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Study of the Prevalence and Severity of Disordered Mineral Metabolism in Patients with Chronic Kidney Disease Stage-5 on Hemodialysis

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Abstract

***Background**: Chronic kidney disease mineral and bone disorder is a systemic disorder that involves bony abnormalities and vascular calcification. The kidney plays an important role in calcium and phosphorus regulation and hence renal dysfunction is necessarily associated with abnormalities in mineral homeostasis which have a wide range of effects not only on the bone but also on extra-skeletal sites. **Methods**: This prospective study was done in the Department of Nephrology, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. CKD Stage-5 adult patients on regular maintenance hemodialysis. Newly diagnosed CKD Stage 5 and prevalent CKD Stage 5 on Dialysis adult patients of 18 years and above were included. **Results**: Calcium level distribution among the observation found that there was 70% of observations had calcium levels < 8.5 mg/dl while 30% of the observation had calcium levels> 8.5 mg/dl. Phosphorous level distribution among the observation showed that there was 100% observation had Phosphorous level < 5.5 and no observation were found phosphorous level >5.5 mg/dl. It was observed that ALP level, 50% of the observation had the ALP level <120 (IU/L) as well as > 120(IU/L). **Conclusion:** The mean calcium levels were lower than KDIGO targets. However, mean PTH levels were higher than targets. The majority of the study population was found to be vitamin D deficient. A unique finding in the present study was serum phosphorus levels were within normal limits, which has been observed in other groups of populations studied in India.*

***Keywords**: Chronic Kidney Disease, Mineral Metabolism, Dialysis, Stage 5 chronic kidney disease.*

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Introduction

Chronic kidney disease (CKD) is estimated to affect more than 10% of the global population, and the prevalence of which has increased in recent years. [1, 2] The most important complication of CKD is cardiovascular disease, which is the primary cause of death in these patients. The kidneys are important for maintaining the body's internal balance of, especially, water and minerals (sodium, potassium, chloride, calcium, phosphorus, magnesium, sulfate). The kidneys also function as a part of the endocrine system and produce erythropoietin and 1,25-dihydroxycholecalciferol (calcitriol). This increase in cardiovascular morbidity/mortality associated with CKD has been described even in patients with no evidence of ischemic heart disease. [3] and is the explanation for the high mortality rate among patients in the initial stages of CKD (20%, 24%, and 46% after 5 years for Stages 2, 3, and 4, respectively), which far surpasses the rate for patients who finally require dialysis. [4] The clinical symptoms develop due to the retention of metabolic

products in the body. If this stage of azotemia/uremia/ progresses it results in the death of the patient if no active measures are taken such as dialysis or transplantation. Bone mineral metabolism abnormalities, which the Kidney Disease Improving Global Outcomes (KDIGO) guidelines. [5] Recently defined as CKD-mineral and bone disorder (CKD-MBD), have been implicated not only in the development of secondary hyperparathyroidism (SHPT) and renal osteodystrophy but have also been associated with the progression of CKD and its complications, including cardiovascular complications. [6] and they ultimately contribute significantly to an increase in morbidity and mortality rates among patients with CKD. [7, 8] CKD-MBD is a systemic disorder that is characterized by abnormal calcium, phosphorous, PTH, and Vitamin D metabolism, which, in addition to affecting the skeletal system, is related to the appearance of cardiovascular and soft tissue calcifications that in turn are associated with cardiovascular pathologies in patients with CKD. [9-12] The biochemical abnormalities are common in CKD and are the primary indicators by which the diagnosis and management of CKD-MBD are made. Despite the high prevalence of MBDs in CKD patients, there are limited data on CKD-MBD from India. [13-16] We in the current study tried to evaluate disordered mineral metabolism in CKD stage 5 patients on hemodialysis.

Materials and Methods

This prospective study was done in the Department of General Medicine/Nephrology, Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical committee permission was obtained for the study. Written consent was obtained from all the participants of the study.

***Inclusion Criteria*:**

1. CKD Stage-5 adult patients on regular maintenance hemodialysis.
2. Newly diagnosed CKD Stage 5 and prevalent CKD Stage 5D adult patients of 18 years and above.

***Exclusion Criteria*:**

1. Patients on hemodialysis with the plan for renal transplant and peritoneal dialysis.
2. CKD Stage 3–5 patients taking a calcium supplement, phosphate binder, Vitamin D or its active metabolites and analogs, calcimimetic.
3. Patients on glucocorticoid, bisphosphonate, nonsteroidal anti-inflammatory drugs, phenytoin, or warfarin.
4. Patients having rheumatologic diseases such as rheumatoid arthritis and ankylosing spondylitis, or primary PTH disorders.
5. Those having liver disease or a history of bone fracture in the preceding 6 months.

The lab investigations were performed for Complete hemogram, blood sugar, renal function tests, Lipid profile, Liver function tests, serum electrolytes, bone profile, serum PTH levels, vitamin D levels, electrocardiography, and ultrasound abdomen. CKD was defined and classified as per kidney disease outcomes quality initiative (KDOQI) criteria. The estimated glomerular filtration rates were calculated from serum creatinine level using the Cockcroft–Gault equation. The diagnosis of underlying basic kidney disease was made on clinical evidence. The biochemical markers of CKD-MBD, namely, calcium, phosphorus, alkaline phosphatase, intact parathyroid hormone (iPTH), and 25- hydroxyvitamin Vitamin D3 (25-OHD), were measured. The total calcium level definitions for hypocalcemia (Ca < 8.5 mg/dl), hypercalcemia (Ca >8.5 mg/dl), hyperphosphatemia (phosphorus >5.5 mg/dl), hypophosphatemia (phosphorus <5.5 mg/dl), elevated alkaline phosphatase level (>120 IU/L), hyperparathyroidism (iPTH > 65pg/ml), hypoparathyroidism (iPTH <10 pg/ml), and Vitamin D deficiency (<20 ng/ml) were used.

***Statistical analysis*:**

Collected data entered in Microsoft excel 2010 for further statistical analysis and presentation of the data. Descriptive statistics including means, standard deviation, and percentages were used to describe the demographic and clinical data. Statistical analysis has been done by using statistical software SPSS (Statistical Package for Social Science) version 22 on windows format.

Results

The age distribution among the patients, in that it was found that maximum observation was

lying in the age group of 35 – 50 years 44% followed by 0-65 years and > 65 years with 38% and 18%. All the observations having a mean age of 53.08 ± 12.24 years, standard given in table 1. In the present study, there were 32 (64%) males, and 18 (36%) females were observed, thus the ratio of males is to females was 1.77:1. Most of the cases were found from a low class of economic status which was 84% followed by the Middle class with 16%

Table 1: Age-wise distribution of patients

Age (Years)	*Frequency*	*Percent*
35 - 50	22	44
50 - 65	19	38
>65	9	18
Total	50	100
Mean	53.08	
SD	12.24	
Range years	35-77	

The Distribution of hemoglobin levels among the observation showed that 96% of the observation had hemoglobin levels < 11 gm/dl and only 4% of the observation had hemoglobin levels>11 gm/dl. The mean hemoglobin level among the patient was found to be 7.67 gm/dl with a standard deviation of 1.98 gm/dl and it was raging from 3.4 to 11.84 gm/dl. The distribution of Blood urea among the observation showed that all the observations which are 100% of the observation had blood urea >40 mg/dl and mean blood urea was found to be 143.47 mg/dl with a standard deviation of 63.13 mg/dl ranging from 63 to 314 mg/dl depicted in table 2.

Table 2: Distribution of Blood Urea among patients.

Blood Urea	*Frequency*	*Percent*
< 40	0	0
> 40	50	100
Total	50	100
Mean	143.47	
SD	63.13	
Range	63 – 314	

Calcium level distribution among the observation found that there was 70% of observations had calcium levels < 8.5 mg/dl while 30% of the observation had calcium levels> 8.5 mg/dl. Phosphorous level distribution among the observation showed that there was 100% observation had Phosphorous level < 5.5 and no observation were found phosphorous level >5.5 mg/dl details depicted in table 3.

Table 3: Distribution of Calcium and phosphorus levels among patients.

Calcium level mg/dl	*Frequency*	*Percent*	*Phosphorus*	*Frequency*	*Percent*
< 8.5	35	70	*< 5.5*	50	0
> 8.5	15	30	*> 5.5*	0	100
Total	50	100	*Total*	50	
Mean	8.02		*Mean*	3.82	
SD	0.91		*SD*	0.50	
Range	5.5 - 9.8		*Range*	2.87 - 5	

From the above table, it was observed that ALP level, 50% of the observation had the ALP level <120 (IU/L) as well as > 120(IU/L). From the above table, it was observed that ALP level, 50% of the observation had the ALP level <120 (IU/L) as well as > 120(IU/L) details depicted in table 4.

Table 4: Distribution of Alkaline Phosphatase and Vitamin D levels among patients.

ALP levels IU/L	*Frequency*	*Percent*	*Vitamin D ng/ml*	*Frequency*	*Percent*
< 120	25	50	*< 20 ng/ml*	26	52
> 120	25	50	*20 – 30 ng/ml*	24	48
Total	50	100	*Total*	50	100
Mean	125.95		*Mean*	20.2	
SD	49.10		*SD*	3.86	
Range	36 – 301		*Range*	12.09 – 29.93	

38% of patients had secondary hyperparathyroidism and an almost equal number of patients had the adynamic bone disease (42%). Less number of patients were in KDIGO targets 20%. All the patients had a serum creatinine level of more than 1.3 mg/dl which is 100% Mean serum creatinine level was found to be 11.52 mg/dl (Table 5).

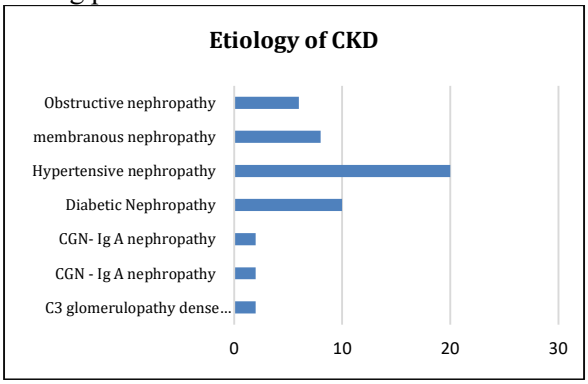
Table 5: Distribution of level of Serum creatinine among patients.

Serum Creatinine mg/dl	**Frequency**	**Percent**
0.6-1.3	0	0
> 1.3	50	100
Total	50	100
Mean	11.52	
SD	4.63	
Range	4.3 - 24.39	

Body mass index among the patients showed that 14% of the patients were underweight, most of the patients were normal that is 64% and 22% of the patients were found within 25-29.9 of BMI. The mean BMI for all observations was 22.14 with a standard deviation of 3.29 ranging between 16-28. Comorbidities distribution among the patients was showing that only 10 %

of the patients had no comorbidities whereas 40% of the patients were hypertensive, 18 % of the patients were suffered from diabetes mellitus, 26% of the patients were suffered from both hypertension as well as Diabetes Mellitus and other rest of the patients nearly 6% of the patients were suffered from other comorbidities like CAD and Bronchial Asthma. Serum albumin among the patients showed that 80% of the patients had serum albumin levels less than or equal to 3.4, and 20% of the patients were found > 3.4 level of serum albumin. Mean serum albumin for all observations was 3.206 with a standard deviation of 0.42 ranging between 2.7- 4.4

Graph 1: Distribution of Etiological Diagnosis among patients



Discussion

In this study, the mean age of the studied population was 53.08 years with the common age group being the fifth decade. In our study male to female sex ratio was 1.77:1. Age distribution and sex ratio were like other studies. [17] In the present study, Hypertensive nephropathy emerged as the commonest etiology of CKD (40%), while non-hypertensive diseases comprised 60% like another study by AL Kakrani et al. [18] These was most likely due to undiagnosed Chronic Glomerulonephritis and Chronic Interstitial Nephritis in rural population. The possible explanation is, almost all these patients had presented late to Emergency Department with symptomatic Chronic Kidney Disease with stage 5. Most of these patients were not diagnosed before having kidney disease and some of them had hypertension which was not evaluated. There was also a common problem of lack of follow-up with the family physician and drug non-compliance. This was unlike in other studies in north India [19] where the most common cause was Diabetic Nephropathy and patients in other studies were a decade older than our cohort. The second common cause of chronic kidney disease was Diabetic Nephropathy. Mean PTH in the study was outside the normal range. In the present study, 38% of patients had secondary hyperparathyroidism and an almost equal number of patients had Adynamic Bone Disease (42%) and few patients were in KDIGO targets – 20%. In patients with CKD stage 3a to stage 5 not on dialysis, the optimal PTH value is not known. However, patients with intact PTH above the normal limit of the assay are first evaluated for hyperphosphatemia, hypocalcemia, and vitamin D deficiency. It is reasonable to correct these abnormalities with any or all the following- reducing dietary phosphate intake and administering phosphate binders, calcium supplements, and/or native vitamin D. Suppression of PTH to normal values is not desirable since it is associate with a higher prevalence of Adynamic bone disease, in which bone turnover is low. The mean calcium levels of the studied population were 8.02 mg/dl. Most of the patients (70%) had serum calcium levels less than the KDIGO target. However, phosphorus levels were within normal limits in all patients of CKD in this study. It was a distinctive observation made in this study, which could reflect variation in dietary habits, nutritional status, and different cultures followed by people living in different regions. As depicted in the table below the values are comparable to similar studies of Diaz et al., [21] Block et al.,[22] and Gupta et al., [20] In the present study, ALP levels were outside the normal range. 50% of CKD patients had high levels of ALP and 50% with low levels. Block GA et al., [22] study ALP values are comparable with these observational studies, where 50% of CKD patients had higher ALP levels. vitamin D insufficiency and deficiency state are highly prevalent in dialysis patients similar to the study by Gonzalez et al., [23] In the present study, mean vitamin D levels were 20.2, with a deficiency in 52%. This could be due to the majority of patients receiving vitamin D supplementation routinely though one-third of patients had an insufficient state. Vitamin D deficiency in patients with CKD 3 and 4 is associated with increased PTH and low mineral

bone density. [24, 25] In CKD 5d patients, vitamin D deficiency is associated with mortality in incident dialysis patients. [26] These studies support the concern raised by KDIGO guidelines that low levels of vitamin D in patients with CKD may contribute to the etiology of secondary hyperparathyroidism. [27] Few studies have shown vitamin D inverse correlation with age, female gender, PTH levels diabetes. Few studies revealed, not much difference in vitamin D levels between different stages of CKD, regardless of treatment with vitamin D. [28, 29] This indicates that vitamin D levels are fundamentally determined by nutritional intake rather than renal function alone.

Conclusion

The most common age group in this study population belonged to the fifth decade. Most of the patients presented with End-Stage Renal Disease with undiagnosed native kidney disease probably Chronic Glomerulo Nephritis and Chronic Interstitial Nephritis. The mean calcium levels were lower than KDIGO targets. However, mean PTH levels were higher than targets. Most of the study population was found to be vitamin D deficient. A unique finding in the present study was serum phosphorus levels were within normal limits, which has been observed in other groups of populations studied in India.

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***Source of support*: Nil**
***Ethical Permission*: Obtained**

References

1. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am J Kidney Dis. 2003; 41:1–12.
2. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, et al. Prevalence of chronic kidney disease in the United States. JAMA. 2007; 298:2038–47.
3. 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.
4. Keith DS, Nichols GA, Gullion CM, Brown JB, Smith DH. Longitudinal follow-up and outcomes among a population with chronic kidney disease in a large managed care organization. Arch Intern Med. 2004; 164:659–63.
5. Moe S, Drüeke T, Cunningham J, Goodman W, Martin K, Olgaard K, et al. Definition, evaluation, and classification of renal osteodystrophy: A position statement from kidney disease: Improving global outcomes (KDIGO) Kidney Int. 2006; 69:1945–53.
6. Danese MD, Belozeroff V, Smirnakis K, Rothman KJ. Consistent control of mineral and bone disorder in incident hemodialysis patients. Clin J Am Soc Nephrol. 2008; 3:1423–29.
7. Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG, Chertow GM. Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. J Am Soc Nephrol. 2004; 15: 2208–18.
8. Russo D, Corrao S, Battaglia Y, Andreucci M, Caiazza A, Carlomagno A, et al. Progression of coronary artery calcification and cardiac events in patients with chronic renal disease not receiving dialysis. Kidney Int. 2011; 80:112–18.
9. Mizobuchi M, Towler D, Slatopolsky E. Vascular calcification: The killer of patients with chronic kidney disease. J Am Soc Nephrol. 2009; 20:1453–64.
10. Kalantar-Zadeh K, Kuwae N, Regidor DL, Kovesdy CP, Kilpatrick RD, Shinabarger CS, et al. Survival predictability of time-varying indicators of bone disease in maintenance hemodialysis patients. Kidney Int. 2006; 70:771–80.
11. Young EW, Albert JM, Satayathum S, Goodkin DA, Pisoni RL, Akiba T, et al. Predictors and consequences of altered mineral metabolism: The dialysis outcomes and practice patterns study. Kidney Int. 2005; 67:1179–87.
12. Wald R, Tentori F, Tighiouart H, Zager PG, Miskulin DC. Impact of the kidney disease outcomes quality initiative (KDOQI) clinical practice guidelines for bone metabolism and disease in a large dialysis network. Am J Kidney Dis. 2007; 49:257–66.
13. Sankarasubbaiyan S, Abraham G, Soundararajan P, Chandrasekaran V, Padma G. Parathyroid hormone and biochemical profile in chronic kidney disease patients in South India. Hemodial Int. 2005; 9:63–67.
14. Jabbar Z, Aggarwal PK, Chandel N, Kohli HS, Gupta KL, Sakhuja V, et al. High prevalence of Vitamin D deficiency in north Indian adults is exacerbated in those with chronic kidney disease. Nephrology (Carlton) 2009; 14:345–49.
15. Ghosh B, Brojen T, Banerjee S, Singh N, Singh S, Sharma OP, et al. The high prevalence of chronic kidney disease-mineral bone disorders: A hospital-based cross-sectional study. Indian J Nephrol. 2012; 22:285–91.
16. Bansal B, Bansal S, Mithal A, Kher V, Marwaha R. Vitamin D deficiency in hemodialysis patients. Indian J Endocrinol Metab. 2012; 16:270–73.
17. Eero Honkanen, Leena Kauppila Abdominal aortic calcification in dialysis patients; results of the CORD study. Nephrol Dial Transplant 2008; 23: 4009 -15.
18. Mukesh Laddha, Vishal Sachdeva, PM Diggikar, PK Satpathy, AL Kakani. Echocardiographic assessment of cardiac dysfunction in patients of End-Stage Renal Disease on Hemodialysis. Journal of the association of physicians of India. 2014; 62(1):28-32.
19. S.K Agarwal, R.K. Srivastava. Chronic Kidney Disease in India Challenges and solutions, Nephron Clin Prac 2009; 11: c197-c203.
20. Gupta A, Kallenbach. The race is a major determinant of secondary hyperparathyroidism in uremic patients. J Am Soc Nephrol 2000;11:330-34.
21. Diaz Corte C, Naes Diaz, et al, Prevention, diagnosis and treatment of renal osteodystrophy in Spain. Preliminary results from a multicenter enquiry. Nephrol Dial Transplant 1998; 13 Suppl 3: 551-56.
22. Block GA, Klassen PS, Lazarus JM, Ofsthun N, Lowrie EG; Mineral metabolism, mortality, and morbidity in maintenance hemodialysis. J Am Soc Nephrol 2004;15: 2208-18.
23. Gonzalez EA. Sachdeva et al, Vitamin D deficiency and insufficiency in Chronic Kidney Disease – a single-center observational study. Am J Nephrol 2004; 24;503-10.
24. La Clair RE, Hellman RN, Karp SL, Kraus M, Ofner S, Li Q, et al. Prevalence of calcidiol deficiency in CKD; Across sectional study across latitudes in the united states. Am J Kidney Dis. 2005; 45:1026 – 33.
25. Elder GJ, Mackun K. 25-Hydroxyvitamin D deficiency and diabetes predict reduced BMD in patients with chronic kidney disease. J Bone Miner Res. 2006; 21:1778-84.
26. Wolf M, Shah A, Gutierrez O, Ankers E, Monroy M, Tamez H, et al. Vitamin D levels and early mortality among incident hemodialysis patients. Kidney Int. 2007; 72:1004.
27. Rolvien T, Krause M, Jeschke A et al. Vitamin D regulates osteocyte survival and perilacunar remodeling in human and murine bone. Bone 2017; 103:78-87.
28. Levin A, Bakris GL, Molitch M, Smulders M, Tian J, Williams LA, et al. Prevalence of abnormal serum Vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: Results of the study to evaluate early kidney disease. Kidney Int. 2007; 71:31-38.
29. Gutierrez OM, Isakova T, Andress DL, Levin A, Wolf M. Prevalence and severity of disordered mineral metabolism in blacks with chronic kidney disease. Kidney 2008; 73:956-62.