, risk factors and precautions.

Sampling Criteria: Inclusion criteria: All the Patients (>18 years) on maintenance haemodialysis coming to Dialysis Unit of Department of Medicine of Gian Sagar Medical College & Hospital, Ramnagar (Patiala) during study period of three years (December, 2012-December, 2015) were enrolled in the study. Each patient was considered only once for the study. Both male and female was included in this study.

Patients with history of previous bone and skeletal disease (e.g. osteopetrosis, achondroplasia, kyphoscoliosis etc.) unrelated to present ailment were excluded on the basis of medical history (present and past) obtained from the patient.

METHOD OF COLLECTION OF DATA

The study was started after proper approval from Institutional Research Ethics Committee. Patients were selected based upon the inclusion and exclusion criteria.

Approach to a Patient was begun by taking informed consent, after proper Medical examination. The detailed Medical history as well as baseline demographic data like Age (Yrs.), Gender(M/F), Weight(kg), Height(cm), BMI(Body Mass Index), Religion, Educational Status (Literate/Illiterate), Environmental Status (Urban/Rural), were recorded as per Performa attached.

Blood sample was collected for laboratory investigations (like Serum calcium, Serum phosphorous, Serum alkaline phosphatase, Serum intact

parathormone (iPTH). Blood sample were collected with aseptic precautions after obtaining informed consent from the patients.

All the above parameters were done on fully automated equipments standardized in Gian Sagar Hospital.

- Dietary history of the patients was taken.
- Detailed history regarding the intake of phosphate binders both calcium based and Non-calcium based and Vitamin–D analogues was taken.

Normal values of serum calcium (corrected for albumin) and phosphate were defined as 8.5-10.5 mg/dl and 2.5-4.5 mg/dl respectively. PTH level >300 pg/ml (2 times the upper limit of the assay) was labelled as hyperparathyroidism (High Bone Turn Over).The detailed data related to CKD-MBD was Collected in Performa and fed into custom built database. Observations and results were compiled at the end of the study. The control of CKD-MBD was assessed in the backdrop of the KDIGO guidelines. All the Demographic and laboratory parameters were compared in all groups by using appropriate statistical method.

Statistical Analysis

The data were analyzed using statistical package for social sciences SPSS (Statistical Package for Social Science) package version 17.0. Descriptive statistics such as range, mean and standard deviation were used to describe continuous variables while numbers and percentages were used to present discreet variables. Chi square test and ANOVA with Post-Hoc Tukey HSD tests were used to test association between clinical and laboratory parameters and Pearson's coefficient of correlation were used to assess the inter-relationship between various examined laboratory markers. The result was statistically significant when the P-value was less than 0.05.

STATISTICAL RESULTS:

The major predictor variables were patient characteristics and laboratory markers of mineral metabolism.

All patients of CKD required dialysis at presentation were grouped into three groups based on serum iPTH results: "Low Pth "relative hypoparathyroidism": serum iPTH<100 pg/ml; "target PTH": iPTH 100-300 pg/ml; and "high PTH": iPTH>300 pg/ml corresponding to hyperparathyroidism disease. The analyzed PTH data (n=263) were based upon iPTH measurements.

RESULTS & DISCUSSION

Chronic kidney disease related mineral and bone disease (CKD-MBD) is a worldwide challenge in haemodialysis patients [3]. Bone abnormalities are found almost universally in patients with progressive loss of renal function in CKD necessitates the eventual use of dialysis ((stage 5D) [5].

The present study was a hospital-based cross-sectional observational study. The study population of 330 patients comprised adults, predominantly belonging to the rural (66.4%)-strata and Sikh community (62.7%) with a mean age of 52.67 ± 15.05 (range 25 to 98 years), of whom mostly patients were taking vegetarian diet (58.2%).The mean age of our study population was similar to other studies like a mean age of 49.3 years with range 17-80[10] and a mean age of 46.6 ± 13.4 years [11]. However, higher mean age was reported in a Western and an Indian study [12-14].

In our study, It was observed that the predominant probable cause of chronic kidney disease was diabetes mellitus (51.8%), followed by drug induce uropathy (27.6%), hypertension (14.5%), and obstructive uropathy (6.1%). Our study was in accordance with other study conducted in 2012 [10].

In the clinical profile of the present study most commonly reported symptoms were Pruritus (6.1%), pedal oedema (40.6%) and proximal muscle weakness (13.9%). In addition, bone pain and bone fracture were found in mild proportion 19.1 % and 4.8 %, respectively. Radiological findings revealed features suggestive of bone fracture on the base of recent medical history/records. In the present study, majority of clinical symptoms related CKD-MBD was found absent in CKD patients undergoing dialysis, reinforcing the fact that CKD-MBD is a clinically silent disease.

Our results were in accordance with observations of Valson T, 2014[11], who reported similar clinical symptoms like bone pain (33.5%), proximal muscle weakness (26.2%) and pruritus (25.5%), but in high percentage as compare to our findings.

The results of our study also revealed that bone pain was significantly association with iPTH levels(both low and high level) (χ^2 = 6.631 and p=0.036). It was observed that the percentage of ckd patients on haemodialysis of bone fracture was slight more in hyperparathyroidism group (46.7 %)as compare to hypo and normal para thyroidism(40.05 ,13.3% ,respectively). This difference was not statistically significant (χ^2= 1.372, P=0.503). Although, the incidence found for fracture was very low, only 5 %(table no 13.). PTH was also significantly associated with other physical symptoms like proximal muscle weakness and eyes problem (p=0.016 and p=0.001). statistically p value was less than 0.05.

Table-1: Proportion of demographic and clinical characteristics of patients

		dialysis patients(n = 330)	%
Age (years)	20 – 40	73	22.10
	41 – 60	159	48.20
	61 – 80	87	26.40
	>80	11	3.30
	52.67 ± 15.05		
Sex	Female	115	34.80
	Male	215	65.20
Religion	Hindu	122	37.00
	Muslim	1	0.30
	Sikh	207	62.70
Educational Status	Illiterate	180	54.50
	Literate	150	45.50
Environmental Status	Rural	219	66.40
	Urban	111	33.60
Dietary History	Non-vegetarian	138	41.80
	Vegetarian	192	58.20
Cause of CKD	Diabetes mellitus	171	51.8
	Drug induce	91	27.6
	Hypertension	48	14.5
	Obstruction	20	6.1
Frequency of dialysis(visit per week)	1	73	22.1
	2	188	57.0
	3	69	20.9
	1.71 ± 1.47		
Bone Pain	Absent	267	80.9
	Present	63	19.1
Bone Fracture	Absent	314	95.2
	Present	16	4.8
Pruritus	Absent	310	93.9
	Present	20	6.1
Relevant Bone Abnormalities	Absent	328	99.4
	Present	2	.6
Intake of Phosphate binders	Not Used	250	75.8
	Used	80	24.2
Pedal Oedema	Absent	196	59.4
	Present	134	40.6
Bony tenderness/ Deformity	Absent	322	97.6
	Present	8	2.4
Proximal Muscle Weakness	Absent	284	86.1
	Present	46	13.9
Irritation in Eyes	Absent	286	86.7
	Present	44	13.3

Table 2: Laboratory findings in haemodialysis patients

Laboratory Investigations:		dialysis patients (n = 330)	%
PTH Level	Below Normal	88	33.5
	Normal	69	26.2
	Above Normal	106	40.3
		(n = 263)	
Ca Level	Below Normal	167	50.6
	Normal	146	44.2
	Above Normal	17	5.2
P Level	Below Normal	3	.9
	Normal	122	37.0
	Above Normal	205	62.1
ALP Level	Below Normal	2	.6
	Normal	165	50.0
	Above Normal	163	49.4

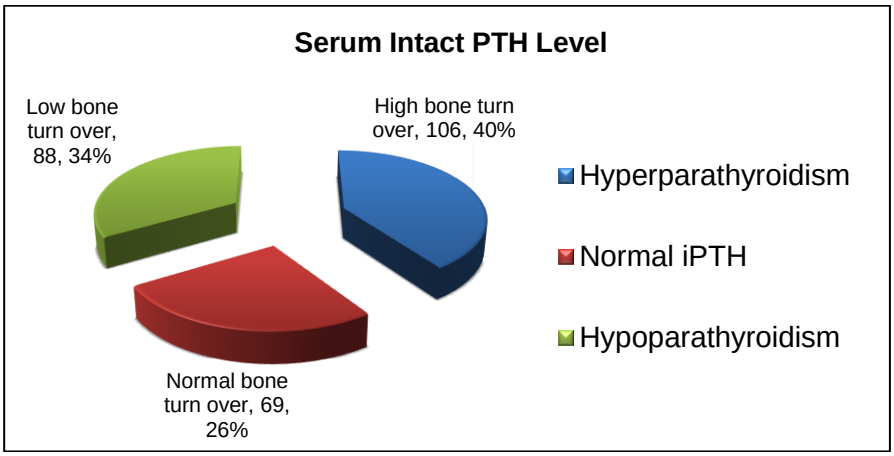

Fig-1: Clinical Pattern of CKD-MBD undergoing Haemodialysis Patients.

Table 3: Association of Parathormone with other clinical & biochemical variables

Table 3.a

Presence of Bone Pain	PTH Level			Total
	<100	100 – 300	>300	
Absent	64 (29.9%)	60 (28.0%)	90 (42.1%)	214
Present	24 (49.0%)	9 (18.4%)	16 (32.7%)	49
Total	88 (33.5%)	69 (26.2%)	106 (40.3%)	263

χ^2 = 6.631; df = 2; P = 0.036; Significant

Table 3.b

Presence of Bone Fracture	PTH Level			Total
	<100	100 – 300	>300	
Absent	82 (33.1%)	67 (27.0%)	99 (39.9%)	248
Present	6 (40.0%)	2 (13.3%)	7 (46.7%)	15
Total	88 (33.5%)	69 (26.2%)	106 (40.3%)	263

χ^2 = 1.372; df = 2; P = 0.503; Not significant

Table 3.c

Proximal Muscle Weakness	PTH Level			Total
	<100	100 – 300	>300	
Absent	69 (30.3%)	64 (28.1%)	95 (41.7%)	228
Present	19 (54.3%)	5 (14.3%)	11 (31.4%)	35
Total	88 (33.5%)	69 (26.2%)	106 (40.3%)	263

χ^2 = 8.220; df = 2; P = 0.016; Significant

Table 3.d

Irritation in Eyes	PTH Level			Total
	<100	100 – 300	>300	
Absent	67 (29.4%)	65 (28.5%)	96 (42.1%)	228
Present	21 (60.0%)	4 (11.4%)	10 (28.6%)	35
Total	88 (33.5%)	69 (26.2%)	106 (40.3%)	263

χ^2 = 13.252; df = 2; P = 0.001; Significant

Tabel 3.e

ALP Level	PTH Level			Total
	<100	100 – 300	>300	
Below Normal	0 (0.0%)	1 (50.0%)	1 (50.0%)	2
Normal	47 (36.2%)	42 (32.3%)	41 (31.5%)	130
Above Normal	41 (31.3%)	26 (19.8%)	64 (48.9%)	131
Total	88 (33.5%)	69 (26.2%)	106 (40.3%)	263

χ^2 = 10.331; df = 4; P = 0.035; Significant

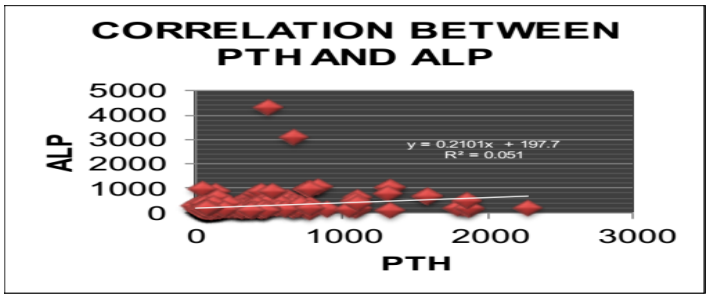

Fig-2: Pearson's Correlation Coefficient between iPTH and tALP

Clinical Pattern of CKD-MBD: MBD presents itself in three forms in CKD patients undergoing haemodialysis in the present study. In clinical pattern most common MBD was found in the present study High bone turn over (40.3%) by taking iPTH >300 pg/mL followed by low bone turn over (33.5 %, iPTH<100 pg/mL) and normal bone turn over (26.2%).In the current study, the other laboratory profile was found Hyperphosphatemia (62.1%) followed by Hypocalcaemia (50.6%) and elevated tALP level (49.4%).

In favour to our results Okoye *et al.;* 2015 [7] concluded that the prevalence of various mineral bone disease abnormalities were 70% hyperphosphatemia and 85% hyperparathyroidism among the patients. But in this study prevalence of hyperparathyroidism were much high as compare to us. Agarwal described hypocalcemia in 49.6%, and hyperphosphatemia in 41.8% CKD -5 patients [15].

In contrast, The PTH levels in the three studies [16-18] have identified patients with normal bone and ABD. Ziólkowska H, 2000[18] found that PTH level of <50 pg/ml was suggestive of ABD, but the difference from normal bone was not significant.

Serum alkaline phosphatase, was found significantly high in CKD patients undergoing haemodialysis in the current study, which is also a biochemical marker of bone turnover and is used to monitor the metabolic bone disease associated with renal insufficiency and also signifies high turnover bone disease when elevated and interpreted in appropriate circumstances. In this study, tALP level >170 IU/L (i.e., upper level of normal) was present in 49.4% of CKD on haemodialysis patients.

Jabbar *et al.;* 2007 found raised bone alkaline phosphatase (>45 IU/L) in 60% of their stage 5 CKD patients [19]. Statistically, it was proved that PTH is directly associated with P and ALP level. Results were evident with the help of statistically analysis (p value was < 0.05, significant).

Overall, the high prevalence of Hyperphosphatemia, hypocalcemia and hyperparathyroidism in this study is consistent with findings from previous hospital based surveys on CKD-MBD in India[14,20].There is positive relationship between PTH and tALP (0.226) which was significant at both 0.05 and 0.01 levels of confidence interval. Statistically, a negative but significant correlation exists between corrected Ca and p (0.05 level of confidence interval). Calcium and phosphate show weak insignificant relationships with PTH.

Impaired phosphate excretion, with the resulting hyperphosphatemia, is one of the earliest consequences of chronic renal failure. Hyperphosphatemia in turn plays an important role in the development of secondary hyperparathyroidism [21, 22]. Moreover, phosphate retention leads to a decrease in serum free calcium levels (hypocalcaemia), which in turn stimulates PTH secretion [23].

CONCLUSION:

The pattern of CKD-MBD is dominated by high bone turn-over disease in our centre. Only a small proportion adheres to the targets as advised in the KDIGO guidelines for bone metabolism and disease in CKD. With the work reported in this thesis we demonstrated that these disorders are associated with important negative clinical outcomes with reduced survival, more muscle and bone problems. Short of a bone biopsy, biochemical tests such as an intact PTH can be used to evaluate bone disease because markedly high or low values do predict underlying bone turnover.Controlling PTH levels prevents damage to bones. Usually, overactive parathyroid glands are controllable with a change in diet, dialysis treatment, or medication.

PTH levels should be evaluated regularly in haemodialysis patients and awareness regarding PTH abnormalities should be there among the treating physicians also.

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COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical standards: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and all patients gave the informed consent prior being included into the study. This study was approved by the Research Ethics Committee (or Institutional Review Board)"

REFERENCES

1. Taj Bakhsh R, Joshaghani HR, Bayzayi F, Haddad M, Qorbani M. Association between pruritus and serum concentrations of parathormone, calcium and phosphorus in haemodialysis patients. Saudi Journal of Kidney Diseases and Transplantation. 2013 Jul 1; 24(4):702.
2. National Kidney and Urologic Diseases Information Clearing house (NKUDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is part of the National Institutes of Health NIH Publication No. 03–4241. Updated July 2003. <http://kidney.niddk.nih.gov/kudiseases/pubs/yourkidneys/>
3. Seck S, Dahaba M, Ka E, Cisse M, Gueye S, Tal AL. Mineral and bone disease in black African haemodialysis patients: a report from Senegal. Nephro-urology monthly. 2012 Sep; 4(4):613-6.
4. Martin KJ, Olgaard K, Group BT, Coburn JW, Coen GM, Fukagawa M, Langman C, Malluche HH, McCarthy JT, Massry SG, Mehls O. Diagnosis, assessment, and treatment of bone turnover abnormalities in renal osteodystrophy. American journal of kidney diseases. 2004 Mar 31; 43(3):558-65.
5. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney international. Supplement. 2009 Aug (113):S1.
6. Uhlig K, Berns JS, Kestenbaum B, Kumar R, Leonard MB, Martin KJ, Sprague SM, Goldfarb S. KDOQI US commentary on the 2009 KDIGO clinical practice guideline for the diagnosis, evaluation, and treatment of CKD–mineral and bone disorder (CKD-MBD). American Journal of Kidney Diseases. 2010 May 31; 55(5):773-99.
7. Okoye JU, Arodiwe EB, Ulasi II, Ijoma CK, Onodugo OD. Prevalence of CKD-MBD in pre-dialysis patients using biochemical markers in Enugu, South-East Nigeria. African health sciences. 2015 Sep; 15(3):941-8.
8. Moe S, Drüeke T, Cunningham J, Goodman W, Martin K, Olgaard K, Ott S, Sprague S, Lameire N, Eknoyan G. Definition, evaluation, and classification of renal osteodystrophy: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney international. 2006 Jun 1; 69(11):1945-53.
9. Muhle FH. Controversies surrounding the use of Parathyroid hormone as a marker of bone metabolism in chronic kidney disease (CKD) patients on haemodialysis in Zimbabwe: The way forward (Doctoral dissertation, University of Zimbabwe).
10. Prasad R, HA KM, Surathkal M. Clinical And Biochemical Spectrum Of Chronic Kidney Disease In Tertiary Care Center. Journal of Evolution of Medical and Dental Sciences. 2012; 1(1):1214-22.
11. Valson AT, Sundaram M, David VG, Deborah MN, Varughese S, Basu G, Mohapatra A, Alexander S, Jose J, Roshan J, Simon B. Profile of incident chronic kidney disease related-mineral bone disorders in chronic kidney disease stage 4 and 5: a hospital based cross-sectional survey. Indian journal of nephrology. 2014 Mar; 24(2):97.
12. Molony DA, Craig JC, editors. Evidence-based nephrology. Wiley-Blackwell; 2009 Jan 22.
13. Agarwal SK, Dash SC, Irshad M, Raju S, Singh R, Pandey RM. Prevalence of chronic renal failure in adults in Delhi, India. Nephrology Dialysis Transplantation. 2005 Aug 1; 20(8):1638-42.
14. Ghosh B, Brojen T, Banerjee S, Singh N, Singh S, Sharma OP, Prakash J. The high prevalence of

chronic kidney disease-mineral bone disorders: A hospital-based cross-sectional study. Indian journal of nephrology. 2012 Jul 1; 22(4):285.

15. Agarwal SK. Assessment Of Renal Bone Mineral Disorder In Naïve Ckd Patients: A Single Center Prospective Study. Indian Journal of Nephrology. 2007 Jul 1; 17(3).
16. Mathias R, Salusky I, Harman W, Paredes A, Emans J, Segre G, Goodman W. Renal bone disease in pediatric and young adult patients on haemodialysis in a children's hospital. Journal of the American Society of Nephrology. 1993 Jun 1; 3(12):1938-46.
17. Salusky IB, Ramirez JA, Oppenheim W, Gales B, Segre GV, Goodman WG. Biochemical markers of renal osteodystrophy in pediatric patients undergoing CAPD/CCPD. Kidney international. 1994 Jan 31; 45(1):253-8.
18. Ziółkowska H, Pańczyk-Tomaszewska M, DęLbiński A, Polowiec Z, Sawicki A, Sieniawska M. Bone biopsy results and serum bone turnover parameters in uremic children. Acta paediatrica. 2000 Jun 1; 89(6):666-71.
19. Jabbar Z, Aggarwal PK, Chandel N, Khandelwal N, Sakhuja V, Jha V. Noninvasive Assessment Of Bone Mineral Status In Indian Ckd Population-A Cross-Sectional Study. Indian Journal of Nephrology. 2007 Jul 1; 17(3).
20. Jabbar Z, Aggarwal PK, Chandel N, Kohli HS, Gupta KL, Sakhuja V, Jha V. High prevalence of vitamin D deficiency in north Indian adults is exacerbated in those with chronic kidney disease. Nephrology. 2009 Apr 1; 14(3):345-9.
21. Ritz E, Matthias S, Seidel A, Reichel H, Szabo A, Hörl WH. Disturbed calcium metabolism in renal failure--Pathogenesis and therapeutic strategies. Kidney International Supplement. 1992 Oct 2(38).
22. Llach F, Bover J. Renal osteodystrophy In: Brenner BM. (editor) Philadelphia, W.b. Saunders Company.The Kidney 1996; 2:2187-2203.
23. Drueke T. The pathogenesis of parathyroid gland hyperplasia in chronic renal failure. Kidney international. 1995 Jul 1; 48(1):259-72.