Section A-Research paper
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Effect of Bone and Mineral Disorder on Morbidity and Mortality in Chronic Kidney Diseased patients in Bundelkhand region- A Prospective Study.

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ABSTRACT
Background: Patients with chronic kidney disease (CKD) continue to have poor management of mineral abnormalities in spite of multiple therapies. Mineral and bone abnormalities associated with Mineral & Bone Disorder (MBD) are a significant source of morbidity and death. The goal of the present study is that examine how the impact of measuring parameters effects on mortality and morbidity in chronic dialysis patients are affected by mineral and bone diseases (MBD) and their components.
Materials and Methods: The study was conducted on Bundelkhand region in MLB Medical College, Jhansi on 170 cases of all adult age group suffering from CKD. Their parameters were detected by evaluating the bone biomarkers.
Observation & Results: It was observed that the cases in stage IV having 32 cases and 18.32% followed by stage V which have 138 and 81.17%. The Mean ± SD in biomarkers of Ca, P, Vit-D and iPTH were found that 3.09 ± 1.68 followed by 9.7 ± 0.14, 10.48 ± 2.51 & 175.5 ± 14.84 respectively. The mortality rate were also calculate that 2 (6.25%) and 9 (6.52%) in both the stages.
Conclusion: This study revealed that it is vey useful tool for the management of CKD-MBD which helps in the knowing about the diagnosis and its pathophysiology for future clinical correlation
Keywords: CKD, Mineral Bone Disorder, Parathormone, Mortality, Morbidity

INTRODUCTION

An independent risk factor for a disturbance of bone and mineral metabolism is chronic kidney disease (CKD) [1,2] A major health issue impacting 5–10% of the world's population is chronic kidney disease (CKD) [3,4] Each element of CKD-MBD is a significant source of morbidity and mortality. These are viewed as risk factors that can be changed [5,6] Recent research has shown that bone cells' embryonic origins give them the capacity to have systemic extra-skeletal impacts

on bone Currently, osteocalcin (OC), FGF23, and sclerostin (SOST) are produced by bone cells, which are an endocrine organ. CKD-MBD relates to cardiovascular events and poor outcomes in end-stage renal disease (ESRD) [1,7,8]. Renal osteodystrophy should only be used to characterise problems in bone morphology linked to CKD, and the term CKD-mineral and bone disorder (CKD-MBD) for the systemic disorder of mineral and bone metabolism caused by CKD [9]. An association between inflammation and bone has also been identified, and chronic inflammation is now more frequently recognised as a CKD characteristic [8,10]. Disorders of the metabolism of calcium and phosphorus can be efficiently treated by dialysis. CKD-MBD is a complex network [1,2]. For these reasons, trends in parathyroid hormone levels, together with those of blood phosphate, calcium, and alkaline phosphatase as indicators of bone turnover, are extensively relied upon by doctors to direct the therapy of mineral bone disorders [11].

MATERIAL AND METHODS

This prospective study was carried out in the Department of Medicine, Maharani Lakshmi Bai Medical College, Jhansi on the patients of CKD during March 2016 to Nov 2017. We included the 170 cases of all age group having CKD and excluded the patients were suffering from acute renal failure. We preceded our study after needful investigations.

OBSERVATIONS AND RESULTS

Table 1. Distribution of cases according to stage of CKD

Stages of CKD	No. of Patients	Percentage
Stage I (eGFR>90%)	0	0
Stage II (eGFR60-89%)	0	0
Stage IIIA (eGFR45-59%)	0	0
Stage IIIB (eGFR 30-44%)	0	0
Stage IV (eGFR15-29%)	32	18.32
Stage V (eGFR<15%)	138	81.17

Fig 1. Distribution of cases according to stage of CKD

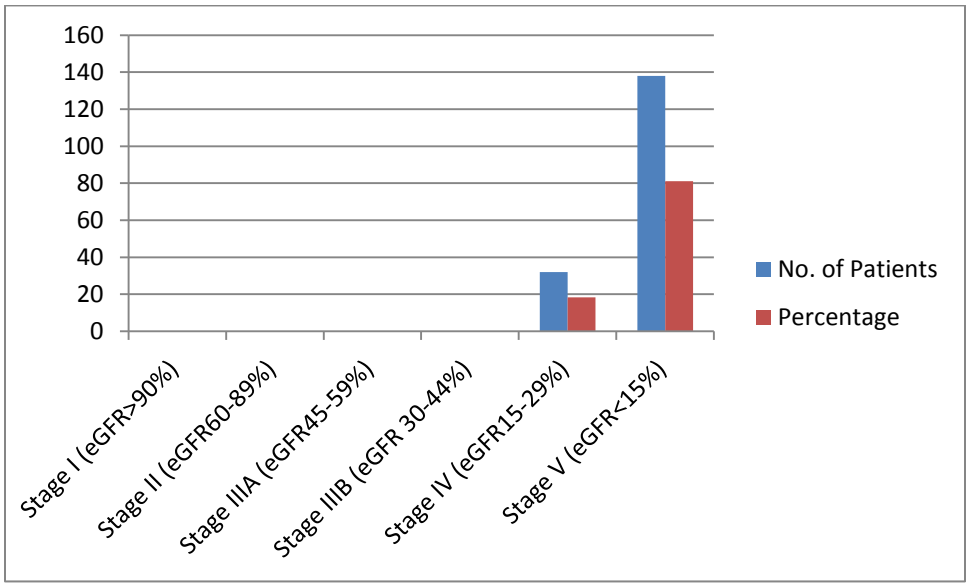

Table 2. Distribution of cases according to age group

Age group (in years)	Total no. of cases (n=170)		Stage IV (32)		Stage V (138)	
	No.	%	No.	%	No.	%
< 18	0	0	0	0	0	0
19 – 29	15	8.8	3	9.3	12	8.6
30 – 39	38	22.35	16	50.0	22	15.94
40 – 49	39	22.94	4	12.5	35	25.36
50 – 59	35	20.58	2	6.25	33	23.91
60 – 69	28	16.47	5	15.62	23	16.66
>70	15	8.8	2	6.25	13	9.42
Mean ±SD	47.33 ± 13.9 Yrs					

Table 3. Distribution of cases according BMD Markers

Parameters		No. of cases				Total	p- value
		Stage IV		Stage V			
		No.	%	No.	%		
S. Calcium (mg/dl) (7.76±2.24)	<8.8	17	17.38	81	82.62	98	<0.001
	8.8-10.6	15	21.12	56	78.88	71	
	>10.6	0	0	1	100	1	
S. Phosphorus (mg/dl) 6.94±1.61	<2.5	0	0	0	0	0	<0.001
	2.5-4.5	5	83.33	1	16.67	6	
	>4.5	27	16.46	137	83.54	164	
Vitamin D	<10	15	17.04	73	82.96	88	0.845

(ng/ml)	10-29	15	22.38	52	77.62	67	
14.33±9.01	30-100	2	13.33	13	86.67	15	
iPTH (pg/ml)	<67	4	100	0	0	4	<0.001
119.94±61.05	>67	28	16.86	138	83.14	166	

Table 4. Effects of BMD Markers on Mortality and Morbidity

Parameters				
	Stage IV (Mean ± SD)	**Mortality**	**Stage V (Mean ± SD)**	**Mortality**
Calcium	3.09±1.68	2 (6.25%)	3.93±2.78	9 (6.52%)
Phosphorus	9.7±0.14		10.1±0.83	
Vit-D	10.48±2.51		11.63±9.37	
iPTH	175.5±14.84		212.27±83.01	

Most of the cases of CKD were found in stage V (81.17%) followed by stage IV (18.32%) [Table 1 & Fig 1]. The cases having the age group of 40-49 yrs (22.94%) followed by age group of 30-69 yrs (22.35%), followed by 50-59yrs (20.58%) followed by 60-69 yrs of age group (16.47%). The least no. of patients are in the age group of 19-29 and >70 yrs age group (8.8%). In stage IV of CKD most of the cases were found in age group of 30-39 yrs (50%) and in stage V of CKD most of the cases were found in range of age group of 40-59 yrs (49.27%) [Table 2]. Table 3 showing that most of the patients in study were presented with hyperparathyroidism 97.6% (119.94±61.05) followed by hyperphosphatemia 96.4% (6.94±1.61) followed by hypocalcemia 57.64% (7.76±2.24) followed by Vitamin D insufficiency 51.76% (14.33±9.01). Table 4 shows that mortality in study was 6.47% in which most of the patient was expired in stage V i.e. 81.82%. Table 10-A shows that most of the mortality occurs in CKD stage V (81.82%). It shows that mortality in stage IV and Stage V occurs mainly in those patients in which phosphorus and iPTH levels are increases.

DISCUSSION

The prevalence of CKD in India has been estimated to range between 0.78% and 0.87%. Despite the efforts of the CKD Registry of India, which collates data from an estimated 199 affiliated centers, data regarding the characteristics of untreated CKD-MBD in pre-dialysis patients in India is scarce; a gap that this study specifically sought to bridge. The inherent limitation of a hospital based survey involving a referred patient population is that it cannot describe the epidemiology of CKD-MBD in the community. In our study most of the cases having the age group of 40-49 yrs (22.94%) followed by age group of 30-69 yrs (22.35%), followed by 50-59yrs (20.58%) followed by 60-69 yrs of age group (16.47%). (Table – 1). Although mean age, gender ratio, etiology of kidney disease, diabetic and socio-economic status of patients in this study is

similar to the standard referred population described in the CKD registry of India decribed by Rajapurkar MM et al [12]. Population based surveys that have assessed the prevalence of CKD in India have shown the mean age of CKD patients to range from 52 to 59 years, 48-61% of whom are males by Agarwal SK et al, 2005 [13].

The high prevalence of 25(OH) D deficiency, hypocalcemia and hyperparathyroidism in this study is consistent with findings from previous hospital based surveys on CKD-MBD in India. This includes, low dietary intake of vitamin D, lack of a national vitamin D food fortification program, increased activity of the 25(OH) D degrading enzyme 25(OH) D 24 hydroxylase in skin fibroblasts of Indians and dark skin pigmentation requiring longer exposure to ultraviolet (UV) rays to achieve adequate 25(OH) D levels. Their prevalence of vitamin D insufficiency (10 to 29 ng/mL) was 39.41 % and vitamin D deficiency (< 10 ng/mL) was 52.76 % deficiency in the CKD group. The reported prevalence of hypovitaminosis D has been consistently and unexpectedly high in almost all populations studied worldwide and across the age spectrum. A previous local study in primary school children aged 7-12 years old (n = 402) showed the prevalence of hypovitaminosis D(< 30 ng/ml) to be 73 %. It was also found in post-menopausal women aged 50 to 65 years the level of 25(OH) D to be significantly lower in the postmenopausal Malay women compared to Chinese women ($p < 0.05$). Whereas, the levels of serum phosphorus, ALP and iPTH rose significantly. consistent with high turnover bone disease. High turnover could contribute to the development of osteoporosis in CKD subjects. Vitamin D are inversely correlated but this correlation is not statistically significant. iPTH and calcium are found to be negatively correlated, i.e., when calcium falls iPTH rises and the reverse occurs in hypercalcemia.

Conclusion

The study acts as useful tool for biomarkers and helps in the management of CKD-MBD. Its clinical outcomes is beneficial for the better knowledge for understanding its diagnosis and pathophysiology for fulfill the future research gaps.

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