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## Relationship between Anemia and Biochemical Parameters of Mineral Bone Disorders in Chronic Kidney Disease Patients

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### ABSTRACT

**Background:** Anemia, electrolyte disturbances and mineral bone disorders are common outcomes of chronic kidney disease (CKD).

**Aim of the work:** To assess relationship between anemia and mineral bone disorder (MBD) parameters in stages 3-5 CKD on conservative treatment patients.

**Patients and Methods:** The current study included a sample of (160) cases, all of whom had chronic kidney disease. All subjects were submitted to full history, clinical examination, and laboratory testing which included complete blood count, Calcium, Phosphorus and Parathyroid hormone (PTH). Quantitative determination of total 25-OH Vitamin D was measured in all patients. Estimated glomerular filtration rate (eGFR) was being calculated.

**Result:** The study revealed a statistically significant association between Hb and eGFR, and also showed a statistically significant negative relationship (p value = 0.001) (r = -0.38) between Hb and serum creatinine. It also revealed a semi-inverse relationship between serum parathormone (iPTH) and hemoglobin level in blood between CKD. Whenever there is an increase in the serum iPTH reflects the decrease in the level of hemoglobin in the blood of the study sample of patients with chronic kidney disease. One of the important statistical results indicated by the study is that blood phosphate is linked to low hemoglobin in kidney patients. Our study agreed with studies that show that vitamin D deficiency is closely related to low hemoglobin level in CKD patients. The lower the calcium level, the lower the hemoglobin level. We found that increased blood calcium is associated with a higher hemoglobin level.

**Conclusion:** Our study showed the significant association between CKD-BMD and anemia. It also showed that increased serum phosphate, parathyroid activity, severe deficiency in vitamin D and a high incidence of anemia among patients with chronic kidney disease.

**Keywords:** Anemia; Chronic kidney disease; Mineral bone disorder.

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### INTRODUCTION

Exacerbation of chronic kidney disease (CKD) is a complex, chronic and long-standing condition whose degree of exacerbation is determined by abnormalities in kidney structure or function for >3 months, with serious health implications.<sup>1</sup>

The kidneys have a great role, the most important of which is the regulation of fluids inside the body, as well as the balance of acid-base, and when kidney disease is severe, metabolic acidosis, and there is also an increased in serum level of potassium, lack of sodium in the blood, and a lack of calcium, which constitutes a reverse risk, including what affects the bones such as disorders of the glossy as well as leads

to calcification of the vessels. Hemorrhagic disease and may even lead to death.<sup>2</sup>

Since one of the most important functions of the kidneys is the regulation of fluids and electrolytes inside the body. When the kidneys are damaged, this leads to electrolyte and mineral imbalances in chronic kidney patients.<sup>3</sup> In addition, kidney damage may sometimes cause anemia, as well as the presence of some disorders.<sup>4</sup> The aim of our study was to assess relationship between anemia and mineral bone disorder (MBD) parameters in stages 3-5 CKD on conservative treatment patients.

### PATIENTS AND METHODS

The current study included a sample of (160) cases, all of whom had chronic kidney disease. All individuals were subjected to a complete history,

clinical examination and laboratory tests, which were conducted in the outpatient department of kidney diseases at the National Institute of Kidney and Urinary Diseases (Egypt).

The inclusion criteria included: Patients between the ages of 18 and 65 years who were proved as having chronic kidney disease.

Exclusion criteria included patients on hemodialysis, patients acute renal failure, congestive heart failure or hepatic disease.

All patients signed written informed consent prior to their inclusion in this study and the institutional ethical committee of the Faculty of Medicine, Al-Azhar University, approved the study.

#### All patients underwent the following:

All patients were subjected to the following: Complete history taking, which include history of comorbid conditions such as DM, HTN and cardiac disease. History of drug intake was taken. Full Clinical Examination: which include manifestations of chronic kidney disease.

As well as measuring the weight of the patients and their suitability for height and the body mass calculator (BMI).

Seven milliliters were collected from the vein of all patients, through sterile plastic syringes, and they are disposed of after completing their function properly. Each sample was divided as follows: Five milliliters of blood was allowed to pass gently along the wall of a clean dry centrifuge tube labeled with the patient name. The blood was allowed to clot for half an hour in a water bath at 37°C, and then it was centrifuged for 15 min at 3000 revolutions/minute for separation of serum by means of a clean dry Pasteur pipette. The serum was fractionated into two clean dry tubes for measuring the following: Estimation of serum creatinine and urea was done using COBAS 501 chemistry autoanalyzer (Roche Diagnostics, USA), Calcium and Phosphorus were assessed by commercial kits available and measured by spectrophotometry, Parathyroid hormone (PTH) measured by Quantitative, electrochemiluminescence (ECLIA) assay (Beckman Coulter, Fullerton, CA), Quantitative determination of total 25-OH Vitamin D was measured in all patients by enzyme-linked immune-sorbent assay (ELISA) commercial kit (Vitamin D Enzyme Immunoassay kit, Monocent, Inc., USA).

Two milliliters of blood was put on EDTA (1mg/ml blood) and mixed thoroughly to perform complete blood picture by Erma Automated Blood Count Machine (Tokyo, Japan).

Version 26 of the statistical program was used, quantitative data and qualitative data were used. The quantitative data is indicated by the standard deviation (SD +) and the qualitative data as a number with a percentage. The t-test was used and the non-parametric data was compared at 0.05 through the Chi-square test.

CKD was indicated as a decrease in eGFR <60 mL/min/1.73 m<sup>2</sup> for more than three months.

## RESULTS

The mean age of all studied patients was 54.9 ± 7.4 years. There were 62 males (38.8%) and 98 females (61.3%). There were 84 diabetic patients (52.5%) and 126 hypertensive patients (78.8%) in the studied patients. The mean eGFR, serum creatinine, serum urea, total calcium, phosphorous, vitamin D, PTH and Hb were 22.3 mL/min/1.73m<sup>2</sup>, 3.3 mg/dl, 102.1 ± 58.9 mg/dl, 8.5 mg/dl, 4.6 mg/dl, 19.1 ng/ml, 185.2 pg/ml and 10.5 g/dl, respectively.

Our results showed statistical significant (**p-value < 0.001**) Positive correlation (**r = 0.48**) between Hb and eGFR, and Statistically significant (**p-value = 0.001**) negative correlation (**r = - 0.38**) between Hb and serum creatinine.

The relationship between serum parathyroid hormone (iPTH) and hemoglobin level was inverse. Whenever there is an increase in serum iPTH, it is the cause of low hemoglobin in patients with chronic kidney disease. .

The single blood phosphate was related to the decrease in the level of hemoglobin in the blood of all patients with chronic kidney disease, and there is an inverse correlation between the blood phosphate and the level of hemoglobin, and therefore the hemoglobin level, whenever it was high in patients, there was a decrease in vitamin D. The statistical results were comprehensive and useful.

Studied patients (N = 160)			
Age (years)	Mean ±SD	54.9 ± 7.4	
	Min - Max	37 – 64	
Sex	Male	62	38.8%
	Female	98	61.2%

**Table 1:** Description of demographic data in all studied patients.

Studied patients (N = 160)			
DM	No	72	47.5%
	Yes	84	52.5%
HTN	No	34	21.2%
	Yes	126	78.8%
Duration of DM (years)	Mean ±SD	12.6 ± 3.6	
	Min – Max	5 – 21	
	Mean ±SD	11.03 ± 4.2	
Duration of HTN (years)	Min – Max	4 – 22	

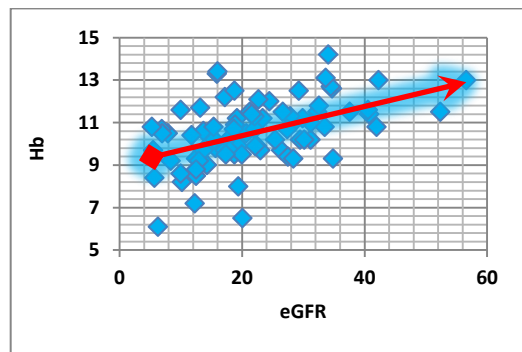
**Table 2:** Description of chronic diseases in all studied patients.

(n = 160)	Minimum	Maximum	Mean	±SD
eGFR	8.3	56.6	22.3	10.8
Creat	1.4	6.6	3.3	1.7
Urea	43	169	102.1	58.9
Total calcium	6.9	10.2	8.5	1.0
Phosphorous	2.8	9	4.6	1.12
Vitamin D	9	29.3	19.1	4.6
PTH	28.7	897.7	185.2	160.4
Hb	8.1	14.2	10.5	1.5
WBCs	3	15.9	7.9	2.3
PLTs	104	560	257.2	91.1

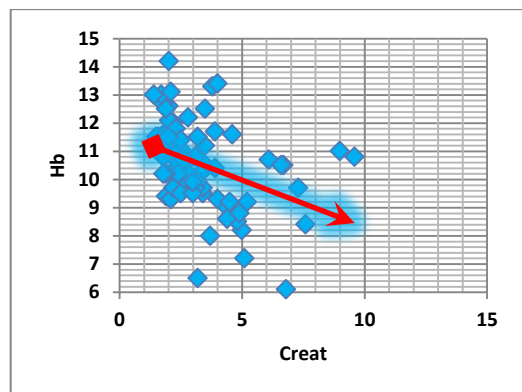
**Table 3:** description of laboratory data in all studied patients.

Variables	(r)	p-value
Hb vs eGFR	0.48	< 0.001 HS
Hb vs Creat	- 0.38	0.001 S
Hb vs Urea	- 0.29	0.009 S
Hb vs Total Ca	0.46	< 0.001 HS
Hb vs Phosphorous	- 0.56	< 0.001 HS
Hb vs Vitamin D	0.42	< 0.001 HS
Hb vs PTH	- 0.26	0.02 S
Hb vs WBCs	0.13	0.247 NS
Hb vs PLTs	- 0.17	0.127 NS

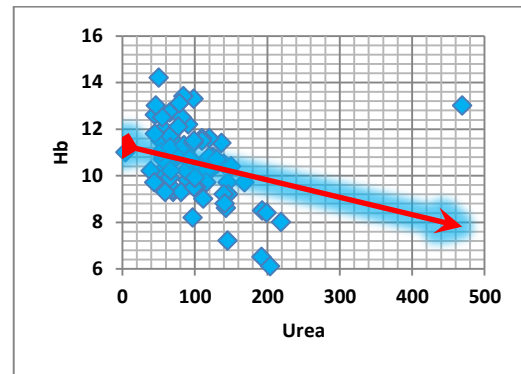
**Table 4:** Correlation study between Hb and other studied laboratory data in all studied patients. (r): Pearson correlation coefficient.



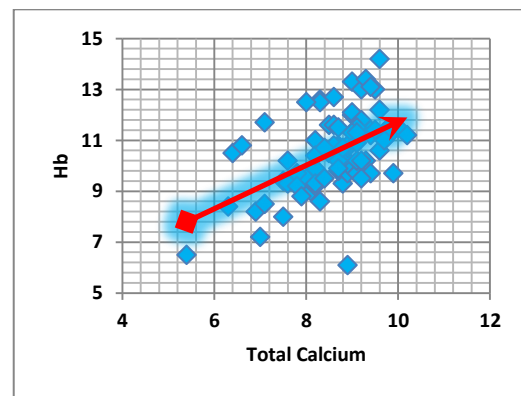
**Fig. 1:** Positive correlation between Hb and eGFR.



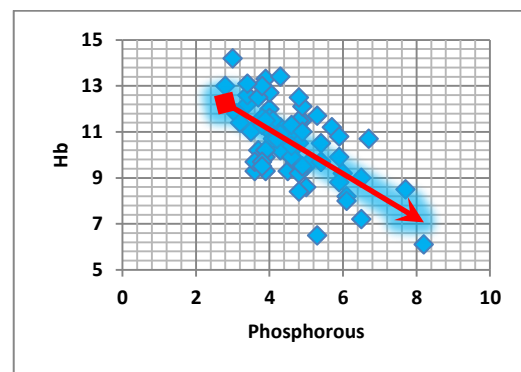
**Fig. 2:** Negative correlation between Hb and Creat.



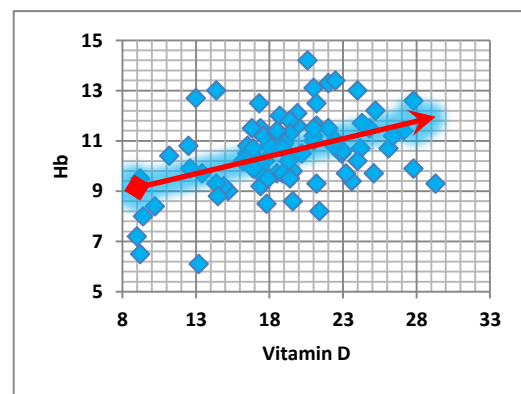
**Fig. 3:** Negative correlation between Hb and Urea.



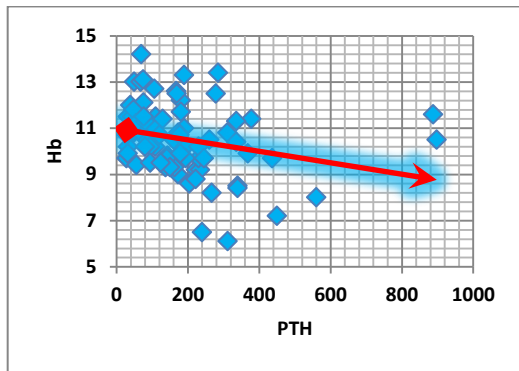
**Fig. 4:** Positive correlation between Hb and total calcium.



**Fig. 5:** negative correlation between Hb and phosphorous.



**Fig. 6:** Positive correlation between Hb and vitamin D.



**Fig. 7:** Negative correlation between Hb and PTH.

## DISCUSSION

Our current research revealed a statistical relationship (p value < 0.001) that expresses a positive correlation ( $r = 0.48$ ) between Hb and eGFR, and a negative correlation (p value = 0.001) ( $r = -0.38$ ) between serum creatinine and hemoglobin.

There was a study by Nalado et al. Which was conducted on a sample of 353 chronic kidney patients, the results of which agreed with the results of this research, where the percentage of anemia patients represented 43.18%, which indicates a statistically significant relationship between anemia and chronic kidney disease (P value < 0.001). It agreed with our study that there was a positive relationship between eGFR and hemoglobin levels ( $r = 0.334$ , P value < 0.0001).<sup>6</sup>

Our study revealed the inverse relationship between hemoglobin level and healthy serum parathyroid hormone (iPTH).

iPTH leads to a decrease in serum level of hemoglobin among CKD patients.

The results of this research also agreed with the study conducted by Keshk et al. Which was conducted on 10 healthy people as a control group and 40 other patients with chronic kidney disease and the aim of this study was to evaluate the relationship of parathyroid hormone (iPTH) and (Hb) level in the patients included in the study and the relationship was negative and statistically significant between iPTH and Hb in the blood.<sup>7</sup>

And the other study that resulted in the same results as ours in this research is the study of Saleem et al., and the results of patients were negatively related and indicate statistical significance between iPTH and Hb, and it was conducted on hemodialysis patients and the control group (P = 0.01).<sup>8</sup>

In the study of Adhikary et al., which included chronic renal patients aged between (29:70) years, it indicated an inverse relationship between normal hematocrit and parathyroid levels, which is the same results revealed by our current research.<sup>9</sup>

More recently, Azeem et al. evaluated 110 Patients undergoing maintenance hemodialysis with PTH

levels greater than 300 ng/L. The authors concluded that patients with hyperparathyroidism frequently develops anemia.<sup>10</sup>

Chutia et al. A cross-sectional study on a sample of (63 chronic renal patients) showed an inverse association between the level of healthy PTH and Hb ( $r = -0.545$ ), indicating that the variables iPTH and Hb are inversely proportional to each other.<sup>11</sup>

The results of the present study showed that hyperphosphatemia is associated with a significantly lower hemoglobin level in CKD-patients. Serum phosphate levels are inversely correlated with levels of hemoglobin.

AbdelAal et al. a case control study included 55 adult patients with end stage renal disease as well as 55 healthy individuals as a control group. This study showed that Hb was inversely correlated with serum iPTH ( $r = -0.359$ , P=0.007) and serum phosphate ( $r = -0.570$ , P<0.001) in the hemodialysis group. In patients with ESRD, an association was found between anemia and each of hyperphosphatemia and hyperparathyroidism.<sup>12</sup>

Our results were concordant with results of Amnuay et al. who showed that higher serum phosphorus levels were associated with low hemoglobin levels in hemodialysis patients among the 43 CKD patients. In multivariate analysis, serum phosphate was associated with a significantly lower hemoglobin level. Serum hemoglobin level is inversely linked with iPTH and serum phosphate level.<sup>13</sup>

Kurniawan et al. The cross-sectional study was conducted in 2176 CKD patients 3–5 miles away. Of the 2176 CKD patients, 67% of the patients were chronic and 56.1% of the patients were chronic. They also found a strong link between hyperphosphatemia and the presence of anemia. They thought that low serum phosphorus could enhance the production of uremic toxin as higher polyamines have been shown to inhibit erythropoiesin secretion and parathyroid hormonal secretion.<sup>4</sup>

A large population-based study conducted by Tran et al. observed that phosphorus levels increase the likelihood of anemia in a population that is associated with early CKD, and phosphorus is biomarginal for anemia and can affect the appearance of hematopoiesis.<sup>2</sup>

The results of the present study showed that vitamin D deficiency was linked to a significantly lower hemoglobin level in patients with CKD.

Results obtained in this study were in agreement with Saha et al. who evaluated 115 patients with CKD including. Mean age was 57.8 years. Most patients were in CKD stage 4 (43, 37.4%) and 5 (45, 39.1%). They observed that Hemoglobin in CKD stages 3-5 pre-dialysis patients had positive correlation with 25(OH)D and negative correlation with phosphate.<sup>14</sup> Kendrick et al. stated that low 25(OH)D3 and elevated CRP levels were independently related with

low hemoglobin concentrations in non-dialysis kidney disease subjects.<sup>15</sup>

The results of current study observed positive relationship between serum calcium and serum hemoglobin level among CKD. We found that an decrease in serum calcium was associated with decrease in serum level of hemoglobin.

This results were in agreement with results of Kimata et al. which found an association between hypocalcemia and presence of anemia.<sup>16</sup>

### CONCLUSION

Our study showed the significant association between CKD-BMD and anemia. It also showed that increased blood phosphate, parathyroid activity, severe deficiency in vitamin D and a high incidence of anemia among patients with chronic kidney disease.

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