Section: Nephrology

Original Research Article

A STUDY ON THE PREVALENCE AND PATTERN OF CHRONIC KIDNEY DISEASE MINERAL BONE DISORDERS AMONG HAEMODIALYSIS PATIENTS FROM A TERTIARY CARE CENTRE IN SOUTH INDIA – RETROSPECTIVE STUDY

Leelavathi V[1], Bhushan C Shetty[2], Sujatha Siddappa[3]

[1]Associate Professor of Nephrology, Institute of Nephrourology, Bangalore, Karnataka, India.
[2]Assistant Professor of Nephrology, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, Karnataka, India.
[3]Professor of Pathology, Institute of Nephrourology, Bangalore, Karnataka, India.

Received : 05/05/2023
Received in revised form : 08/06/2023
Accepted : 17/06/2023

Keywords:
chronic kidney disease, mineral bone disease, secondary hyperparathyroidism.

Corresponding Author:
Dr. Bhushan C Shetty,
Email: shettycbhushan@gmail.com

DOI: 10.47009/jamp.2023.5.3.414

Source of Support: Nil,
Conflict of Interest:None declared

Int J Acad Med Pharm
2023; 5(3); 2102-2107

Abstract

Background: Chronic kidney disease – Mineral bone disease (CKD-MBD) refers to a systemic disorder of mineral and bone metabolism. Patterns and the prevalence of these factors should be studied among our population for better quality of life. **Aims/Objectives:** (1) To study the demographic profile; (2) To distinguish between high turnover bone disease, normal bone disease, and dynamic bone disease based on iPTH values (3) To study the association between iPTH values and alkaline phosphatase levels; (4) To know the multiple regression analysis to find potential risk factors for CKD/MBD. **Materials and Methods:** Patient details regarding physical examinations and blood investigation reports were reviewed. Analyses of 25(OH) D3 and intact PTH (iPTH) were performed using electrochemiluminescence immunoassay. **Results:** The present study comprised 99 patients, of whom 58 (58.59%) were men and 41 (41.41%) were women. The patients had mean iPTH values of 537.63 pg/ml, with 6 (6.06%) having dynamic bone disease and 45 (45.45%) having high turnover bone disease. 23 subjects had their vitamin D levels checked, and all exhibited severe deficiencies. A logistic regression analysis of the prediction of CKD MBD showed age, sex, duration of dialysis, anaemia, and acidosis are the risk factors for the development of MBD. Spearman's rank correlation revealed a link between iPTH values and alkaline phosphatase levels. **Conclusion:** In the present study, in CKD patients, secondary hyperparathyroidism, hyperphosphatemia, hypocalcaemia, elevated alkaline phosphatase, vitamin D insufficiency were frequent conditions. The early stages of CKD should be the first time that MBD should be monitored.

INTRODUCTION

The term "chronic kidney disease-mineral bone disorder" (CKD-MBD) refers to a systemic disorder of mineral and bone metabolism caused by abnormalities in the metabolism of calcium, phosphorus, parathyroid hormone (PTH), or vitamin D, abnormalities in bone turnover, mineralization, volume, linear growth, or strength, and vascular or soft tissue calcification.[1] These endocrine and mineral processes play a crucial role in the regulation of adult bone structure and function as well as the beginning of bone creation during growth (bone modelling) (bone remodeling. As a result, people with CKD who require dialysis (stage 5D) and the vast majority of those with CKD stages 3-5.[2] both have abnormalities in their bones. Long before the necessity for renal replacement therapy, anomalies in bone mineral metabolism appear during the early stages of chronic kidney disease (CKD). The chosen therapeutic approach might have a favourable or negative impact on these abnormalities. As a result, it is advised that attending doctors keep an eye on and manage biochemical markers early in the onset of CKD before the requirement for dialysis. The possibility of extra skeletal calcification because of CKD's aberrant mineral and bone metabolism and the treatments used to treat these abnormalities has become a growing source of worry. According to several cohort studies, there are links between problems with mineral metabolism and fractures, cardiovascular disease, and death in people with CKD.[3]

Due to variations in ethnicities and dialysis methods, there is a lack of representative data on the prevalence of CKD-MBD and its range. With different dialysis

ISSN(O): 2687-5365; ISSN(P): 2753-6556

modalities and in different populations, each of these categories' relative prevalence varies.[4] There are few data on CKD and MBD in India, despite the significant frequency of MBDs in CKD patients. This research's objective was to examine the prevalence and distribution of MBDs in CKD patients at various stages.

MATERIALS AND METHODS

This is a cross-sectional study of 99 patients with chronic kidney disease who visited the institute of nephrourology in Bangalore and was in varying stages of the disease.

Inclusion Criteria

The patients diagnosed with CKD and above 18 years of age who gave written consent for treatment were selected for the study.

Exclusion Criteria

Refusal to consent, being under the age of 18, having thyroid or liver disease, having primary or metabolic bone disease, or being on hormone replacement treatment were excluded from the study.

Method

The patients were asked about and provided with details about suspected CKD causes, the length of time spent receiving dialysis, the usage of phosphate binders, and vitamin D supplements. All patient details regarding physical examinations, and blood investigation reports such as albumin, creatinine, bicarbonate, potassium, calcium, phosphorus, alkaline phosphatase, PTH, and 25-hydroxyvitamin D3 (25[OH]D3) were reviewed. Based on a documented history of progressive oedema, early hypertension, proteinuria of > 1gm/day, and red cell cast in urine, it was thought that the patient had chronic glomerulonephritis. And bilaterally shrunken kidneys on ultrasonography, bland urine sediment with proteinuria of < 1 gm/day, are taken as presumed chronic interstitial nephritis. A known diabetic (5 years old) with microalbuminuria or proteinuria, hypertension, azotemia, and normal or enlarged kidneys on ultrasonography was considered to have diabetic nephropathy. The diagnosis of obstructive uropathy was made using clinical and biochemical indicators of kidney disease in a patient with a history of kidney disease, ultrasonography signs of hydronephrosis, and clinical evidence of urinary obstruction. Analyses of 25(OH) D3 and intact PTH (iPTH) were performed using electrochemiluminescence immunoassay. Based on the serum level of iPTH, patients were classified into:

1. SHPTH; iPTH>400 pg/ml
2. Adynamic bone disease (ABD); iPTH<65 pg/ml

The duration of the study was from January 2022 to December 2022.

Statistical Analysis

The Statistical Package for the Social Sciences Version 20 was used to analyse the data. The mean and standard deviation were used to present quantitative variables. Nonparametric variables' means were compared using the Mann-Whitney U-test, and the relationship between several groups was identified using Spearman's rank-order correlation. To find potential CKD-MBD risk variables, multiple regression analysis was employed. Significant values were noted. The statistical analysis was carried out in SPSS software. The ratio of male and female was 2:1.

RESULTS

Table-1: The study comprised 99 patients in total, of whom 58 (58.59%) were men and 41 (41.41%) were women. The majority of them were between the ages of 51 and 60.

Table 2: The patients had mean iPTH values of 537.63 pg/ml, with 6 (6.06%) having a dynamic bone disease and 45 (45.45%) having a high turnover bone disease. Twenty-three subjects had their vitamin D levels checked, and they all exhibited severe deficiencies.

Table 3: Prevalence of CKD MBD according to Native kidney disease included ADPKD, A typical HUS, C3GN, CAKUT, CIN, CPN, DKD, FSGS, IGA nephropathy, IRGN with severe IFTA, Nephronophthisis, Obstructive uropathy, Presumed CGN, Presumed CIN and Total 99 patients.

Table 4: Logistic regression analysis of the prediction of CKD MBD showed that age, sex, duration of dialysis, anemia, and acidosis are the risk factors for the development of MBD, though they were not statistically significant in our study.

Table 1: Prevalence of CKD MBD according to age

Age groups	Without CKD MBD	%	With CKD MBD	%	Total	%
<=30yrs	0	0.00	26	100.00	26	26.26
31-40yrs	1	6.67	14	93.33	15	15.15
41-50yrs	1	6.25	15	93.75	16	16.16
51-60yrs	3	11.11	24	88.89	27	27.27
>=61yrs	1	6.67	14	93.33	15	15.15
Total	6	6.06	93	93.94	99	100.00
Mean age	54.00		43.72		44.34	
SD age	12.62		16.06		16.01	

ISSN(O): 2687-5365; ISSN(P): 2753-6556

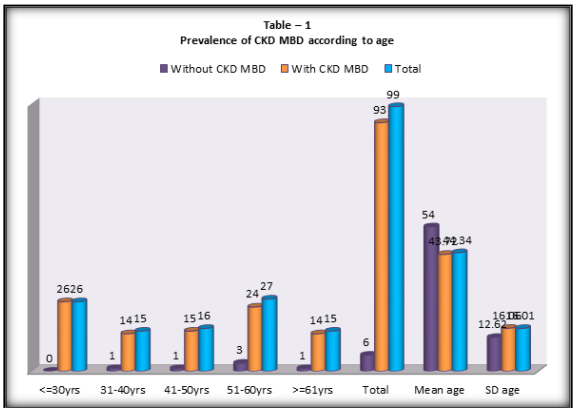
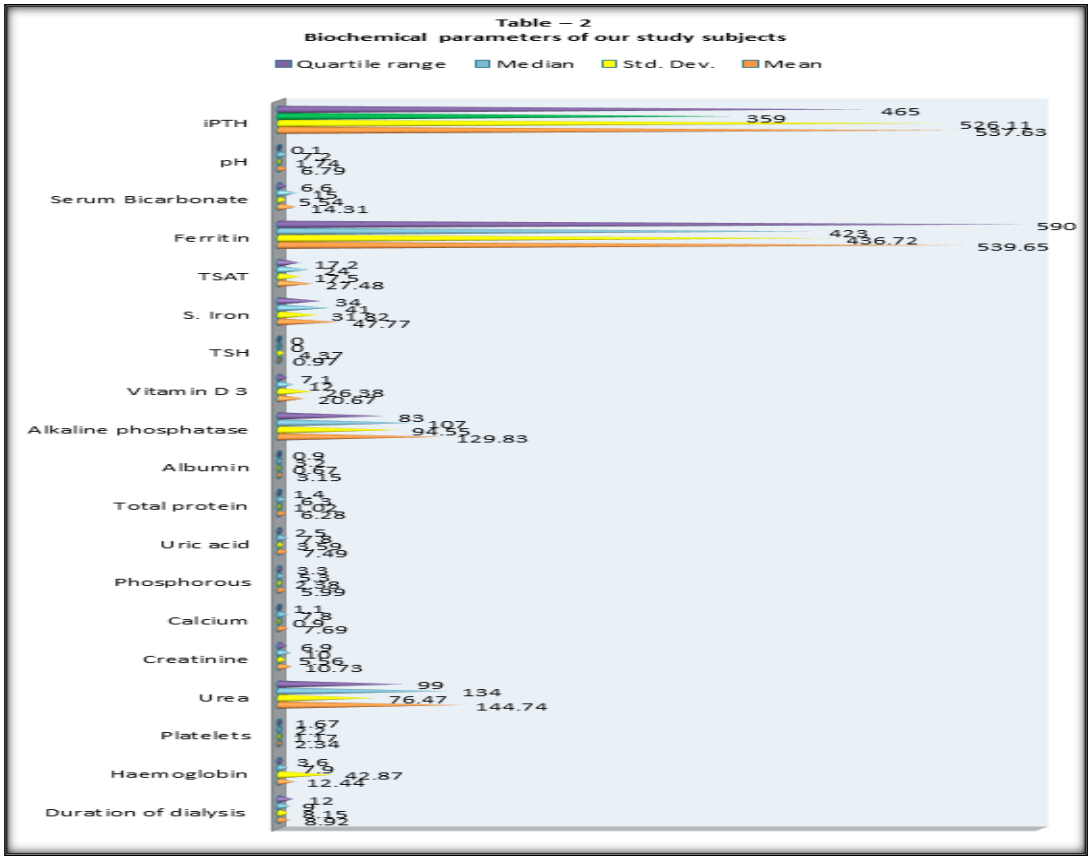


Table 2: Biochemical parameters of our study subjects

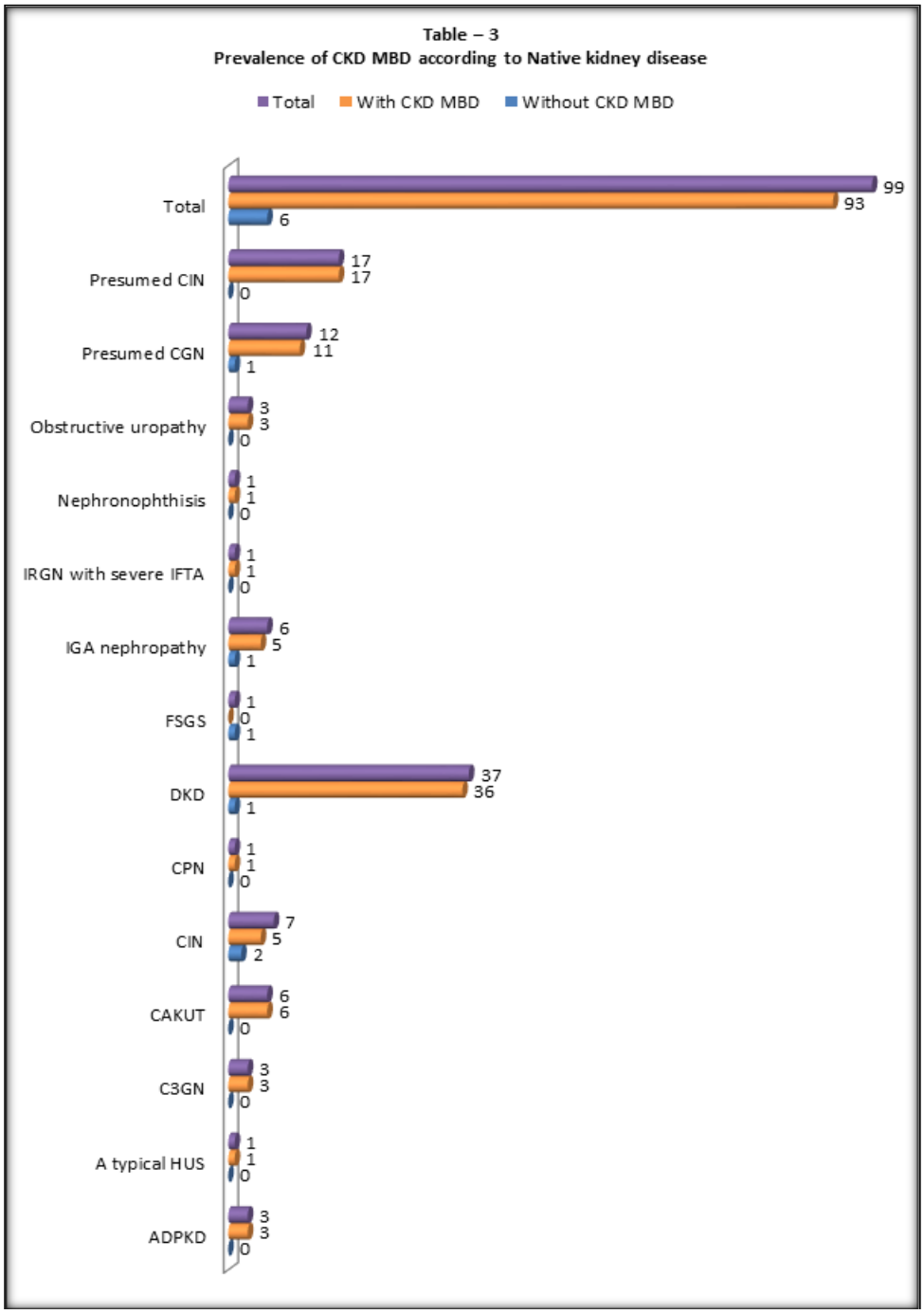
Numerical variables	Mean	Std. Dev.	Median	Quartile range
Duration of dialysis (in months)	8.92	8.15	9.00	12.00
Haemoglobin	12.44	42.87	7.90	3.60
Platelets	2.34	1.17	2.20	1.67
Urea	144.74	76.47	134.00	99.00
Creatinine	10.73	5.56	10.00	6.90
Calcium	7.69	0.90	7.80	1.10
Phosphorous	5.99	2.38	5.30	3.30
Uric acid	7.49	3.59	7.80	2.50
Total protein	6.28	1.02	6.30	1.40
Albumin	3.15	0.67	3.20	0.90
Alkaline phosphatase	129.83	94.55	107.00	83.00
Vitamin D 3	20.67	26.38	12.00	7.10
TSH	0.97	4.37	0.00	0.00
S. Iron	47.77	31.82	41.00	34.00
TSAT	27.48	17.50	24.00	17.20
Ferritin	539.65	436.72	423.00	590.00
Serum Bicarbonate	14.31	5.54	15.00	6.60
pH	6.79	1.74	7.20	0.10
iPTH	537.63	526.11	359.00	465.00



ISSN(O): 2687-5365; ISSN(P): 2753-6556

Table 3: Prevalence of CKD MBD according to Native kidney disease

Native kidney disease	Without CKD MBD	%	With CKD MBD	%	Total	%
ADPKD	0	0.00	3	100.00	3	3.03
A typical HUS	0	0.00	1	100.00	1	1.01
C3GN	0	0.00	3	100.00	3	3.03
CAKUT	0	0.00	6	100.00	6	6.06
CIN	2	28.57	5	71.43	7	7.07
CPN	0	0.00	1	100.00	1	1.01
DKD	1	2.70	36	97.30	37	37.37
FSGS	1	100.00	0	0.00	1	1.01
IGA nephropathy	1	16.67	5	83.33	6	6.06
IRGN with severe IFTA	0	0.00	1	100.00	1	1.01
Nephronophthisis	0	0.00	1	100.00	1	1.01
Obstructive uropathy	0	0.00	3	100.00	3	3.03
Presumed CGN	1	8.33	11	91.67	12	12.12
Presumed CIN	0	0.00	17	100.00	17	17.17
Total	6	6.06	93	93.94	99	100.00



ISSN(O): 2687-5365; ISSN(P): 2753-6556

Table 4: Logistic regression analysis of prediction of CKD MBD by different risk factor

Risk factors	Odds Ratio	Std. Err.	Z-value	P-value	95% CI for OR	
Age in yrs	0.96	0.03	-1.3300	0.1830	0.91	1.02
Sex	0.79	0.71	-0.2600	0.7940	0.13	4.64
Duration of dialysis	0.98	0.05	-0.4200	0.6770	0.90	1.07
Haemoglobin	1.00	0.02	-0.0100	0.9910	0.96	1.04
Serum bicarbonate	1.04	0.08	0.5300	0.5960	0.89	1.22

DISCUSSION

Patients with CKD frequently experience problems with their bones' and minerals' metabolism. Regarding the prevalence, aetiology, and management of CKD-MBD, industrialised and developing nations differ from one another. These disparities included ethnoracial variables, dialysis quality, varieties of dialysis membrane, and dialysis water, as well as economic factors such as restricting the usage of efficient modern phosphate binders, calcimimetics, and Vitamin D. In patients receiving maintenance hemodialysis, this study clarified the prevalence, pattern, and risk factors for CKD and MBD.[5]

58% of the participants in our study were men, while the remaining participants were women. Diabetic renal disease, like in the study, was the most common cause of CKD. In our study, the overall prevalence of CKD MBD was 93.94%, compared to 58% in earlier studies.[6]

According to previous studies, hypocalcemia occurs in 29.9% and 49.6% of patients with CKD stages 4 and 5, respectively. In our study, the mean serum calcium of 7.69 mg/dl noted, had similar findings.[7]

The growth and progression of SHPT depend on hyperphosphatemia. In contrast to the study, the mean serum phosphorus levels in our sample were roughly 6 mg/dl. A robust and substantial predictor of the serum iPTH level was the combination of blood phosphorus and alkaline phosphatase levels. iPTH's impact on phosphorus control and bone remodelling makes it crucial in the pathophysiology of CKD and MBD. If there is no liver abnormality, alkaline phosphatase is a marker that reflects osteoblastic activity. Although only weakly associated, abnormal serum levels of these two markers are associated with the rate of bone turnover, fracture risk, and other clinical occurrences, such as mortality.[8] For the identification of the type of renal osteodystrophy, bone biopsy remains the gold standard; however, it is not easily accessible for most patients. Instead, bone or total alkaline phosphatase and iPTH can be used to estimate bone turnover.[9]

It was reported that, in 57 of 118 (48%) patients receiving hemodialysis, secondary hyperparathyroidism was shown to be the most common cause of CKD-MBD, similar to our study.[10] It was found to have a similarly high prevalence of SPTH. When analysing the trends in renal osteodystrophy among 2248 dialysis patients from 1983 to 1995, it was discovered that there was a steadily rising prevalence of ABD. 6.06% of the patients in our research study developed ABD, compared to 18% in the study.[11]

Age, dialysis duration, gender, serum bicarbonate, and haemoglobin were all identified by logistic regression analysis as being risk factors for the development and severity of CKD-MBD, which is consistent with findings from other studies.[12]

With normal serum iron profiles and mean serum ferritin levels of 539 in our study patients, TSAT theorises that inflammation may also play a role in the development of CKD and MBD.

CONCLUSION

Our study revealed a range of CKD-MBD in CKD Stages 3–5D. It revealed that among Indian CKD patients, secondary hyperparathyroidism, hyperphosphatemia, hypocalcemia, elevated alkaline phosphatase, and vitamin D insufficiency were frequent conditions. Secondary hyperparathyroidism was the most prevalent kind of MBD. In Indian CKD patients compared to western ones, these abnormalities of mineral metabolism, in particular SHPT and 25D insufficiency, are more prevalent, more severe, and manifest sooner in the course of CKD. The early stages of CKD should be the first time that MBD should be monitored.

Limitation of study

Owing to tertiary location of research centre to the small number of patients, we have limited findings and results.

- There is no conflict of interest.
- Self-Funded.

REFERENCES

1. Ketteler M, Elder GJ, Evenepoel P, et al. Revisiting the KDIGO clinical practise guideline on chronic kidney disease—mineral and bone disorders: a commentary from a kidney disease: Improving Global Outcomes controversies conference Kidney Int. 2015;87:502–528. 2. Alem
2. M, Sherrard DJ, Gillen DL, et al. Increased risk of hip fracture among patients with end-stage renal disease. Kidney Int. 2000;58:396–399
3. Blayney MJ, Pisoni RL, Bragg Gresham JL, Bommer J, Piera L, Saito A, et al. – High alkaline phosphatase levels in haemodialysis patients are associated with a higher risk of hospitalisation and death. Kidney Int. 2008; 74: 655–63
4. Furuhashi T, Moroi M, Joki N, Hase H, Masai H, Kunimasa T, et al. – The impact of chronic kidney disease as a predictor of major cardiac events in patients with no evidence of coronary artery disease. J Cardiol 2010; 55: 328–36
5. K. Agarwal and R.K. Srivastava b. Nephron – chronic kidney disease in India: Challenges and Solutions, ClinPract 2009, 111: c197–c203, DOI: 10.1159/000199460
6. Alhaji Abdu, Aliyu Abdu1, Fatiu A – Prevalence and Pattern of Chronic Kidney Disease Mineral Bone Disorders among Haemodialysis Patients in Kano, Northwest Nigeria.

ISSN(O): 2687-5365; ISSN(P): 2753-6556

Arogundade 2. Annals of African Medicine, Volume 18, Issue 4, October-December 2019.
7. Ghosh, T. Brojen, S. Banerjee1, N. Singh2, S. Singh, O. P. Sharma3, J. Prakash – The high prevalence of chronic kidney disease and mineral bone disorders: a hospital based cross sectional study.
8. Coen G, Ballantine P, Bonucci E, Calabria S, Constantine S, Ferrannini M, et al. – Renal osteodystrophy in predialysis and haemodialysis patients: comparison of histological patterns and diagnostic productivity of intact PTH. Nephron 2002; 91: 103–11.
9. Lehmann G, Ott U, Kaemmerer D, Schuetze J, Wolf G. – Bone histomorphometry and biochemical markers of bone turnover in patients with chronic kidney disease stages 3-5. ClinNephrol 2008; 70: 296-305.
10. Harris SS, Seferiades E, Dawson, and Hughes B – Framingham Heart Study, Boston Low Income Elderly Osteoporosis Study Secondary hyperparathyroidism and bone turnover in elderly blacks and whites. J. Clin. EndocrinolMetab 2001; 86: 3801-4.
11. Sanjay Vikrant, AnupamParashar – Prevalence and severity of disordered mineral metabolism in patients with chronic kidney disease: A study from a tertiary care hospital in India
12. Mizobuchi M, Towler D, Slatopolsky E – Vascular calcification: The killer of patients with chronic kidney disease J Am SocNephrol. 2009; 20: 1453-64.

ISSN(O): 2687-5365; ISSN(P): 2753-6556