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Research Article

USAGE OF DRUGS IN THE TREATMENT OF CHRONIC KIDNEY DISEASE WITH MINERAL BONE DISORDER

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ABSTRACT

CKD-MBD, or chronic kidney disease-mineral and bone disorder, is a systemic condition resulting from kidney disease, characterized by abnormalities in calcium, phosphorus, parathyroid hormone (PTH), and vitamin D metabolism. The objective of this prospective study, conducted at Sagar Hospital's nephrology department, was to identify patterns of drug usage in managing CKD-MBD. The study included 182 patients. It revealed a higher prevalence of CKD-MBD in men (67%) compared to women (33%), with a larger number of patients falling in the 51-70 age range. The most common comorbidities observed were hypertension and diabetes mellitus (DM), with a prevalence rate of 90% in males and 30.8% in females. Abnormal levels of calcium, phosphorus, and PTH served as diagnostic criteria for MBD due to their association with CKD-MBD. Non-pharmacotherapy treatment involved a renal diet comprising 1500 kcal and 50g of protein. Among pharmacotherapy options, furosemide was the preferred medication for CKD treatment (39%), followed by cholecalciferol (30.9%) and vitamin supplements (38.38%) for managing MBD. The study highlighted that bone-related problems tend to increase as individuals age and their lifestyle patterns change. Overall, both pharmacotherapy and non-pharmacotherapy approaches were employed to improve patients' conditions and prevent further complications in the majority of CKD-MBD cases.

KEYWORDS: CKD-MBD, parathyroid hormone, vitamin supplements, cholecalciferol, calcium.

INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health problem, with adverse outcomes of kidney failure, cardiovascular disease (CVD), and premature death. According to Kidney Disease: Improving Global Outcomes (KDIGO), CKD is defined as kidney damage or glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 for 3 months or more, irrespective of cause. Kidney disease severity is classified into five stages according to the level of GFR.[1-3]

The kidney plays a vital role in the metabolism of minerals and bone health. It is not only the target organ of several regulating hormones such as parathormone (PTH) and fibroblast growth factor-23 (FGF-23), but it is also the main organ that activates vitamin D. CKD-MBD was further expanded to include cardiovascular diseases (CVD), left ventricular hypertrophy (LVH), hypertension, immune dysfunction, inflammation and iron deficiency anaemia, and thus its treatment is still a major challenge for the nephrologist that necessitates further pushing for the development of new agents with high specificity to the treatment of CKD induced MBD. Thus, the abnormal mineral metabolism occurs in chronic kidney diseases (CKD) and sequentially affects the bone health. Recently it is renamed chronic kidney disease-mineral and bone disorder (CKD-MBD) as a systemic syndrome and is called renal osteodystrophy (ROD), if the disease is limited to the bone. CKD-MBD is manifested by an abnormality of any one or a combination of the following: laboratory-abnormalities of calcium, phosphorus, PTH, or vitamin D metabolism; bone-changes in bone turnover, mineralization, volume, linear growth, or strength; and calcification-vascular or other soft-tissue calcification.[4]

Absent or low bone resorption and formation and could be an early finding of CKD. It is often associated with low PTH level and the patients are more vulnerable to develop fractures. A slow turnover of bone with an increased

unmineralized osteoid matrix that in turn will lead to decreased bone strength. It is often attributed to deficiency of vitamin D, metabolic acidosis and hypocalcaemia. Bone resorption in turn will increase Phosphorus production and lowers Phosphorus deposition inducing hyperphosphatemia. Hyperphosphatemia stimulates transition of osteoblasts in the vessels contributing to extra skeletal mineralization and increasing Ca x P product. In stage IV-V CKD, GFR <30% of normal, this adaptation will be no longer adequate, and hyperphosphatemia develops despite high PTH. Calcium and vitamin D as CKD advances and functioning nephron mass decreases together with hyperphosphatemia and increased FGF-23, suppression of 1a hydroxylase activity occurs, resulting in calcitriol deficiency with subsequent decreasing intestinal Ca absorption and decreased Ca. Parathormone Calcitriol deficiency also decreases VDRs. In parathyroid gland (PTG), it results in resistance to calcitriol mediated regulation and stimulation of PTH secretion leading to SHPT, due to direct stimulation of parathyroid cells contributing to elevation of PTH. Secondary hyperparathyroidism (SHPT) is a prominent hazard of CKD, that will lead to vascular calcification (VC) and CVDs with an increased PTH, leading to Ca and P metabolism imbalance.[5]

FGF23 is produced by osteocytes and osteoblasts, and it represents direct bone-kidney and bone– parathormone. The prime objective of CKD-MBD management is to maintain bone and cardiovascular health. Optimal treatment involves normalizing serum phosphate and calcium and preventing parathyroid hyperplasia with appropriate fine-tuning of PTH. In addition, vitamin D therapy probably has an important role. Controlling Hyperphosphatemia Diet Phosphate is ubiquitous in the diet and dietetic input to limit excessive phosphate intake should be a part of any management strategy. Phosphate Binders Oral phosphate binders reduce intestinal absorption of phosphate by rendering dietary phosphate less absorbable. Broadly they can be divided into two classes – calcium based (generally cheap) and calcium free (generally expensive). These are suboptimal therapies, being bulky, unpalatable, of low potency, and all must be taken with meals to maximize efficacy. It is hardly surprising that compliance with phosphate binders is poor. To state the obvious, the best phosphate binder is one that the patient will take – and this may require a certain amount of trial and error at the outset. Calcium-containing agents are relatively cheap and have the advantage that they will suppress PTH. They augment the overall calcium burden, and they are best avoided in patients with known vascular calcification, hypercalcaemia, a history of calciphylaxis or ABD.[5-6]

MATERIALS AND METHODS

Materials

Study site: The study was conducted in the Nephrology department of Sagar Multi-Specialty Hospital, Bengaluru.

Study design: This was a Prospective study on 182 patients.

Sample size: A total of 182 patients from the Nephrology department of Sagar Hospital, who satisfied the study criteria and consented to participate in the study were included for the study.

Study period: The study was conducted over a period of 06 months starting from February 2022 to July 2022

Ethical approval: Ethical committee clearance has been obtained by the Institutional Ethical Committee (IEC) of Sagar Hospitals.

Study criteria

Inclusion criteria

- All chronic kidney disease patients along with mineral bone disorder along with both inpatients and outpatients
- Patient aged above 18 years.
- Previously and newly diagnosed CKD with mineral bone disorders patients.

Exclusion criteria

- Pregnancy and lactating women.

Study Materials: Data Collection Form and Patient Consent Form.

Source of data

- Patient case notes
- Treatment charts/Medication chart
- Laboratory reports
- Interaction with patients.

Method of collection of data/study procedure

Patient Enrolment

Patients having CKD along with Mineral Bone Disorder (MBD) were admitted in the Endocrinology and Nephrology Department of Sagar Hospital in Bengaluru. Based on the inclusion and exclusion criteria patients were screened.

Methods of data collection

A prospective study was conducted in the Department of Medicine and Nephrology of Sagar hospital – Bengaluru. The patients who meet the criteria were enrolled for the study. To assess the efficacy of drugs; laboratory parameter such as renal function test; calcium, urea, creatinine, BUN, hematology data; haemoglobin, RBC, PCV, electrolyte such as sodium, potassium and chloride is used and other parameters like parathyroid hormone, alkaline phosphate were used. To assess the pattern of drug, drug related data were collected such as drug name, doses, frequency, and route of administration and documented in suitable designed data collection form. Data was analysed

using a suitable statistical tool. We had used a treatment chart, laboratory reports and patient counselling to assess the laboratory parameter and evaluate the management in CKD-MBD patients. This was collected and documented in a suitable designed data collection form – to assess the outcome of efficacy, effects, and safety of the drugs used in CKD with MBD. The follow up was documented up to discharge.

Statistical method

Statistical analysis has been carried out in the present study. Mean has been used to measure the central tendencies of given data. Microsoft Word and Excel are used to generate tables and graphs respectively. Chi-square test was defined at 5% level of significance i.e., p-value <0.05.

Statistical software

The statistical software namely IBM SPSS version 27 was used for the analysis of the data and the drawn charts.

RESULT AND DISCUSSION

Males have shown highest prevalence than females.

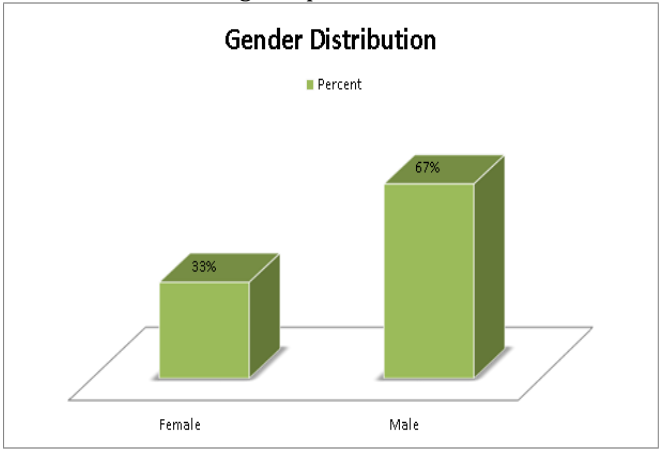

Figure no. 01: Subjects are distributed based on gender

Age group between 51-70 have shown highest prevalence.

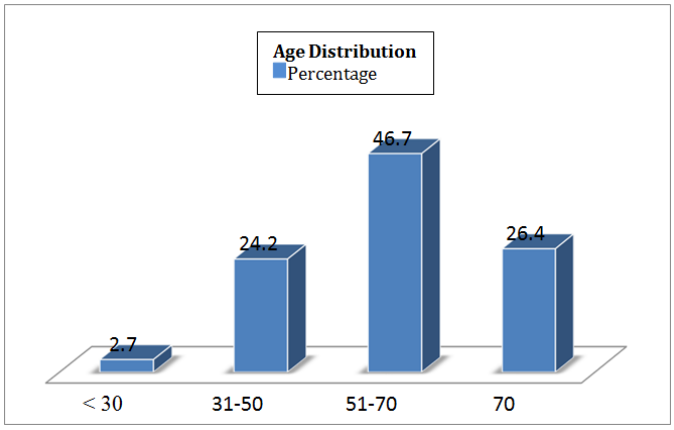

Figure no. 02: Subjects are distributed based on age group.

Majority of patients have diabetes as comorbidity.

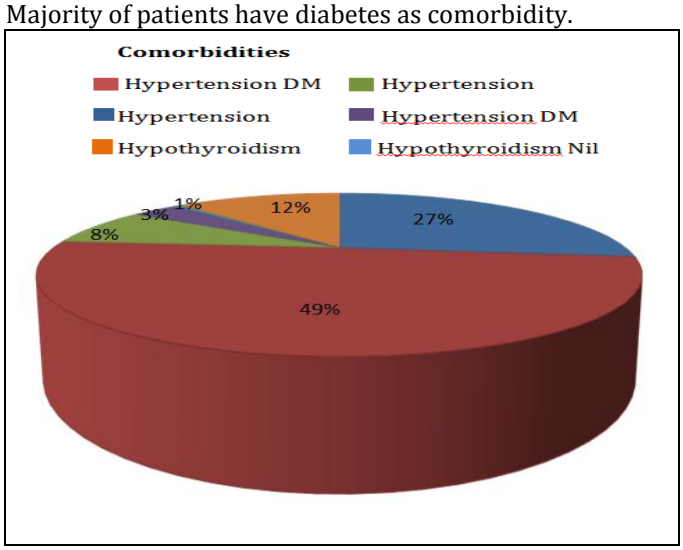

Figure no. 03: Subjects are distributed based on comorbidities.

Table no. 01: Subjects are distributed based on calcium level before and after the treatment.

Before	After			Total	Significance
	Below Normal	Normal	Above Normal		
Below Normal	119	26	0	145	Chi-square = 262.29 P<0.001 significant
	65.4%	14.3%	0.0%	79.7%	
Normal	01	34	0	35	
	0.5%	18.7%	0.0%	19.2%	
Above Normal	00	00	02	02	
	0.0%	0.0%	1.1%	1.1%	
Total	**120**	**60**	**02**	**182**	
	65.9%	**33.0%**	**1.1%**	**100.0%**	

After the treatment patients showed increased levels of calcium

Table no. 02: Subjects are distributed based on phosphorus level before and after treatment.

Before	After			Total	Significance
	Below Normal	Normal	Above Normal		
Below Normal	09	02	00	11	Chi-square = 188.027 P<0.001 significant
	5.3%	1.2%	0.0%	6.5%	
Normal	00	56	01	57	
	0.0%	33.1%	0.6%	33.7%	
Above Normal	00	43	58	101	
	0.0%	25.4%	34.3%	59.8%	
Total	**09**	**101**	**59**	**169**	
	5.3%	**59.8%**	**34.9%**	**100.0%**	

After the treatment majority of patients showed normal phosphorous level.

Table no. 03: Subjects are distributed based on alkaline phosphate level before and after treatment.

Before	After	Total	Significance
	Below Normal		
Below Normal	06	06	------
	3.4%	3.4%	
Normal	133	133	
	75.6%	75.6%	
Above Normal	37	37	
	21.0%	21.0%	
Total	**176**	**176**	
	100.0%	**100.0%**	

After the treatment alkaline phosphate levels were normal.

After the treatment patient showed better Parathyroid hormone.

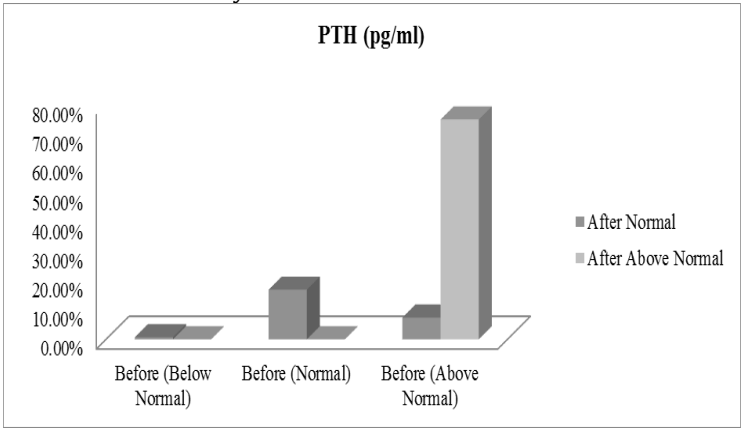

Figure no. 04: Subjects are distributed based on parathyroid hormone (PTH) level before and after treatment.

Table no. 04: Subjects are distributed based on creatinine level before and after treatment.

Before	After			Total	Significance
	Below Normal	Normal	Above Normal		
Below Normal	01	01	01	03	Chi-square = 58.592 P<0.001 Significant
	0.6%	0.6%	0.6%	1.7%	
Normal	00	03	00	03	
	0.0%	1.7%	0.0%	1.7%	
Above Normal	01	14	158	173	
	0.6%	7.8%	88.3%	96.6%	
Total	**02**	**18**	**159**	**179**	
	1.1%	**10.1%**	**88.8%**	**100.0%**	

Creatinine levels of patients were normal after the treatment.

Table no. 05: Subjects are distributed based on potassium level before and after treatment.

Before	After			Total
	Below Normal	Normal	Above Normal	
Below Normal	09	17	00	26
	5.0%	9.4%	0.0%	14.4%
Normal	04	105	03	112
	2.2%	58.0%	1.7%	61.9%
Above Normal	03	27	13	43
	1.7%	14.9%	7.2%	23.8%
Total	**16**	**149**	**16**	**181**
	8.8%	**82.3%**	**8.8%**	**100.0%**

After the treatment patient showed normal levels of potassium.

Table no. 06: Subjects are distributed based on sodium level before and after treatment.

Before	After			Total	Significance
	Below Normal	Normal	Above Normal		
Below Normal	56	32	02	90	Chi-square = 21.080 P<0.001 Significant
	30.8%	17.6%	1.1%	49.5%	
Normal	29	62	00	91	
	15.9%	34.1%	0.0%	50.0%	
Above Normal	00	01	00	01	
	0.0%	0.5%	0.0%	0.5%	
Total	**85**	**95**	**02**	**182**	
	46.7%	**52.2%**	**1.1%**	**100.0%**	

Sodium levels are normal after the treatment.

Renal soft diet upto 1500Kcal and 50g protein showed more effect during CKD-MBD treatment.

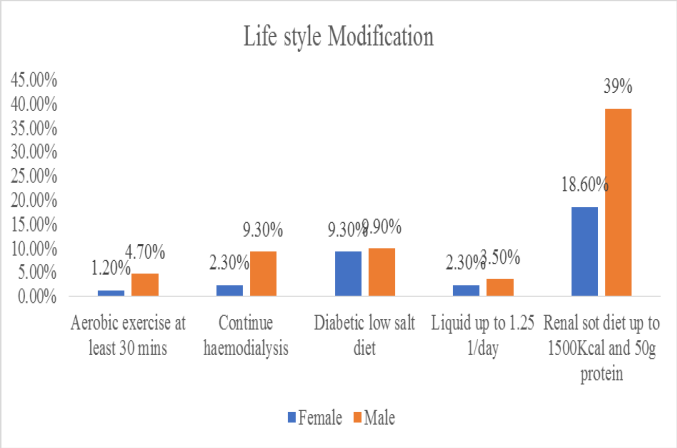

Figure no. 05: Subjects are distributed based on lifestyle modification.

Furosemide and Erythropoietin showed a higher range of usage during the treatment.

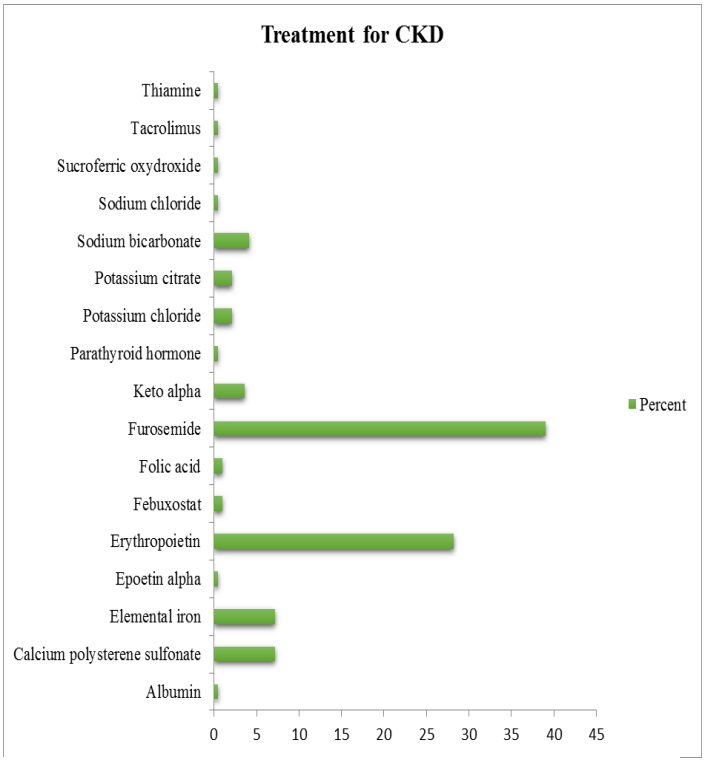

Figure no. 06: Drugs are distributed based on their usage for chronic kidney disease treatment.

Vitamin supplements showed higher range of frequency during the treatment.

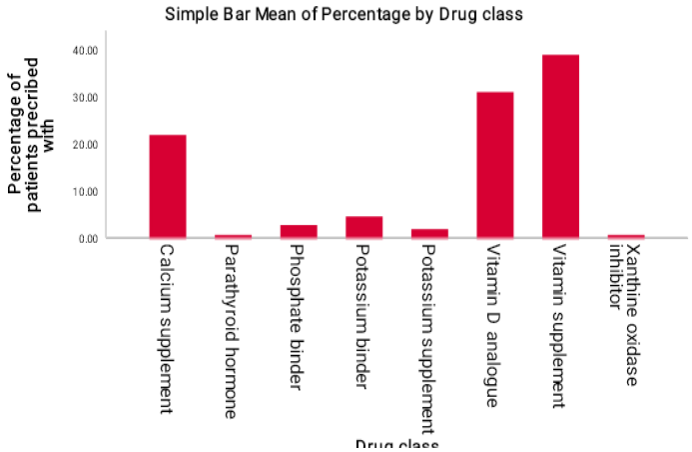

Figure no. 07: Drugs are distributed based on their usage for mineral bone disorder (MBD) treatment.

DISCUSSION

Our study findings indicate that individuals with chronic kidney disease (CKD) and mineral bone disorder (MBD) are commonly aged between 51 and 70. The majority of participants in our study were male, as they face a higher risk of comorbidities compared to females. Hypertension was the most prevalent comorbidity, particularly among males. Abnormal levels of calcium, phosphorus, alkaline phosphate, and parathyroid hormone (PTH) were observed in most participants.

Regarding medication, furosemide was frequently prescribed for CKD treatment, while Vitamin D analogues were commonly used for managing mineral bone disorder. The effectiveness of these medications was determined by comparing laboratory values of calcium, phosphorus, alkaline phosphate, and PTH before and after therapy, showing a significant p-value (<0.001).

Non-pharmacotherapy in the form of lifestyle modifications played a crucial role, with a renal diet of up to 1500 kcal and 50g protein being preferred. Additionally, continuous hemodialysis was recommended based on individual patient conditions.

It is essential to provide proper care for CKD patients with a focus on mineral bone disorder, as it significantly affects their quality of life and increases the risk of bone fractures. Both medication and lifestyle changes are important in preventing further damage.

CONCLUSION

The study at Sagar Hospital focused on treatments for patients with chronic kidney disease (CKD) and mineral bone disorder (MBD). It included 182 participants, primarily men aged 51-70. Vitamin D analogues and vitamin supplements were commonly prescribed for MBD management, while furosemide was highly prescribed for CKD. Both pharmacotherapy and non-pharmacotherapy significantly improved parameters such as calcium, parathyroid hormone, phosphorus, albumin, and potassium. Renal diet and protein intake were recommended as lifestyle modifications, while aerobic exercise was less advised. CKD-MBD is more prevalent in males, often caused by comorbidities like hypertension and diabetes. Treatment aims to improve patients' condition and prevent further complications.

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