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Hani Ismail

*Internal medicine, faculty of medicine, Alazhar university ,cairo, Egypt, haniismail52@yahoo.com*

Ahmed Alaa Eldin Ahmed M. Saad

*Internal Medicine, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt*

El-Sayed Muhammad Rashed

*Internal Medicine, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt*

Mohamed Farok Ibrahim Mosa

*Clinical Pathology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt*

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# Disorders of Calcium Metabolism and its Relation to Anemia in Chronic Kidney Disease Patients

Hani I. H. Abu Khalil <sup>a,\*</sup>, Ahmed A. A. M. Saad <sup>a</sup>, El-Sayed M. Rashed <sup>a</sup>, Mohamed F. I. Mosa <sup>b</sup>

<sup>a</sup> Department of Internal Medicine, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

<sup>a</sup> Department of Clinical Pathology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

## Abstract

*Background: Chronic kidney disease (CKD) is frequently complicated by anemia & mineral bone disorders.*

*Aim and objectives: To evaluate the connection between anemia & markers of calcium metabolism in stages 3-5 CKD nondialysis-dependent on dialysis individuals.*

*Subjects and methods: A sample of sixty patients participated in the current investigation, all of whom had CKD on conservative treatment. All understudied patients were submitted to full medical history taking, apparent clinical examination, and laboratory investigations, including full blood picture, total serum calcium, serum phosphorus, Parathormone hormone (PTH), and total 25-OH Vitamin D.*

*Results: A statistically significant correlation between hemoglobin concentration (Hb) and serum total calcium (Ca) was found in the current investigation. Hemoglobin levels decrease with decreasing calcium levels. The study's key statistical findings include the connection between CKD patients' low hemoglobin and high blood phosphate (PO<sub>4</sub>) levels. Our research supported other studies that demonstrate a strong correlation between low hemoglobin levels in CKD patients and vitamin D insufficiency. Additionally, it showed that in CKD patients, serum parathormone (iPTH) and hemoglobin level were inversely correlated. Any time there is a rise in serum PTH, there is a corresponding drop in hemoglobin levels. Hemoglobin & eGFR have a statistically significant association in the current investigation (p-value = 0.005) (r = 0.36).*

*Conclusion: Correcting renal osteodystrophy is thought to be a therapeutic target for anemia, since we reported finding a correlation between blood bone metabolic indicators & anemia in individuals CKD.*

*Keywords:* Haemoglobin; Mineral bone disorders ; Glomerular filtration rate

## 1. Introduction

Decreased renal function lasting more than three months is known as CKD & identified by reduced estimated GFR below sixty ml per minute per 1.73 m<sup>2</sup> or by blood, urine, or image markers of renal injury.<sup>1</sup> Patients with CKD frequently have disorders in the metabolism of minerals and bones, which may be related to increased cardiovascular calcification and a great chance of complications & death.<sup>2</sup> The main causes of anemia linked to chronic kidney illness are inadequate erythropoietin production, iron store depletion, and a shortened half-life of red blood cells.<sup>3</sup>

## 2. Patients and methods

A sample of sixty patients participated in the

current investigation, all of whom had CKD. All individuals were subjected to a complete history of medical importance (such as comorbid conditions and drug intake), physical examination, and medical tests, which were conducted in the outpatient & inpatient department of Internal Medicine, Al-Hussein Hospital, Al-Azhar University (Egypt). The inclusion criteria included Patients between 18 and 60 years of age who were proven as having CKD on conservative treatment. Exclusion criteria included hemodialysis, acute kidney injury, congestive heart failure, or chronic liver disease patients. Before being included in this study, every patient signed a written informed consent form, and the study was authorized by the Al-Azhar Faculty of Medicine's institutional ethical council. Venous blood samples containing seven milliliters were taken from all understudied individuals through sterile plastic syringes and then disposed of immediately.

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\* Corresponding author at: Internal Medicine, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt.  
E-mail address: [Haniismail52@yahoo.com](mailto:Haniismail52@yahoo.com) (H. I. H. Abu Khalil).

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Exclusion criteria included hemodialysis, acute kidney injury, congestive heart failure, or chronic liver disease patients. Before being included in this study, every patient signed a written informed consent form, and the study was authorized by the Al-Azhar Faculty of Medicine's institutional ethical council. Venous blood samples containing seven milliliters were taken from all understudied individuals through sterile plastic syringes and then disposed of immediately. Every specimen was divided in the following manner: A dry, clean centrifuge tube labeled with the patient's name was gently filled with five milliliters of blood. After allowing the blood to coagulate for thirty minutes at 37°C in a water bath, it was centrifuged for fifteen minutes at 3000 revolutions per minute to separate the serum using a dry, clean Pasteur pipette. Two dry, clean tubes were separated from the serum to measure the following: In order to estimate serum creatinine & urea, Roche Diagnostics, USA's COBAS 501 chemistry autoanalyzer was utilized. Commercial kits were used to test Ca & PO<sub>4</sub> & measured by spectrophotometry. Parathyroid hormone (PTH) was measured using the quantitative electrochemiluminescence (ECLIA) assay (Beckman Coulter, Fullerton, CA). Using a commercial enzyme-linked immune-sorbent assay (ELISA) kit (Vitamin D Enzyme Immunoassay kit, Monocent, Inc., USA), the total 25-OH Vitamin D was quantitatively determined for each patient. An automated Blood Count Machine (Tokyo, Japan) was used to perform a complete blood picture after two milliliters of blood were added to EDTA (1 mg/ml blood) and properly mixed. Statistical analysis: Version 24 of the SPSS (Statistical Program for Social Science) was applied to analyze the data. Frequency and percentage were used to report both quantitative & qualitative data. Quantitative data were expressed as mean± standard deviation (SD). A measure of a set of data's dispersion is the standard deviation (SD). In contrast to a greater SD, which suggests that the results are dispersed over a larger range, a lower standard deviation (SD) suggests that the values are more likely to be near the established mean. The Pearson's correlation coefficient (r) test was applied to correlate data among two parameters. Significance is indicated by a P value less than 0.05. Glomerular filtration rate (GFR) calculation: The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula is applied to determine the estimated glomerular filtration rate (eGFR).<sup>4</sup> Decreased eGFR of below sixty ml/min/1.73 m<sup>2</sup> for greater than 3 months was the definition of CKD .<sup>5</sup>

### 3. Results

We found that the mean age of all patients under study was 53.33 ± 6.44 years, 24 were males (40%) while females were 36 (60%) (Table 1), 33 were diabetic (55%) while 47 were hypertensive (78.7%) (Table 2). The mean total Ca, PO<sub>4</sub>, 25-OH Vitamin D, Parathormone hormone (PTH), haemoglobin, eGFR, serum creatinine and serum urea, were, 8.88 mg/dl, 4.37mg/dl, 19.97 ng/dl, 144.66 pg/ml, 10.88g/dl, 26.42 ml/min/1.73m<sup>2</sup>, 4.5 mg/dl and 83.3 mg/dl respectively (Table 3). A statistically significant correlation between haemoglobin concentration (Hb) & serum total calcium (Ca) (p- value < 0.001) was found as well as Positive correlation (r = 0.55). Haemoglobin levels decrease with decreasing calcium levels. The study's key statistical findings include the connection between CKD patients' low haemoglobin & high blood (PO<sub>4</sub>) levels as there was inverse correlation (p-value less than 0.001) & (r = - 0.47) among both parameters. Our investigations demonstrate a strong correlation between low haemoglobin levels in CKD patients & vitamin D insufficiency. Additionally, it showed that in CKD patients, serum parathormone (iPTH) & haemoglobin level were inversely correlated. Any time there is a rise in serum PTH, there is a corresponding drop in haemoglobin levels. Haemoglobin & eGFR have a statistically significant association in the current investigation (p value = 0.005) (r = 0.36) (Table 4).

Table (1): Demographic information of under studied patients.

| PATIENTS UNDER STUDY<br>(NUMBER = 60) |           |             |     |
|---------------------------------------|-----------|-------------|-----|
| AGE<br>(YEARS)                        | Mean ± SD | 53.33± 6.44 |     |
|                                       | Range     | 37 – 59     |     |
| SEX                                   | Male      | 24          | 40% |
|                                       | Female    | 36          | 60% |

Table (2): Chronic diseases in all patients under study.

| PATIENTS UNDER<br>STUDY (NUMBER =<br>60) |     |    |       |
|--|-----|----|-------|
| DM                                       | No  | 27 | 45%   |
|  | Yes | 33 | 55%   |
| HTN                                      | No  | 13 | 21.3% |
|  | Yes | 47 | 78.7% |

Table (3): laboratory results of all patients under study

|                       | Range    | Mean ± SD      |
|-----------------------|----------|----------------|
| S. Calcium(mg/dl)     | 5.4-10.2 | 8.88±0.78      |
| S. Phosphorous(mg/dl) | 3-7      | 4.37±0.85      |
| PTH (Pg/ml)           | 29-560   | 144.66 ± 108.7 |
| Vitamin D(ng/ml)      | 10-30    | 19.97±4.35     |
| S. Creatinine(mg/dl)  | 1.4-4.4  | 2.5±0.09       |
| eGFR                  | 15-56    | 26.42±1.12     |
| Urea(mg/dl)           | 41-190   | 83.3±29.1      |
| HB (g/dl)             | 6.7-14.1 | 10.88±1.32     |
| WBC (cell/cmm)        | 3.8-12.8 | 7.84± 2.01     |
| Platelets(cell/cmm)   | 105-400  | 243.5±67.17    |

Table (4): The relationship between haemoglobin and other laboratory results in all under studied patients.

| VARIABLES                      | PEARSON CORRELATION COEFFICIENT (R) | P-VALUE                      |
|--------------------------------|-------------------------------------|------------------------------|
| HAEMOGLOBIN VERSUS TOTAL CA    | 0.55                                | < 0.001 (highly significant) |
| HAEMOGLOBIN VERSUS PHOSPHOROUS | - 0.47                              | < 0.001 (highly significant) |
| HAEMOGLOBIN VERSUS PTH         | - 0.27                              | 0.03 (significant)           |
| HAEMOGLOBIN VERSUS VITAMIN D   | 0.32                                | < 0.12 (significant)         |
| HAEMOGLOBIN VERSUS CREATININE  | - 0.26                              | 0.04 (significant)           |
| HAEMOGLOBIN VERSUS EGFR        | 0.36                                | < 0.001 (highly significant) |
| HAEMOGLOBIN VERSUS UREA        | - 0.46                              | < 0.001 (highly significant) |
| HAEMOGLOBIN VERSUS WBCS        | 0.1                                 | 0.8 (non-significant)        |
| HAEMOGLOBIN VERSUS PLTS        | - 0.05                              | 0.8 (non-significant)        |

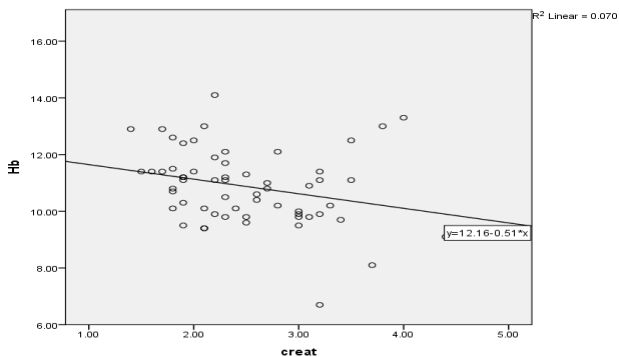


Figure 1. Inverse relationship among haemoglobin & Creatinine.

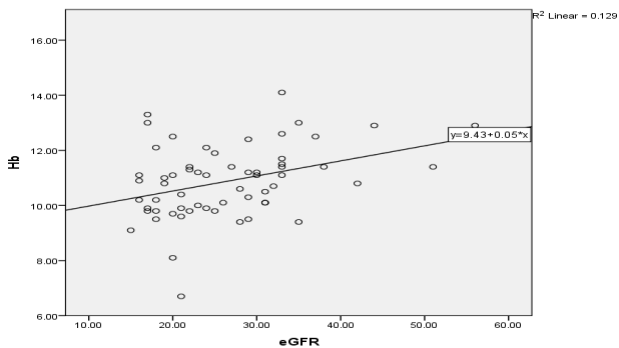


Figure 2. Positive correlation among haemoglobin & eGFR.

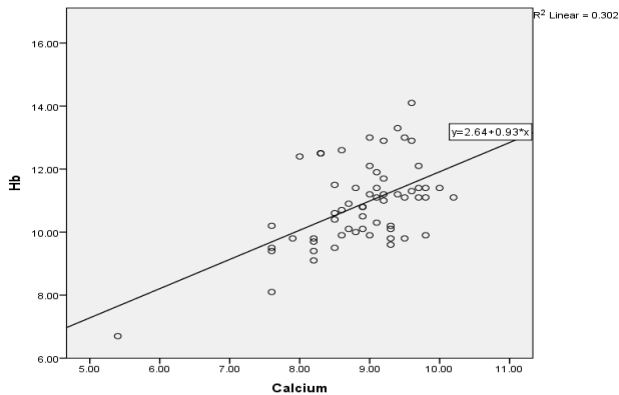


Figure 3. Positive correlation among haemoglobin & total Ca.

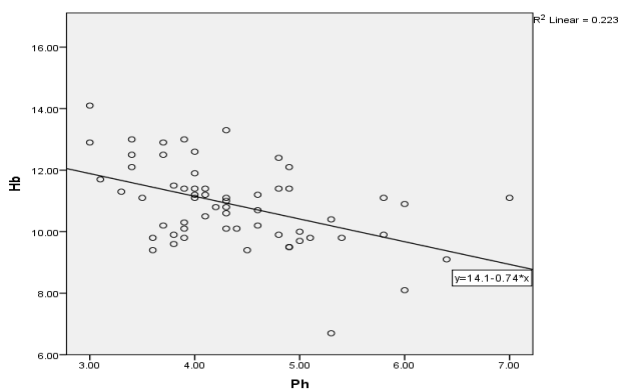


Figure 4. Inverse relationship among haemoglobin & PO4.

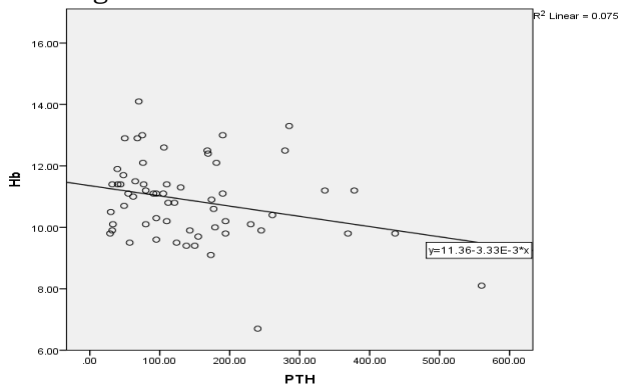


Figure 5. Positive correlation among haemoglobin & PTH.

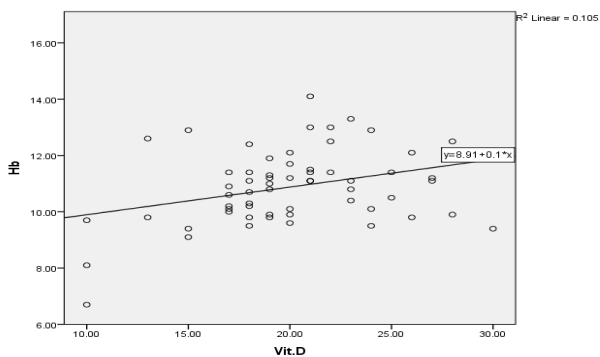


Figure 6. Positive correlation among haemoglobin & 25-(OH) Vitamin D.

#### 4. Discussion

The purpose of this research was to investigate the connections between anemia & blood bone biomarkers in CKD patients receiving conservative treatment. We demonstrated that there was an inverse relationship between serum levels of PO<sub>4</sub>, total Ca & Hb. According to Mauro et al., anemia in nondialysis dependent CKD individuals was closely correlated with both elevated serum PO<sub>4</sub> & a reduction in total Ca levels.<sup>6</sup> Additionally, Tran et al. reported on the associations between anemia and hyperphosphatemia.<sup>7</sup>

The current study's findings showed that serum intact parathormone (iPTH) & anemia were inversely correlated. Tran et al. previously found these relationships.<sup>7</sup>

The current study's findings showed that blood levels of hemoglobin among individuals with CKD and intact parathormone (iPTH) were inversely correlated. We discovered that among CKD patients, a rise in blood iPTH levels is accompanied by a fall in serum hemoglobin levels. Increased iPTH has been shown to reduce hematological function by inhibiting erythropoietin production, shortening the half-life of red blood cells & causing Bone Marrow (BM) fibrosis.<sup>8</sup> Our research revealed a substantial correlation between a vitamin D deficit and a decreased hemoglobin level in CKD individuals, which concurred with those of Saha et al., who assessed over a hundred CKD individuals. The average age was 57.8. The majority of patients had stages 4 (43, 37.4%) and 5 (45, 39.1%) of CKD. They found that hemoglobin had a positive connection with 25-(OH) Vitamin D & an inverse relationship with PO<sub>4</sub> in pre-dialysis patients with CKD stages 3-5.<sup>9</sup>

#### 4. Conclusion

Correcting renal osteodystrophy is thought to be the treatment focus for anemia, as blood-bone metabolic indicators have been linked to anemia in CKD individuals.

#### Disclosure

The authors have no financial interest to declare in relation to the content of this article.

#### Authorship

All authors have a substantial contribution to the article

#### Funding

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#### Conflicts of interest

There are no conflicts of interest.

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