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Study of mineral and bone disorders in Minia University Hospital dialysis patients

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Abstract

Background: Chronic renal disease – mineral bone disease (CKD-MBD) is characterized by irregularities in the metabolism of calcium, phosphorus, parathormone hormone (PTH), or vitamin D, and abnormalities in mineralization, bone turnover, and the calcification of soft tissues or blood vessels. Serum parathormone or bone-specific alkaline phosphatase measurements are used to evaluate bone disease, as elevated or diminished values indicate underlying bone turnover. **Methods:** The study included ninety patients with end stage renal disease (ESRD) undergoing regular hemodialysis at the hemodialysis unit at Minia University Hospital from May 2022 to December 2023, the aim is to study MBD in those patients and the diagnostic value of plasma b-ALP as a marker of bone turnover. After obtaining informed consent, laboratory tests conducted, including a complete blood count, blood sugar, lipid profile, CRP, blood urea, serum creatinine, albumin, total calcium, phosphate, bone specific alkaline phosphatase, and PTH level evaluation. **Results:** High PTH level was prevalent in 23.3% of the studied patients and low parathyroid level in 10% and Serum calcium and bone-specific alkaline phosphate levels show high significant correlation with PTH level. Symptoms of MBD were common in both low and high bone turnover populations. In the study, 57% of the individuals had hypocalcemia. In 66.7% of the patients, PTH was within the normal range. **Conclusion:** The percentage of MBD among the HD patients under study was 33.3%, majority of patients with low PTH levels had high serum Ca and low bone specific alkaline phosphatase.

Keywords: chronic kidney disease-mineral bone disorder, Bone specific alkaline phosphatase, mineral bone disorder, Hypocalcemia

Introduction:

Chronic kidney disease (CKD) is a significant public health issue that has a substantial impact on health and healthcare expenses. CKD is diagnosed in adults when there is a persistent abnormality in kidney structure or function, such as abnormal albuminuria or an abnormal estimated glomerular filtration rate (eGFR), lasting for longer than three months (1). CKD-MBD presents with symptoms such as bone pain, calcification of blood vessels and soft tissues in the initial stages of the disease. (2) As renal impairment increases, patients typically have increasingly severe disruptions in bone and mineral metabolism. The abnormalities encompass renal osteodystrophy (ROD), a condition marked by bone pain, muscle-tendon rupture, pruritus, and more susceptibility to fractures, along with CKD-MBD (3). The laboratory diagnosis of CKD-MBD includes measuring the levels of serum calcium, phosphate, PTH, calcitriol, alkaline phosphatase (ALP) (total or bone-specific), and

assessing the acid-base balance. Additionally, various serum and urine markers that are often employed in monitoring patients with CKD are also evaluated. (4)

Aim of the work:

The study of mineral bone disorders (MBDs) among hemodialysis (HD) patients in EL-Minia University Hospital and the diagnostic value of plasma b-ALP as a noninvasive marker of the degree of bone turnover in hemodialysis patients.

Patient and Methods:

This is a cross-sectional hospital-based descriptive study conducted to study mineral bone disorders on 90 patients with end stage renal disease (ESRD) on regular HD in hemodialysis unit of Minya university hospital, Egypt in the period from May 2022 to December 2023.

Patients having acute infections, connective tissue disease, malignancy, chronic liver disease, recent myocardial infarction, and recent trauma in preceding 6 months were excluded from the study.

Ethical consideration:

The hospital's medical ethics committee gave the study permission to proceed (Approval No.315/2022 Date: 27 March 2022) and All patients gave their informed consent. The study was conducted among a cohort of hemodialysis patients who willingly consented by themselves to be interviewed and actively engaged in the study.

Data collection:

Information was gathered through a meticulously designed questionnaire. The questionnaire encompassed demographic information, social information, medical disorder history, duration of dialysis treatment, clinical and laboratory information, and smoking history. Full medical History taking and Clinical examination was done. The height and weight of patients was measured and body mass index was calculated.

Pre-dialysis blood samples were taken to determine metabolic parameters and complete blood count (CBC). Standard laboratory techniques were used to measure CBC, blood urea, serum creatinine, albumin, total Ca, phosphate, blood sugar, and serum lipids. The serum PTH assay was conducted using electrochemiluminescence immunoassay on the fully automated COBAS e 411 system (Roche Diagnostics GmbH, Mannheim, Germany). The measurement of bone-specific alkaline phosphatase is conducted using an enzyme-linked immunosorbent assay (ELISA), specifically with the Cat. No E1493Hu kit.

The patients were divided into three groups according to serum PTH level: the first group patients with PTH level less than 150 pg/ml (low bone turnover), the second group patients with PTH level between 150 and 600 pg/ml (normal bone turnover), and the third group patients with PTH level more than 600 pg/ml (high bone turnover)

The diagnosis of MBD among the studied patients was made according to the following: suggestive MBD–related symptoms (bone pain, muscle weakness, and combination of both symptoms) and MBD-related laboratory indicators (serum PTH, serum Ca, serum phosphorus, and serum bone specific alkaline phosphatase levels).

Statistical analysis:

The data were gathered, reviewed, coded, and entered into the Statistical Package for Social Science (IBM SPSS) version 20. The qualitative data were represented using numbers and percentages, whereas the quantitative data were represented using mean, standard deviations, and ranges, but only if their distribution was found to be parametric. The comparison of two groups with qualitative data was conducted using the Chi-square test. However, if the predicted count in any cell was less than 5, the Fisher exact test was employed instead of the Chi-square test. One Way ANOVA was employed to compare multiple independent groups with quantitative data and a parametric distribution. The confidence interval was established at 95% with a corresponding margin of error of 5%. The p-value was deemed significant for the following reasons: A p-value less than 0.05 is considered significant, while a p-value less than 0.001 is considered very significant. Correlation analysis, utilizing Pearson's and Spearman's rho methodologies, is employed to evaluate the magnitude of the relationship between two numerical variables. The correlation coefficient, represented by the symbol "r",

quantifies the size and direction of the linear association between two variables.

Results:

The study included 90 cases with 50 males and 40 females aged from 21 to 80 years (mean 48.99 years). 63.3% of cases had Ca < 8.4 mg/dl, 20% had Ca 8.4 – 9.5 mg/dl and 16.7% had Ca > 9.5 mg/dl, while 55.6% of cases had Pi 3.5 – 5.5 mg/dl and 12.2% of cases had Pi > 5.5 mg/dl. In 10% of cases PTH was < 150 pg/ml, 66.7% cases had PTH 150 - 600 pg/ml and 23.3% cases had PTH > 600 pg/ml **(Table 1,2**).

There were 77 cases taking oral Calcium acetate, 65 cases taking Erythropoietin, 16 cases taking H2 blockers, 8 cases taking vitamine D, 7 cases taking PPI, 4 cases taking Cinacalcet, 3 cases taking oral Anti coagulation and 2 cases taking Phosphorus chelators and Oral NaHCO3. **(Table 3)**

Fifty-nine patients (65.6%) were suffering from bone pain, 35 (38.9%) of them had diffuse pain, 19 (21%) in lower limb, 4 (4.4%) back pain and 1 case (1.1%) with upper limb pain. It was frequent in 54.4 % of cases, despite that it caused limitation of activity in only 30 % of cases with fracture occurring in 13.3 %, while muscle weakness occurring in 22 patients (24.4 %) **(Table 4).**

There was a highly significant negative correlation between serum Ca and parathormone level (p value= 0.0001). Also, there were a highly significant positive correlation between parathormone level and both blood urea and bone specific alkaline phosphatase (p value =0.000). There was a significant positive correlation between parathormone and inorganic phosphate (p value= 0.011). **(Table 5)**

Patients with higher PTH levels, the level of corrected calcium was significantly lower as hypocalcaemia with low serum Ca less than 8.4 mg/dl was present in 4 patients (44.4%) with low PTH (less than 150 pg/ml), and 36 patients (60 %) with PTH level between 150_ 600 pg/ml and 17 patients (81 %) with PTH more than 600 pg/ml which was statistically significant .While normal Ca level was found in 1 case (11.1%), 14 cases (23.3 %) and 3 cases (14.3 %) of patients with low, normal and high PTH level respectively. There was an increase in bone specific alkaline phosphatase with the increase of PTH level which was highly significant statistically. **(Table 6, fig1)**

There was highly significant negative correlation between serum Ca and both blood urea and bone specific alkaline phosphatase **(Table 7, figures 2,3).**

Table (1): Some demographic data of studied patients:

Variables	Total No. 90
Age	
Mean± SD	48.99 ± 14.28
range	21 – 80
Sex	
Males	40 (44.4%)
Females	50 (55.6%)
Residence	
Rural	73 (81.1%)
Urban	17 (18.9%)
Body mass index	
Underweight ((< 18)	4 (4.4%)
Normal weight (18.5-24.9)	28 (31.1%)
Overweight (25-29.5)	47 (52.2%)
Obese ((≥ 30)	11 (12.2%)
Drinking water	
Tap water	37 (41.1%)
Filtered water	53 (58.95)
Cooking pan (Aluminum)	70 (77.8%)

Table (2): Laboratory data of studied patients

Laboratory Investigation	No. = 90
Corrected calcium Mean ± SD (Range) < 8.4 8.4 - 9.5 > 9.5	 7.66 ± 2.58 (1.4 – 13.2) 57 (63.3%) 18 (20.0%) 15 (16.7%)
Pi (inorganic phosphate) Mean ± SD (Range) < 3.5 3.5 - 5.5 > 5.5	 4.15 ± 1.27 (2 – 8) 29 (32.2%) 50 (55.6%) 11 (12.2%)
Parathormone hormone (PTH) Median (IQR) < 150 150 – 600 > 600	 408.5 (284 – 587) 9 (10.0%) 60 (66.7%) 21 (23.3%)
Hemoglobin (Hb) Mean ± SD (Range)	9.43 ± 2.16 (3.3 – 15.2)
Total leukocytic count (TLC) Median (IQR) Range	5.45 (4.4 – 6.8) 2.4 – 12
Platelets Median (IQR) Range	220.5 (170 – 283) 44 – 798
Urea Mean ± SD	100.24 ± 39.13
Creatinine Mean ± SD (Range)	6.61 ± 0.71 (3.3 – 8.1)
Random blood sugar Mean ± SD (Range)	138.89 ± 21.85 (90 – 210)
Bone specific alkaline phosphate Mean ± SD (Range)	164.22 ± 76.35 (33 – 367)
Cholesterol Mean ± SD (Range)	177.51 ± 54.20 (95 – 450)
Low density lipoprotein (LDL) Mean ± SD	107.67 ± 35.56
Triglyceride Mean ± SD (Range)	143.78 ± 87.76 (40 – 457)
High density lipoprotein (HDL) Mean ± SD	0.79 ± 17.89
C-reactive protein (CRP) Positive Negative	 39 (43.3%) 51(56.7%)
Serum albumin Mean ± SD (Range)	4.28 ± 0.78 (2.7-6.2)

Table (3): Drug history of studied patients

Medication	No.	%
Calcium acetate	77	85.6%
Erythropoietin	65	72.2%
H2 blockers	16	17.8%
Vit D	8	8.9%
Proton pump inhibitor	7	7.8%
Cinacalcet	4	4.4%
Anti coagulation (warfarin)	3	3.3%
Phosphorus chelators (sevelamer)	2	2.2%
Oral NaHco3	2	2.2%

Table (4): **Bone mineral disease related symptoms and signs**

	No. = 90
Bone pain	
Yes	59 (65.6%)
No	31 (34.4%)
Site of pain	
Diffuse	35 (38.9%)
Lower limb	19 (21%)
Back	4 (4.4%)
Upper limb	1 (1.1%)
Frequency of pain	
Frequent	49 (54.4%)
Not frequent	41(45.6%)
Impact of pain on activity	
Yes	27 (30.0%)
No	63 (70%)
Fractures	
Yes	12 (13.3%)
No	78 (86.7%)
Cause of fracture	
Major trauma	9 (10.0%)
Minor trauma	2 (2.2%)
Spontaneous	1 (1.1%)
Site of fracture	
Lower limb	8 (8.8%)
Upper limb	2(2.2%)
Multiple sites	2(2.2%)
Muscle weakness	22 (24.4%)

Table (5): Correlation Between PTH and other variables

	PTH	
	r	**P-value**
Corrected total calcium	-0.366**	0.0001
Pi (inorganic phosphate)	0.268*	0.011
Hemoglobin (Hb)	0.066	0.536
Total leukocytic count (TLC)	-0.057	0.592
Platelets	-0.106	0.322
Urea	0.513**	0.0001
Creatinine	0.003	0.981
Bone specific alkaline phosphatase	0.796**	0.000
Cholesterol	0.086	0.419
low density lipoprotein (LDL)	-0.003	0.975
Triglyceride	0.030	0.778
High density lipoprotein (HDL)	0.007	0.945
Serum albumin	-0.011	0.917

Table (6): Distribution of MBD and laboratory finding according to PTH level

	PTH < 150	**PTH 150 – 600**	**PTH > 600**	**test value**	**P-value**
	No. = 9	**No. = 60**	**No. = 21**		
Corrected total calcium (mg/dl) < 8.4 8.4 - 9.5 > 9.5	 4 (44.4%) 1 (11.1%) 4 (44.4%)	 36 (60.0%) 14 (23.3%) 10 (16.7%)	 17 (81.0%) 3 (14.3%) 1 (4.8%)	8.626	0.051
Pi (inorganic phosphate) (mg/dl) < 3.5 3.5 - 5.5 > 5.5	 5 (55.6%) 2 (22.2%) 2 (22.2%)	 19(31.6%) 37(61.7%) 4 (6.7%)	 5 (23.8%) 11 (52.4%) 5 (23.8%)	6.073	0.194
Bone specific alkaline phosphatase (IU/L) Mean ± SD Range	 89.89 ±61.6 33 – 221	 142.83 ± 54.7 34 – 225	 257.20 ± 51.6 125 – 367	43.25	0.0001

Table (7): Correlation Between Corrected ca and other variables

	Corrected total Ca	
	r	**P-value**
Parathormone hormone (PTH)	**-0.366****	**0.0001**
Age	0.158	0.137
Duration of hem dialysis (Years)	0.084	0.430
Onset of pain (Months)	0.074	0.583
Onset of fracture (Year)	0.336	0.461
Systolic blood pressure	-0.193	0.068
Diastolic blood pressure	-0.101	0.346
Pulse	0.079	0.461
Respiratory rate	-0.123	0.247

Temperature	0.091	0.400
Random blood sugar	-0.117	0.279
Pi (inorganic phosphate)	**-0.236***	**0.025**
Hemoglobin (Hb)	0.195	0.065
Total leukocytic count (TLC)	0.195	0.065
Platelets	0.027	0.804
Urea	**-0.628****	**0.0001**
Creatinine	-0.021	0.844
Bone specific alkaline phosphatase	**-0.320****	**0.002**
Cholesterol	0.039	0.713
low density lipoprotein (LDL)	0.057	0.594
Triglyceride	0.118	0.269
High density lipoprotein (HDL)	0.110	0.302
Serum albumin	-0.181	0.087

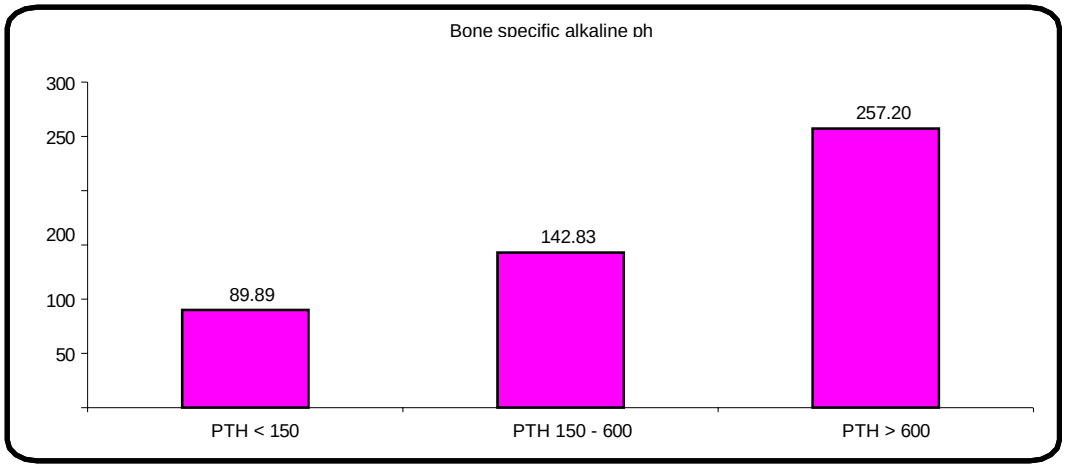

Figure (1): Comparison Between PTH and Bone specific alkaline phosphatase

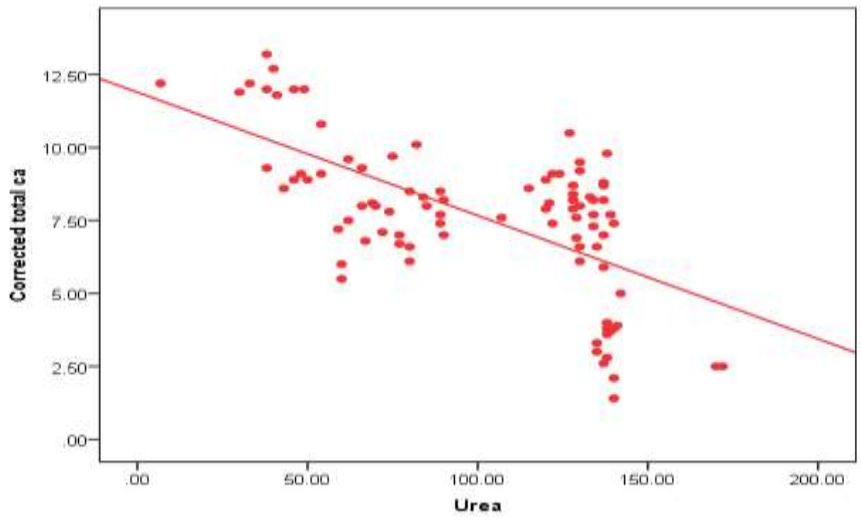

Figure (2): Negative Correlation Between Corrected total ca and Urea

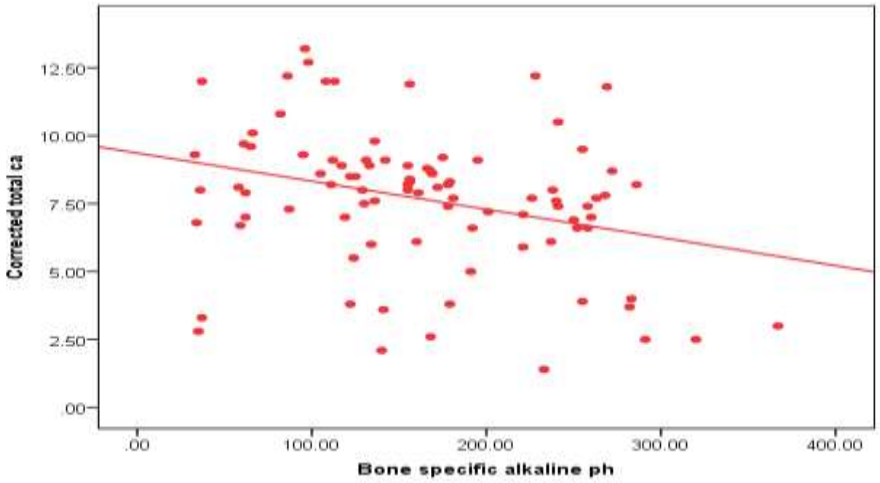

Figure (3): Negative Correlation Between Corrected total ca and Bone specific alkaline phosphatase

Discussion

CKD-mineral bone disorder (CKD-MBD) is a systemic condition that affects the metabolism of minerals and bones as a result of deteriorating renal function. These changes can be detected by examining alterations in the metabolic processes of calcium, phosphorus, parathyroid hormone (PTH), and vitamin D, as well as irregularities in bone remodeling, mineralization, and strength. Furthermore, it might result in the deposition of calcium salts in blood vessels and soft tissues (6)

As renal function declines, patients frequently experience progressively more severe changes in bone and mineral metabolism. The disturbances include renal osteodystrophy (ROD), which commonly presents as bone pain, muscle-tendon rupture, and an increased susceptibility to fractures, as well as CKD-mineral and bone disorder (CKD-MBD). (7)

Torregrosa et al. found that individuals in stages 3a–5D of chronic kidney disease (CKD) had lower bone mineral density (BMD) and were twice as likely to experience fractures compared to the general population and patients without CKD who had normal BMD. Moreover, it establishes a robust association between CKD-MBD and elevated rates of death, illness, and diminished quality of life. (8)

Chronic kidney disease (CKD-MBD) mostly arises from renal insufficiency, which leads to secondary hyperparathyroidism and subsequent hyperphosphatemia (9).

Bone alkaline phosphatase (BALP) is a dimeric protein that is attached to the outer surface of osteoblasts. When used as a biomarker, it acts as a valuable indicator of bone formation. PTH

and BSAP demonstrate similar diagnostic precision in differentiating between low and non-poor bone turnover. (10)

The aim of our study was to examine mineral bone disorders (MBDs) in hemodialysis (HD) patients at EL-Minia University Hospital and evaluate the degree to which the recommended levels, as specified by KDIGO criteria, were achieved.

According to the 2017 KDIGO guidelines, patients with CKD stages 5 and 5D should aim for specific levels of certain substances in their blood. These targets include a serum corrected calcium level between 8.4-9.5 mg/dL, a serum inorganic phosphate level between 3.5-5.5 mg/dL, and a parathyroid hormone (PTH) level for Stage 5 CKD HD patients that is 2- to 9-fold higher than the upper normal limit (11), which corresponds to a range of up to 600 pg/ml. (12)

According to the laboratory results in this study, 21 patients (23.3%) exhibited signs of hyperparathyroid bone disease, characterized by high levels of intact parathyroid hormone (iPTH >600 pg/ml). On the other hand, 9 patients (10%) had low-turnover bone disease, indicated by reduced levels of iPTH (<150 pg/ml). The data revealed that the combined occurrence of high and low turnover bone disease among the patients analyzed is 33.3%. Furthermore, there were 60 cases where the PTH levels fell within the desired range of 150 to 600 pg/mL.

In a study conducted by Hedgeman et al. across 13 nations, it was discovered that the occurrence of secondary hyperparathyroidism varied significantly, ranging from 30% to 50% among patients dependent on dialysis (13). Agarwal et al. found that 39.4% of individuals diagnosed with stage 5 chronic kidney disease (CKD) exhibited hyperparathyroidism (14).

In Senegal, Seck et al. found that among 118 individuals, 57 cases showed high-turnover illness (secondary hyperparathyroidism), while 22 cases showed low-turnover bone disease (15).
The hyperparathyroidism cohort was divided into three subgroups according to the amounts of calcium in their blood. The frist subgroup comprised 17 individuals, accounting for 81% of the total, who displayed increased parathyroid hormone (PTH) levels and low calcium levels. This could be ascribed to the low effectiveness of vitamin D, either because of inadequate treatment or noncompliance by the patients. Furthermore, individuals suffering from chronic renal illness demonstrated a resistance to parathyroid hormone (PTH). also, the decline in osteoblastic parathyroid hormone (PTH) receptors in chronic kidney disease (CKD) has been associated with PTH resistance in CKD. Three individuals (14.3%) in the second group had serum calcium levels within the normal range. the third group, there was one patient (4.8%) who exhibited high levels of both parathyroid hormone (PTH) and calcium. This can be related to the advancement of secondary hyperparathyroidism, which required surgical intervention on the parathyroid glands.

Patients exhibiting low bone turnover were subsequently classified into three groups according to their serum calcium levels. Out of these groups, 4 cases (44.4%) had low levels of serum calcium, 1 case (11.1%) had normal levels of serum calcium, and 4 cases (44.4%) had high levels of serum calcium. The observed phenomenon in this group involved an increased intake of calcium, which explains the rise in calcium levels in the blood despite the low levels of parathyroid hormone (PTH).

The study revealed a successful iPTH blood level in 66.7% of the subjects. Only 23.3% of the patients displayed serum calcium levels that were within the required range. In their research, Buargub et al. found that a mere 17.4% of the patients achieved the intended blood level of iPTH, while only 30% of the patients had serum Ca levels that met the appropriate range (16). In a study conducted by Jabbar et al., it was discovered that only 9% of patients had parathyroid hormone (PTH) levels that fell within the normal range. (17)

According to the KDIGO standards, 57 out of our total cases (63.3%) had hypocalcemia, which means their calcium levels were below 8.4 mg/dl. Out of the total of 15 patients, which accounts for 16.7% of the cases, hypercalcemia was seen. In these cases, the calcium levels exceeded 9.5 mg/dl. In addition, 18 patients, which accounted for 20% of the total, achieved the desired calcium level range of 8.4-9.5 mg/dl.

Our investigation, following the KDIGO recommendations, revealed that 29 cases (32.2%) exhibited hypophosphatemia, characterized by inorganic phosphate levels below 3.5 mg/dl. In addition, 11 cases (12.2%) exhibited elevated levels of inorganic phosphate (hyperphosphatemia), with a value exceeding 5.5 mg/dl. Out of the total of 50 cases, which accounts for 55.6% of the sample, the serum inorganic phosphate levels were found to be within the target range of 3.5-5.5 mg/dl.

This discovery aligns with the research carried out by Ahmed et al., which likewise encompassed three separate cohorts. The original group included of two patients (3.6%) experiencing hypercalcemia, 46 patients (83.6%) experiencing hypocalcemia, and seven patients (12.7%) having normal levels of calcium in their blood serum. (18).

In Nafar et al.'s study, it was discovered that 46% of the patient's exhibited hypoparathyroidism, whereas 29.3% of the patient's displayed hyperparathyroidism. Hypercalcemia was found in 20.6% of the patients, whilst hyperphosphatemia was observed in 34.2% of the patients. (19)

The results of our experiment revealed a statistically significant positive correlation between parathyroid hormone (PTH) and bone-specific alkaline phosphatase. Compared to PTH, serum BALP shows less variation and hence may be more suited for detecting and tracking changes in bone turnover over a period of time.
Significant correlation was found between parathyroid hormone (PTH) and both phosphate (Pi) and urea. Additionally, a statistically significant inverse correlation was found between corrected total calcium levels and the following variables: parathyroid hormone (PTH), bone-specific alkaline phosphatase, and urea.
Li et al. discovered a strong correlation between serum PTH levels and an elevated risk of hyperphosphatemia and high serum ALP levels. The connection between these variables is robust, progressive, and exhibits a consistent linear pattern (20).

Furthermore, Nafar et al. established a statistically significant and favorable correlation. The correlation between parathyroid hormone (PTH) and serum phosphorus (Pi) levels is positive, while the correlation between PTH and blood calcium (Ca) levels is negative. A negative correlation was seen between the mean serum Pi concentration and the mean serum adjusted Ca concentration (19).

In addition, Ahmed et al. found a clear positive correlation between parathyroid hormone (PTH) and alkaline phosphatase (ALP), as well as between blood urea and PTH. On the other hand, a significant inverse correlation was found between the levels of calcium in the blood and the amount of urea in the blood(18).
Jadoul et al. observed a positive correlation between elevated parathyroid hormone (PTH) levels and a higher probability of decreased bone mineral density (BMD).(21)

Haarhaus et al. discovered a positive correlation between bone-specific alkaline phosphatase (bALP) and parathyroid hormone (PTH) (22).

In a separate study, Agarwal et al. investigated a cohort of 87 patients who were receiving hemodialysis, he found that the increase in PTH level was accompanied by rise in bone specific alkaline phosphatase and decrease in calcium level (15).

In our research, 59 cases (65.6%) reported the occurrence of bone pain, with 30% of these cases reporting a negative impact on their daily functioning, and 13.3% of cases reporting the occurrence of fractures. Two individuals exhibited PTH levels beyond 600 pg/dl, whilst 10 individuals displayed PTH levels within the range of 150-600 pg/dl. This pertains to the possible etiology of the fracture. Among the entire set of occurrences, 9 were characterized by severe trauma, 2 were associated with mild trauma, and 1 case occurred without any apparent cause. In addition, 24.4% of the cases displayed muscular weakness. Subjects with low, normal, and high PTH levels experienced bone soreness in 55.6%, 66.7%, and 66.7% of cases, respectively. Despite the apparent control of the parathyroid hormone (PTH) level, the regulation of serum calcium and phosphate levels in this group is inadequate, resulting in the emergence of symptoms of mineral bone disorder (MBD) in the patients. This can be partially attributed to inadequate

vitamin D intake and unhealthy eating habits, as well as the use of medications that affect parathyroid hormone (PTH).

83.3% of cases with bone fractures displayed parathyroid hormone (PTH) values within the range of 150-600 pg/ml. When dealing with fractures, it is important to consider issues beyond irregularities in parathyroid hormone (PTH). This includes drugs or dietary sources that include aluminum, as it can build up in the bones and cause osteomalacia.

The study comprised a total of 77 participants who were administered oral Calcium acetate, 65 participants who were administered Erythropoietin, 16 participants who were administered H2 blockers, 20 participants who were administered Vit D, 7 participants who were administered PPI, 4 participants who were administered Cinacalcet, 3 participants who were administered oral Anti coagulation, and 2 participants who were administered Phosphorus chelators and Oral $NaHCO_3$.

Hanudel et al. found that Erythropoietin affects the production and breakdown of FGF23, which could have important implications for individuals with chronic kidney disease (23).
Adachi et al. discovered that prolonged use of H2-receptor antagonists (HRA) had negligible influence on bone mineral density (BMD), and the length of HRA administration did not have an impact on the degree of BMD. (24).

Proton pump inhibitors (PPIs) are associated with a higher probability of hip fractures in the general population. The proposed mechanisms primarily revolve around reduced calcium absorption, as well as the activation of parathyroid glands through gastrin, deficiency of vitamin B12, and altered activity of osteoblasts and osteoclasts (25). Vangala et al. found that approximately 75% of patients who suffered a hip fracture had been using a proton pump inhibitor (PPI) in the three years prior to the fracture. Furthermore, almost 15% of these individuals had acquired prescriptions for PPIs that were used for more than 80% of the days within that specific period (26).

The research conducted by Louie et al. on a notable European patient group with chronic HD found that 67% of those who were given cinacalcet experienced hypocalcemia. This patient has been interpreted as a medically induced equivalent to the "hungry bone syndrome," which is commonly observed after parathyroidectomy in individuals with advanced secondary hyperparathyroidism (27). When compared to "hungry bone syndrome," cinacalcet-induced hypocalcemia is generally less intense, more prolonged, and frequently asymptomatic (28).

Fusaro et al. conducted a cross-sectional study with a 3-year follow-up to investigate the disparities between hemodialysis patients who received warfarin treatment for more than 1 year and those who did not receive any treatment. The study revealed that male patients who were administered warfarin had a greater prevalence of vertebral fractures in comparison to the control group (77.8% vs. 57.7%, $p<0.04$) (29).
Binding et al. shown that the use of new oral anticoagulants was more effective than vitamin K dependent anticoagulation in preventing bone fractures in patients with atrial fibrillation. Additionally, these new anticoagulants had good effects on bone health and reduced the risk of fractures. (30)
Rasheed et al. found that giving a small amount of oral sodium bicarbonate supplementation improved protein metabolism. Furthermore, correcting metabolic acidosis in hemodialysis patients improves serum albumin levels, which is essential for maintaining a normal total calcium level (31)

Regarding the consumption of drinking water, 37 individuals used tap water while 53 individuals consumed filtered water. In terms of the usage of cooking pans, there were 70 patients of individuals utilizing aluminum pans.

Mohammed et al. found that aluminum sulfate, commonly referred to as alum, is the primary water coagulant utilized in Egypt. Nevertheless, the excessive use of alum during the water treatment procedure may lead to more concentrations of aluminum in tap water (32).

Jabeen et al. cautioned against heating aluminum pans in the absence of any liquid, since this may lead to the release of metal, particularly aluminum, into the food. Exposure to this substance has the potential to cause harm to persons. The analysis revealed that all the samples subjected to aluminum exhibited

increased quantities of aluminum metal subsequent to marination and cooking (33).

According to the KDOQI Clinical Practice Guidelines issued by the National Kidney Foundation, medical professionals should take action if the blood aluminum levels in patients on long-term hemodialysis surpass 2 µg/dL (34).

Aluminum has been identified in the bones of individuals with chronic renal failure who are undergoing hemodialysis. Aluminum has an inclination to specifically bind to the unmineralized variant of type I collagen, impeding the calcification process and resulting in the formation of osteomalacia. (35)

Conclusion: Our results revealed that the percentage of MBD among the studied patients in Minia university hospital hemodialysis unit was 33.3% depending on abnormal PTH levels (23.3% of patients with high PTH level and 10% with low PTH levels). The rise of b-ALP is synchronized to the rise of PTH as most of patients with high PTH level (high bone turnover) had high level of b-ALP and patients with low PTH level had low serum b-ALP level.

Recommendations: Regular follow up of hemodialysis patients for MBD should be done. bone-ALP is metabolized by the liver so it can be used as a more sensitive diagnostic marker to CKD-MBD than PTH. Drinking water, cooking pans and drugs used frequently by hemodialysis patients may have a role of MBD so it should be considered and patient education about their risk should be done to be avoided.

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