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Original Research Paper

Biochemical and Hematological Alterations in Chronic Kidney Disease in Iraqi Patients

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Abstract: In patients with stages five of chronic kidney disease, the clinical syndrome known as chronic kidney disease–mineral bone disorder dysfunction includes the development of secondary hyperparathyroidism hormone, as well as abnormalities in vitamin D as well as mineral metabolism is characterized by biochemical and hormonal It is the alterations to hyperphosphatemia and hypocalcemia that cause it with that cause it elevated risk for mortality, cardiovascular disease, bone fractures, and the advancement of chronic kidney diseases.

Methods: For this research, 120 blood samples were collected from patients with chronic kidney disease and 60 volunteers. A sandwich Enzyme-linked immunosorbent assay was used to estimate the serum levels of human parathyroid hormone, and use competitive Enzyme-linked immunosorbent assay was used to estimate Vitamin D, and Urea, creatinine, albumin, Calcium, phosphorus, glucose, and bilirubin were measured using a spectrophotometer. Glomerular filtration rate was estimated indirectly, and a hematocytometer measured Hematological Parameters, and the results were statistically processed in SPSS.

Results: The study showed no significant difference ($p>0.407$) in the mean age among patient groups was 44.51±12.33 years, while the control group was 41.13±10.22 years. the study also examined body weight distribution, finding no significant difference(p->0.32) between patients 24.54±3.44 and the control group 25.11±3.21. and finding no significant difference in Total serum bilirubin ($P>0.067$). The resulting data showed a significant difference ($P<0.001$) in the increase in the mean levels of urea, creatinine, phosphorus, glucose, and parathyroid hormone in chronic kidney disease patients compared to the healthy control group. The results showed a decrease in the mean ± SD of hemoglobin, packed cell volume, white blood cells, platelets, albumin level, glomerular filtration rate, calcium, and vitamin D in kidney failure patients compared to the healthy control group.

Conclusions: The disease known as chronic kidney disease-mineral bone disorder is complex; knowing the actual cut-off for risk-related factors such as vitamin D deficiency, calcium, high Parathyroid hormone, and phosphate disorders, as well as their implications for future cardiovascular disease, bone health, and mortality risk, deserves further study.

Keywords: chronic kidney disease (CKD), parathyroid hormone (PTH), chronic kidney disease-mineral bone disorder (CKD-MBD), secondary hyperparathyroidism (SHPT), Renal failure (RF), Cardiovascular diseases (CVD), fibroblast growth factor 23 (FGF23), hemodialysis (HD), Enzyme-linked immunosorbent assay (ELISA).

1. Introduction

One of the main causes of vitamin D insufficiency is chronic kidney disease (CKD) [1] indicates that a large number of people are susceptible to problems brought on by a lack of vitamin D. These problems include the emergence of metabolic bone, cardiovascular disease (CVD), autoimmune and infectious disorders, neoplasms, hyperparathyroidism, type 2 diabetes, and elevated albuminuria[2, 3]Vitamin D is a secosteroid [4], A group of compounds that dissolve in fat and have a backbone made up of four rings of cholesterol. The two primary sources of vitamin D are intestinal absorption and dermal production[5], It plays a significant part in the equilibrium of phosphate and calcium[4], The creation, growth, and preservation of bone, as well as the stability of the cellular cytoskeleton, depend on the calcium macroelement, which affects several extracellular and intracellular processes[6], calcium contributes in neural conduction via the ion channels and controls the activity of intracellular enzymes[7], [8], Intestinal absorption, renal reabsorption, and bone exchange all control calcium homeostasis[9]. More than 9% of people worldwide suffer from CKD, which frequently results in abnormalities in calcium metabolism. In the context of CKD, calcium homeostasis is complex[10]. Serum calcium levels are typically kept within the normal range until the advanced stages of CKD, at which point they fall in tandem with a decline in vitamin D levels[10, 11]. The primary risk factor for osteoporosis is an inadequate supply of calcium. Variations in the serum calcium[7,12]include modifications to bone remodeling, such as increased bone resorption brought on by low blood calcium levels[13]One factor that leads to the development of hyperparathyroidism is the low vitamin D levels and reduced calcemic response to parathyroid hormone (PTH)[14]PTH is the peptide has 84 amino acids, in physiological PTH decreases renal calcium clearance, increases intestinal calcium absorption by synthesis 1,25-dihydroxevitamin D [15] in CKD The elevated PTH secretion increases calcium outflow from bone[16]. Potentially lead to hyperphosphatemia and increase intestinal sensitivity to vitamin D in CKD[16]Phosphorus is the second most important component of bone tissue, after calcium[7]The intestines absorb dietary phosphorus, Phosphorus homeostasis is mainly regulated by the kidneys, and the body's main store of phosphorus is found in the bone. PTH, fibroblast growth factor 23 (FGF23)[17], and vitamin D are the primary recognized phosphorus-regulating hormones, and they are also produced by the kidney, bone, and parathyroid glands. These hormones control phosphorus homeostasis through intricate tissue-level processes[18]. The kidneys' capacity to effectively eliminate phosphorus is diminished, and kidney function deteriorates. In patients with CKD, elevated serum phosphorus has been linked to the advancement of the disease [13], and the retention of phosphorus leads to secondary hyperparathyroidism (SHPT), which causes osteopenia and all of the other bone and mineral abnormalities that lead to vascular calcification and higher mortality [19], As an external etiology, SHPT is rather prevalent and can be brought on by liver disease, vitamin D insufficiency, lithium medication, or, most frequently, CKD. Hypocalcemia and hyperphosphatemia are the main causes of SHPT in CKD [20, 21] It is typified by increased glandular size and PTH production and secretion, which impairs bone and mineral metabolism[22], The clinical condition known as chronic kidney disease-mineral bone disorder (CKD-MBD) includes the development of SHPT as well as abnormalities in vitamin D and mineral metabolism [23]Changes in hormones and biochemistry are hallmarks of CKD-MBD[24] a disorder marked by elevated vascular calcifications, bone disease, and anomalies in test data on calcium and phosphorus metabolism [25]. These interact and raise the risk of death, bone fragility fractures, and CVD [13] People with stage 5 CKD in the context of Renal failure (RF) exhibit this the most [19]. Because circulating PTH and vitamin D bind to their respective receptors on osteoblasts [26], they enhance the production of a receptor activator of nuclear factor _ B ligand that stimulates the resorption of osteoclastic bone and the bloodstream's release of phosphorus and calcium [7, 27].

2. Methodology

In this research, 120 Iraqi patients undergoing dialysis were studied. The patients' mean BMI was 24.54±3.44, and their ages varied from 44.51±12.33. From October to December 2024, at Al-Sadder Hospital in Najaf, Iraq, these patients were diagnosed with kidney diseases. The

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current study excluded patients with liver illnesses and anti-HCV Ab. The control group consisted of 60 participants. Their mean BMI was 25.11±3.21, and their ages varied from 41.13±10.22.

Collecting blood, and using enzymatic methods to determine Urea, creatinine, albumin, Calcium, phosphorus, glucose, and bilirubin, and hematocytometer measured Hematological Parameters. and the use of Enzyme-linked immunosorbent assay (ELISA) was used to estimate the serum levels of PTH, Vitamin D, Glomerular filtration rate was estimated indirectly.

In the study, the Student's T-test was used to assess differences in variables among diagnostic groups. A two-tailed test was performed to ascertain statistical significance at a 0.01 level. All statistical analyses were conducted using the Windows platform's IBM SPSS version 26 software.

3. Results and discussion

The results in Table 1 shows no significant (P-value > 0.05) difference in the mean age of patients, 44.51 ± 12.33 years, compared with the mean age of the healthy group, 41.13 ± 10.22 years. The study also examined body weight distribution finding no significant difference between patients and the control group in BMI (p>0.32) across normal weight (18.5-24.9 kg/m2), overweight (25- 29.9 kg/m2), and higher than (30 kg/m2) was considered obese. These studies are in agreement with previous studies [28] finding no significant difference in Total serum bilirubin (P>0.067). The data suggested that there are significant differences in vitamin D, PTH, phosphorus, and Calcium of the patients and controls, as shown in p-value sequentially (<0.001), and this value is less than 0.05 (P<0.05) and which agrees with previous studies[29],[30]The results in the Table showed a significant decrease (p < 0.001) in HB, PCV, platelets, and WBC in kidney disease patients as compared with the control group aligning with the study[31].

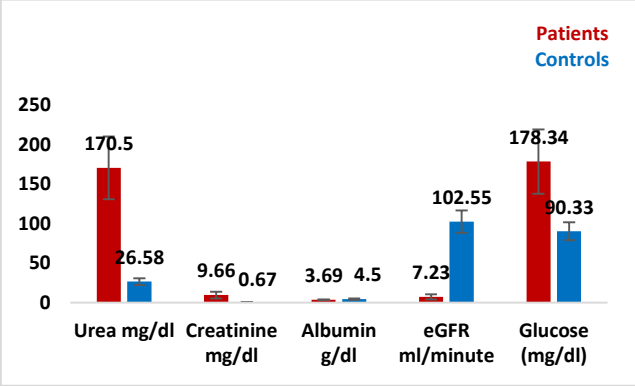

Figure 1: shows urea, creatinine, Albumin, GFR, and glucose in the patient group compared with the control group.

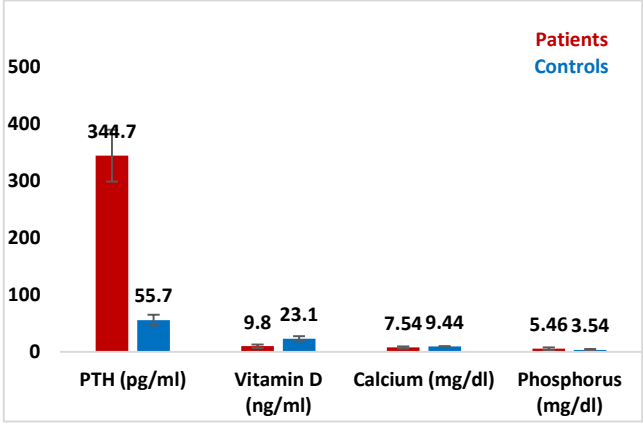

Fig 2: shows vitamin D, Calcium, phosphorus, and PTH in kidney disease patients as compared with the control group

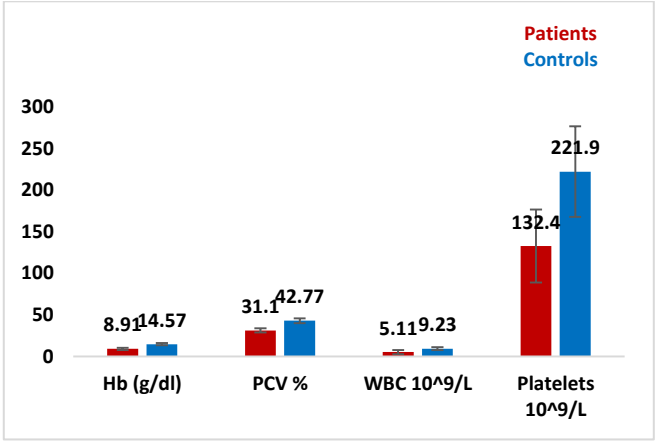

Fig 3: shows Hematological Parameters in the patient group compared with the the control group.

Glomerular filtration rate decreases as age increases. This is a traditional risk factor for people with RF. It is

vital for clinical practice because it helps interpret the indications, symptoms, and abnormalities in the laboratory that may indicate renal disease. Serum levels of endogenous filtration indicators are used to determine GFR [32].

Anemia in RF patients is prevalent due to the reduced production of erythropoietin in the kidneys, due to the reduction of renal mass[33], and is diagnosed in more than 50% of stages 4 and 5 of CKD. The World Health Organization's definition of anemia was Hb <13 g/dL for men and Hb <12 g/dL for women[34]. It is primarily linked to a major decrease in GFR and is an independent risk factor for heart failure and death in CKD patients[35].

Although there are several possible causes for the patient group's high blood sugar levels, CKD is often associated with diabetes, This causes the body to lose its ability to regulate blood sugar levels that are regulated by the kidneys; this condition is known as diabetic nephropathy[36]Without diabetes, however, because injured kidneys have lower insulin clearance and insulin resistance, the disease can impact glucose metabolism. These disturbances lead to hyperglycemia in HD patients[37].

The patient group's significantly higher urea and creatinine levels than those of the control group are most likely caused by the more severe kidney damage that results in CKD, renal aging, concomitant conditions, and the length and effectiveness of HD treatment[38]Artificial HD removes toxins from the blood, although not as consistently as healthy kidneys do[39]. Some biochemical markers, such as urea and creatinine, were shown to be highly significant in the serum of RF patients on HD before dialysis[40]. This is because the number of nephrons is decreasing. When the kidneys are unable to remove nitrogenous waste products from the bloodstream, these compounds build up in the blood[41]. Levels of urea and creatinine constitute essential markers since they are crucial for both diagnosing and following RF[42].

Patients with ESCKD are known to have a significant issue with hypoalbuminemia, which is one of the best indicators of death and other unfavorable outcomes[43]In HD patients, hypoalbuminemia is a sign of a poor prognosis since it is linked to depression in older people, adverse outcomes, and increased mortality. According to a study, patients who had plasma albumin levels of 3.8 g/dL were twice as likely to experience anxiety and depression, and Low levels of serum albumin may reflect malnutrition[44].

The CKD–MBD complex can arise from bone demineralization and soft tissue calcification caused by dysregulation of the calcium–PTH–phosphorus–vitamin D axis[45].

Patients with CKD frequently have low vitamin D levels, which are linked to increased risks of morbidity and all-cause mortality[5]because kidney 1a'-hydroxylase facilitates the final hydroxylation step of Vitamin D from 25-hydroxy to 1,25-hydroxy[29], Moreover, vitamin D deficiency in CKD causes nonskeletal conditions like metabolic syndrome, immunological dysfunction, hypertension, diabetes, and anemia in addition to skeletal conditions like osteoclast cell abnormalities, imbalanced bone turnover, and loss of bone quality[5]. Vitamin D levels fall as renal function deteriorates[10], lowering the ability to reabsorb calcium, leading to increased calcium excretion in the urine[46]. When calcium levels fall along with vitamin D concentrations, maintaining calcium homeostasis in the context of CKD becomes more difficult. and significantly decreases in advanced CKD[10], [47]. The main cause of osteoporosis is a calcium deficit. Variations in serum calcium levels include adjustments in bone remodeling, such as increased bone resorption brought on by low serum calcium levels[7], [48]PTH is the main regulator of serum calcium, and the interaction between calcium and the calcium-sensing receptor on the parathyroid gland's cell surface controls PTH release[16] Enhancing the calcemic response to PTH at the bone, the increased PTH secretion raises calcium outflow from bone[16],[49] and hyperphosphatemia becomes increasingly noticeable[14]and the kidneys' capacity to properly eliminate phosphorus is reduced[13]either because of bone disorders in CKD, which are all marked by excessive bone resorption, or because of a diminished capacity to filter phosphate as a result of renal function decline[50], Due to tubular reabsorption being already maximally disabled by FGF23 and PTH, the phosphate reservoir is shifted to soft tissue (such as the vasculature) due to bone disease[51]. This is caused by several bone-

specific signaling pathways, many of which are directly activated by phosphate itself, resulting in elevated levels of FGF23. Phosphate also stimulates the release of PTH[20], [52]Hyperphosphatemia is observed in stages 4-5 of CKD and may start earlier in some people, heightened dialysis regimens are necessary to effectively control it, and treatments to regulate serum phosphorus levels must start in pre-dialysis CKD stages[53], Phosphorus retention is a contributing factor to SHPT, which results in osteopenia and all of the associated abnormalities of bones and minerals[19], Hypocalcemia and hyperphosphatemia are the main causes of SHPT in CKD[20] SHPT, which is difficult to reverse These people may have numerous adenomas made of monoclonal or polyclonal clusters of parathyroid cells, or they may have hyperplasia of the parathyroid gland. The SHPT of CKD is linked to several RF problems, such as fractures, vascular calcification, and accelerated CVD[14],[54] According to a study, depression is linked to elevated PTH levels in CKD patients, and the likelihood of meeting the criteria for depression increases by 6.3% for every 100 pg/dL increase in PTH levels[44], higher PTH levels and hypoalbuminemia were the main factors linked to depression. QoL scores were similarly lower among depressed patients[55] Patients receiving hemodialysis are even more likely to experience cognitive impairment. RF patients had a 4- to 10-fold higher chance of being admitted to the hospital for ischemic and hemorrhagic stroke, as well as a higher risk of dementia and cognitive impairment[56].

Chronic kidney disease is a micro-inflammatory state. Vascular calcification and bone loss may be common outcomes of this inflammation. C-reactive protein and inflammatory cytokines[57]can enhance the osteo-chondrogenic differentiation of vascular smooth muscle cells by activating the Msx2-Wnt/catenin signaling pathway, induce oxidative stress, and facilitate the endothelial-to-mesenchymal transition. Inflammatory cytokines, including Interleukin-6, Tumor necrosis factor-α, and Interleukin-1β, which are produced either locally in the bone or circulate systemically, have been found to accelerate bone resorption[58].

Table 1: shows the Biochemical parameters in chronic kidney disease compared to the control group

Parameters	Means± SD		
	Patients N=120	Controls N=60	p-value
Age (Yrs.)	44.51±12.33	41.13±10.22	P>0.407
BMI (Kg/m^2)	24.54±3.44	25.11±3.21	P>0.32
Urea (mg/dl)	170.5±39.66	26.58±4.33	P<0.001
Creatinine (mg/dl)	9.66±4. 23	0.67±0.10	P<0.001
eGFR (ml/minute)	7.23±3.31	102.55±14.11	P<0.001
Albumin (g/dl)	3.69±0.55	4.5±0.66	P<0.001
T.Billirubin (mg/dl)	0.51± 0.22	0.74±0.31	P>0.067
PTH (pg/ml)	344.7±45.6	55.7±9.3	P<0.001
VitD (ng/ml)	9.8± 3.32	23.1±4.4	P<0.001
Calcium (mg/dl)	7.54±1.89	9.44±0.85	P<0.001
Phosphorus (mg/dl)	5.46±2.12	3.54±1.22	P<0.001
Hemoglobin (g/dl)	8.91±1.22	14.57±1.29	P<0.001
PCV (%)	31.11±2.56	42.77±2.87	P<0.001
WBC (10^9/L)	5.11±2.57	9.23±1.55	P<0.001
Platelets (10^9/L)	132.4±43.89	221.9±54.3	P<0.001

Data represented as Mean ±SD, NS non-significant differences at (P≥0.05). *=significant differences at (P< 0.05), **=significant differences at (P< 0.01).

Conclusion

Millions of people worldwide suffer from the health issue of chronic kidney disease. The increasing incidence of chronic kidney disease and its numerous, serious consequences is linked to its interconnected relationship with cardiovascular and metabolic conditions. The focus on chronic kidney disease–mineral bone disorder highlights the intricate relationships between mineral metabolism, bone health, and cardiovascular outcomes. Chronic kidney disease–mineral bone disorder is a complex and multifactorial disease. In particular, understanding the true cut-off for risk factors such as vitamin D deficiency, calcium, high Parathyroid hormone, phosphate disorders, and fibroblast growth factor 23, as well as their implications for future cardiovascular disease, bone health, and mortality risk, deserves further study.

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Author's Contributions

Muntadher Mohammad Ali, Sana Atiyah designed this project. analysed and contributed to the interpretation of the data. Sana Atiyah. wrote the first draft of the article. Muntadher Mohammad Ali provided critical revision for important intellectual content. All co-authors approved the final version of the article.

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