# Study of Serum Biomarkers in Females Hemodialysis Patients

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## Abstract

Renal bone disease is one of the metabolic disorders in renal failure patients that causes morbidity. The aim was to study the biomarkers and the incidence of renal osteodystrophy (bone turnover diseases) in hemodialysis patients. Method: 50 females' patients from Al Basra-Teaching Hospital in Iraq who maintained hemodialysis (at least 1 year) and healthy females (n=30) as a comparison group were included. Serum vitamin D, parathyroid hormone, osteocalcin, and some bone parameters were tested. Results: a significant decrease in serum vitamin D in female patients under dialysis (12.770 ng/ml) compared to the control group (20.8167 ng/ml). Osteocalcin levels increased in patients (54.3114 ng/ml) compared to the healthy group. In general, the PTH level was elevated significantly in dialysis patients (262.211pg/ml), and an elevation in ALP level (221.084IU/L) was also found. The patients, according to their PTH level, showed renal bone disease. About 30 females' patients (60%) revealed high bone turnover, followed by 20 patients (40%) with low bone turnover disease. Conclusion: deficiency in vitamin D with incidence of renal osteodystrophy in female hemodialysis patients.

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## 1. Introduction

The patients with chronic kidney disease CKD developed many metabolic abnormalities including the renal bone disease [1]. The bone disease result from mineral and hormonal alternations that initiate in early stage of renal disease [2]. The bone disease reached to 90 – 100% with the occurrence of the progressing of kidney disease, especially in patients undergoing dialysis [3, 4]. Vitamin D involved in calcium homeostasis by conjunction with parathyroid hormone (PTH) regulate the plasma levels of ionised calcium and phosphate [5,6]. Vitamin D have important role as modulator (cell differentiating and anti-proliferative factor) in body system involving renal, cardiovascular and immune systems [7,8]. The kidney is responsible for converting the non-active form of vitamin D (25-(OH) vitamin) into the active form 1, 25 dihydroxy-vitamin D. There is a similar deficiency in vitamin D in chronic kidney disease and general population [9], but this deficiency is effected not only to lower kidney function, but to other factors including sex, age, diabetes mellitus, and body adiposity [10]. The decreasing in vitamin D contributed to develop hypertension, cardiovascular disease and bone complications [11]. The bone turnover diseases in renal diseases had two forms the low and high turnover disease that called the renal osteodystrophy (ROD), which associated with high risk of bone fracture, tissue calcification that leading to mortality [12].

The disturbance in calcium, phosphorus, and vitamin D levels lead to common complication in chronic kidney diseases called renal hyperparathyroidism [13]. In response to hypocalcemia induced by phosphate retention and reduced vitamin D synthesis as reduced renal function, leading to develop Secondary hyperparathyroidism [14]. Therefore, the early diagnosis of hyperparathyroidism was essential to prevent renal bone complications. The accurate detection of bone status in CKD is bone biopsy, but it's painful, cost and need a trained staff. The alternative is used the biochemical guideline of bone metabolism which correlated with bone histomorphology [15]. Because the alternations in both parathyroid activity and vitamin D metabolism in renal failure patients and the prevalence of bone pain symptoms in dialysis patients [16], therefore, the aim of study was to determine the vitamin D status in renal failure females' patients undergoing hemodialysis and the incidence of renal bone diseases.

## 2. Material and Methods:

### 2.1 Patients

50 females' patients with average age (29-74 years) undergoing dialysis treatment in Al Basrah-Teaching hospital of Basrah province during 2/1/2019 – 1/5/2019 were included in this study. The patients were in the end stage renal failure whom diagnosis by the Urologist and maintenance on hemodialysis for at least one year (3 time /week). The patients divided into 3 age groups (29-44y), (45-59y), and (60-74y). The control group consist of healthy female (n=30) with average age (29-74 years). The control group was not suffered from any diseases or had any symptoms, and divided with the same age groups. All patients and control were asked by questionnaire and exclusion whom receiving nutritional supplement. All patients and control were not received vitamin D.

### 2.2 Sample Collection

The blood samples from patients were collected before dialysis operation. (4 ml) of venous blood sample was drown at (8-10 Am) by the nurse. The blood collected in gel tube and left for 15minute at room temperature for clotting then centrifuged at (3000 rpm) for 15 minutes to obtain serum that stored at -20C$^{o}$ for biochemical and hormonal measurements [17]. The blood sample from healthy subjects were collected out of the hospital by clinical laboratory scientist.

### 2.3 Serum Assay

The renal function (creatinine, urea, uric acid, albumin) were measured by commercial Roche using COBAS INTEGRA 400 plus /Roche/Germany. Electrolytes profile (potassium, chloride, sodium) were measured by DRI-CHEM 4000 Chemistry Analyzer/ FUJIFILM/Japan. The serum ALP measured by the Colorimetric assay in accordance with a standardized method by using commercial Kit (COBAS INTEGRA 400 plus, Catalog no. 03333752). The serum calcium measured by using commercial Kit (COBAS INTEGRA 400 plus, Catalog no. 05061482). The serum phosphorus measured by the endpoint method with sample blanking assay by using commercial Kit (COBAS INTEGRA 400 plus, Catalog no. 03183793). The parathyroid hormone was measured by Elisa kit using COBAS e411/Roche /Germany. Vitamin

D by Elisa kits from Monobind Inc., USA (Cat. No.92630), osteocalcin by Elisa kit (My Bio Source, USA, Cat. No.RDEEH3468).

### 2.4 Determine of renal bone disease

The type of bone turnover in dialysis patients was determined by the level of PHT [18]. The high bone turnover when PTH>300 pg/ml [18, 19], low bone turnover when PTH<150 (149-60) pg/ml [19], adynamic low bone turnover when PTH< 60 pg/ml [20,21].

### 2.5 Statistical Analysis

The data were analysis by t- test for comparing two groups and by ANOVA one way test for comparing the age groups by using (SPSS) program version 22. Data expressed by (mean ±S.D). Comparison between means by least significant differences (P≤0.05) [22].

## 3. Results

### 3.1 Hormonal and biochemical parameters in dialysis and control groups

There was significant decreasing ($p \leq 0.05$) in serum vitamin D3 (12.7700 ng/mI), in comparison with healthy females control group (20.816 ng/ml) **Table 1**. The concentrations of osteocalcin increased significantly (P≤0.05) in female dialysis patients group (54.3114 ng/ml) compared to control group (17.060 ng/ml). In general the PTH concentration was increased significantly (P≤0.05) in dialysis patients 262.211 pg/ml compared to control group 53.022 pg/ml. the levels of PTH showed variations either more than 300 pg/ml (459.163pg/ml) and less than 150 pg/ml (65.259pg/ml). The concentration of ALP and phosphorus increase significantly (P<0.05) in female dialysis patients group (221.0846 u/dI), and (5.8936 mg/dI) respectively, while decreased serum calcium (9.040 mg/ dl) in comparison with healthy females control group (102.5040 u/dI), (9.4740 mg/dI), and (3.9437 mg/dI) respectively. The Levels of potassium, and chloride increase significantly (P<0.05) in females dialysis patients group (5.3978 mmol/L), (107.5592 mmol/L) respectively, while no significantly in sodium level (141.3698 mmol/L), in comparison with healthy females control group (4.5043 mmol/L), (98.8220 mmol/L) and (137.1233 mmol/L) respectively. The levels of creatinine , urea ,and uric acid increase significantly (P<0.05) in females dialysis patients groups (7.7364 mg/dI) , (108.7232 mg/dI),and (6.5156 mg/dI) respectively, while albumin decrease significantly (P<0.05) in females dialysis

patients group (3.7414g/dI) ,in comparison with healthy females control group (0.2617 mg/dI), (35.3760 mg/dI), (4.0843 mg/dI) and (4.3717 g/dI) respectively.

**Table 1: Various hormonal and biochemical parameters in females' dialysis patients and healthy control group.**

| Treatment | Dialysis N= 50 | Control N = 30 | P≤ 0.05 |
|---|---|---|---|
| | Mean ±SD | Mean ± SD | |
| Vitamin-D (ng/ml) | 12.770 ±5.13810 | 20.816 ± 4.499 | 0.000 |
| PTH (pg/ml)Total | 262.211±87.276 | 53.022 ± 4.615 | 0.000 |
| Osteocalcin (ng/mL) | 54.311 ±8.41240 | 17.060 ±3.647 | 0.000 |
| Alkaline phosphatase (U/L) | 221.084 ±83.464 | 102.504 ±12.708 | .000 |
| Calcium (mg/dL) | 9.040 ±.835 | 9.474 ±0.248 | 0.017 |
| Phosphorus (mg/dL) | 5.893 ±.888 | 3.943 ±0.391 | 0.000 |
| PotassiumK (mmol/L) | 5.397 ±1.1061 | 4.504 ±0.507 | 0.000 |
| Chloride Cl (mmol/L) | 107.559 ±4.858 | 98.822 ± 7.724 | 0.000 |
| Sodium Na (mmol/L) | 141.369 ±7.942 | 137.123 ± 4.959 | 0.086 N.S |
| Creatinine (mg/dL) | 7.7364 ±2.327 | 0.261 ±0.051 | 0.000 |
| Urea (mg/dL) | 108.723 ±37.241 | 35.376 ±9.167 | 0.000 |
| Uric acid (mg/dL) | 6.5156 ±1.79385 | 4.084 ±0.964 | 0.000 |
| Albumin (g/dL) | 3.741 ±.7132 | 4.371 ±0.197 | 0.000 |

The significant when p-value at p≤0.05.

## 3.2 Hormonal and biochemical parameters among age groups in dialysis patients

In hormones parameters according to age groups in females' dialysis, there are significant increase ($p < 0.05$) in serum PTH, especially in the second age group which was higher than the other age groups. Statistically, no significant difference in vitamin D and osteocalcin among all age groups, (**Table 2)**. The previous table shows the mean values of serum Ca, P, and ALP in

dialysis patients in female dependent on age groups. There are significant increasing ($p < 0.05$) in serum ALP. ALP in the third group is higher than the other age groups. The phosphorus and calcium concentration showed insignificant in all age groups. According to age groups in females' dialysis, there is significant increase ($p < 0.05$) in serum Na in the third group age, no significant was found in serum $K^+$ and $Cl^-$ concentration. According to age groups in females' dialysis, there are significant increase ($p < 0.05$) in serum urea and uric acid. The urea in the first age group is higher than the other age groups, while uric acid is higher in the third age group than the other ages. Statistically, no significant were observed in creatinine and albumin levels.

**Table 2: Various hormonal and biochemical parameters in females' dialysis patients according to age groups.**

| Treatment | First age group (29 - 44) N=14 | Second age group ( 45 – 59 ) N=15 | Third age group ( 60 – 74 ) N= 21 | P≤ 0.05 |
|---|---|---|---|---|
| | Mean ±SD | Mean ±SD | Mean±SD | |
| Vitamin-D (ng/ml) | 14.714 ±5.793 | 10.633 ±1.351 | 13.000 ±2.915 | 0.097 N.S |
| PTH (pg/mL) | b277.01 ±95.101 | a283.102 ±187.655 | c227.012 ±71.121 | 0.003 |
| Osteocalcin (ng/mL) | 52.546 ±8.467 | 55.073 ±11.026 | 54.943 ±6.216 | 0.660 N.S |
| Alkaline phosphatase (U/L) | c179.445 ±65.966 | b215.333 ±34.979 | a252.951 ±85.250 | 0.033 |
| Calcium (mg/dL) | 8.820 ±0.579 | 9.101 ±0.859 | 9.200 ±0.867 | 0.621 N.S |
| Phosphorus (mg/dL) | 5.813 ±0.810 | 5.886 ±1.047 | 5.952 ±0.855 | 0.906 N.S |
| PotassiumK (mmol/L) | 5.172 ±1.655 | 5.506 ±.770 | 5.470 ±.866 | 0.675 N.S |
| Chloride Cl | 107.846 | 107.066 | 107.721 | 0.897 |

| | | | | |
|---|---|---|---|---|
| (mmol/L) | ±8.132 | ±2.333 | ±3.280 | N.S |
| Sodium Na (mmol/L) | c136.330 ±12.783 | b142.776 ±4.370 | a143.725 ±3.144 | 0.016 |
| Creatinine (mg/dL) | 8.161 ±2.280 | 7.768 ±2.460 | 7.430 ±1.131 | 0.668 N.S |
| Urea (mg/dL) | a121.445 ±29.163 | c89.853 ±35.192 | b113.720 ±36.163 | 0.050 |
| Uric acid (mg/dL) | b6.431 ±1.692 | c5.234 ±1.091 | a7.486 ±1.720 | 0.000 |
| Albumin (g/dL) | 3.892 ±.496 | 3.720 ±.820 | 3.655 ±.768 | 0.631 N.S |

Small letters referred to significant (Significant when p-value at p≤0.05). N.S: no significant

### 3.3 The percentage of renal bone diseases in patients and vitamin D according to PTH levels

According to PTH levels, all females' hemodialysis patients revealed a renal bone diseases. The high bone turnover showed high percentage (30, 60%) in females undergoing hemodialysis. The low bone turnover disease showed (12, 24%). The more specific adynamic low bone turnover disease consist (8, 16%) as shown in Table 3.

**Table 3: The percentage of renal bone diseases in patients and vitamin D according to PTH levels.**

| Range of PTH (pg/ml) | Female | | |
|---|---|---|---|
| | PTH level | The patients number and percentage | Vitamin D (ng/ml) |
| High bone turnover PTH>300 | 459.163 ± 213,267 | 30 (60%) | 10.256 ± 4.856 |
| low bone turnover PTH(60-149) | 84.927 ± 39.573 | 12 (24%) | 13.384 ± 6.673 |
| Adynamic bone turnover | 45.592 ± 20.873 | 8 (16%) | 15.130 ± 7.412 |

| | | | |
|---|---|---|---|
| PTH<60 | | | |
| P≤ 0.05 | 0.002 | 0.007 | 0.090 N.S |

## 4. Discussions

The present study showed a decrease in the level of calcitriol in dialysis patients compared with healthy control. These consistent with other studies of [23,24,25],which indicated that the main cause of the low level of vitamin D is kidney dysfunction, because the kidney is the main site for conversion of 25(OH)D to circulating 1,25(OH)2D. Although decreased 1,25(OH)2D synthesis has been classically related to CKD, the circulating concentration of both metabolites, 25(OH)D and 1,25(OH)2D, begins to decrease from the earliest stages of CKD [26]. Several factors are associated with this phenomenon including reduced renal mass, dietary restrictions and nutritional deficiencies, reduced sunlight exposure, skin hyperpigmentation, diabetes mellitus, obesity, accumulation of uremic toxins, impaired skin synthesis of cholecalciferol, proteinuria, and increased FGF23 [27]. Additionally, vitamin D is transported in conjugation with vitamin D binding protein (VDBP) and filtered through the glomerulus. Tubular reabsorption of vitamin D bound to DBP is facilitated by the multi-ligand receptor megalin. In proteinuric CKD subjects, megalin is occupied by an extensive albumin load, and therefore fewer receptors are available to uptake 25(OH)D-DBP, which contributes to vitamin D deficiency. In addition to 25(OH)D, 1,25(OH)2D levels are also reduced in CKD [28].

Renal 1α-hydroxylase activity reduces as the renal mass decreases. Other down-regulating factors that are present in CKD patients include low availability of 25(OH)D, hyperphosphatemia, metabolic acidosis, and uremia itself. Additionally, elevated FGF23 activates the enzyme 24-hydroxylase (CYP24), hydroxylating both 25(OH)D and 1,25(OH)2D. 24- hydroxylase limits the amount of 1,25(OH)2D in target tissues both by producing 24,25(OH)2D (thus decreasing the availability of 25(OH)D for 1 hydroxylation) or by accelerating the catabolism of 1,25(OH)2D to 1,24,25(OH)3D resulting in calcitroic acid, which is biologically inactive [29,30]. The combination of vitamin D and / or 1,25(OH)2D3 insufficiency and end organ resistance to vitamin D contribute to the development of chronic kidney disease - minerals bone disease (CKD-MBD). Additional mechanisms include the impairment of vitamin D dependent osteocalcin production and change in osteoblasts and

osteocytes observed in CKD [31], which is associated with bone loss and vascular calcification [32,33]. High levels of phosphorous in the blood with low calcium levels that stimulate the parathyroid gland to secrete the PTH hormone. This hormone stimulates the bone cells (osteoblasts and osteocytes) to secrete FGF-23, which reduces NTP2 action to transport blood phosphorous [34], and the secretion of phosphorous outside the body, inhibiting hormone production 1-alpha hydroxylase which reduces the production of vitamin D [35]. Vitamin D3 deficiency lead to many of disease , the first of this disease is a bone turnover , also, increase the chance of asthma , risk of death from cardiovascular disease, infect of high cholesterol ,and diabetes type 2 [36,37]. When the kidneys lose their function, a phosphorus retention stimulates the parathyroid gland to secrete the enzyme FGF23, which is excreted from the bone cells. This enzyme prevents the kidneys to produce an enzyme 1α-hydroxylase which converts vitamin D from the picture 25(OH)D to the active form [38].When the production of vitamin D decreases, the percentage of calcium in the blood decreases as a result of the lack of calcium absorption from the small intestine or reabsorption from the kidneys. Thus, parathyroid gland PTG is stimulated to secrete a large amount of PTH hormone, which releases calcium from the bones to the bloodstream to maintain the normal level of calcium, and the liberation continues Calcium from the bone, which leads to turnover and deformities in the bone [39].Our study shows that serum PTH concentrations increase in patients with dialysis compared with healthy control .This result agree with [40,41,42,43]. When GFR falls, the phosphorus clearance decreases significantly, leading to phosphorus retention, this hyperphosphatemia, subclinical when estimated GFR is < 30 mL/min, is thought to be the principal cause of secondary hyperparathyroidism SHPT [39]. Secondary hyperparathyroidism is caused by any condition associated with a chronic depression in the serum calcium level, because low serum calcium leads to compensatory over activity of the parathyroid, so renal failure is by far the most common cause of secondary hyperparathyroidism [44]. Hyperphosphatemia, hypocalcaemia and vitamin D3 deficiency (needed to absorb calcium) a major reason for raising a PTH level [45].

Secondary hyperparathyroidism occurs early in the course of chronic renal failure. Early in the course, a decrease of calcitriol and an abnormality in the calcium sensor receptor may be the important factors; later, with advanced renal failure, hyperphosphatemia becomes an additional important pathogenic factor [46]. SHPT begins due to a lower GFR rate of less than 60mL/min ,and the inability of the kidneys to produce the active vitamin D responsible for the

reabsorption of calcium and a return to the blood, as well as a major reason is phosphorus retention in the blood that stimulates the parathyroid gland to secrete the PTH hormone. Normally PTH act as stimulates cells Osteogenesis of the hormone FGF-23 and stimulation of the kidneys by secretion of the 1-alpha hydroxylase , hormone FGF-23 prevents the re-transfer of phosphorous to the bloodstream, 1-alpha hydroxylase works to convert vitamin D into the active image, which works to reabsorb calcium into the blood [47]. Three reasons cause the parathyroid gland to be enlarged in early renal failure are decrease of calcitriol and calcium , and excessed of phosphorue in serum . Alteration in vitamin D metabolism, decreased levels of calcitriol and moderate decreases in ionized calcium may allow greater synthesis and secretion of PTH. As the disease progresses, there is a decrease in the number of vitamin D receptors (VDR) and calcium receptors (CaR). The decreased number of VDR and CaR makes the parathyroid glands more resistant to calcitriol and calcium ,then Phosphorus induces hyperplasia of the parathyroid glands independent of calcium and calcitriol, and by a post-transcriptional mechanism increases PTH synthesis and secretion. Calcium and phosphorous homeostasis is tightly regulated between bone, the kidney, and the parathyroid gland [48]. Key modulators of calcium and phosphorous include FGF-23, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, and parathyroid hormone. FGF-23 is released from bone due to increasing serum phosphorus levels and acts in the kidney to increase phosphorous excretion and decrease 1 alpha hydroxylation of 25-hydroxyvitamin D [39]. FGF-23, along with serum phosphorous, also decreases parathyroid hormone secretion, to maintain calcium and phosphorous balance [35,45]. In CKD, stages 3-5 (eGFR < 59 mL/min), FGF-23 levels increase, initially leading to phosphaturia and decreased parathyroid hormone excretion [41]. As the CKD progresses, there is a resistance in the kidney and parathyroid gland to FGF-23 and a deficiency in the kidney of 1 alpha hydroxylation of vitamin D, both of which result in reduced phosphorous excretion[49]. The deficiency of 1,25-dihydroxyvitamin D, along with the decreased phosphorus excretion, results in hypocalcemia and hyperphosphatemia, thereby stimulation of parathyroid hormone synthesis and parathyroid gland hyperplasia , hyperplasia leads to the constant release of calcium from the bones to the bloodstream and thus leads to bone turnover [50].

Our study shows that serum osteocalcin OCT concentrations increase in patients with dialysis compared with healthy control ,this result agree with [51,52],whom explain , in chronic renal failure, that the a circulating osteocalcin is elevated. This elevation is due to decreased

renal clearance and, in some patients, increased bone turnover secondary to renal osteodystrophy. Osteocalcin (OC) is a bone-specific protein produced primarily by osteoblasts during bone formation, besides its role in bone formation, osteocalcin may play a role in the regulation of energy metabolism and male fertility [53].

Serum osteocalcin levels are high in patients with chronic kidney failure . The increased serum accumulation of osteocalcin in patients with chronic renal disease can be related to decreased renal clearance, increased bone metabolism, or a combination of both [54]. In patients with chronic renal failure ,the progressive increase in serum osteocalcin levels closely corresponded with intact PTH and alkaline phosphatase levels. More importantly, such increases in serum osteocalcin levels reflect the severity of the bone harm [51,55]. Due to renal failure and a decrease in GFR (phosphorus retention and low calcium level in the blood), and increased bone metabolism, it leads to an elevated level of PTH and alkaline phosphate that stimulates osteoblast cells to secrete the osteocalcin hormone, which is called the bone hormone [56]. Osteocalcin plays an important role in regulating metabolism in the body, as it has an important role in bone mineralization and the balance of sodium ions, it also works as a hormone in the body as it stimulates the beta cells of the pancreas to secrete insulin, as well as stimulates the fat cells to secrete the hormone adiponectin, which increases the rate of insulin sensitivity [57]. Osteocalcin stimulates the cells of the leydig cells (interstitial cells) in the testicle to produce testosterone, which has a role in a man's fertility rate [58]. Osteocalcin also regulates the presence of energy in muscle cells [59]. There is higher level of ALK-P serum concentration in dialysis patents compared with healthy group and this result agree with [60,61] ,which explain higher level of Serum alkaline phosphatase (Alk-P) is associated with vascular calcification and mortality in hemodialysis patients, [62]who conclusion ALP level higher in CKD patients both without and with ESRD .Higher serum ALk-P activity was associated with increased mortality in the peritoneal dialysis PD patients [61].

The main reasons for the high level of ALk-P are bone and liver diseases. When the kidneys function decreases, the level of calcium in the blood decreases, and as a result of renal insufficiency it leads to preventing the formation of vitamin D3 in the active form that helps to reabsorb calcium, so release calcium stored from the bones with production alkaline phosphatase from osteoblast cells contributing to its high levels in plasma as the renal function or GFR declines [63,64]. On the other hand, plasma ALk-P levels can originate from liver, bone,

intestine and placenta. In general, the isoenzymes from liver and bone contribute to the majority of the circulating enzyme levels. Therefore, in a patient of liver disease serum ALk-P level is an important marker for screening and monitoring. However in a CKD patient, renal osteodystrophy could result in a significant increase in the bone isoenzyme of ALk-P contributing to high serum ALk-P level. In fact, higher ALk-P has been associated with increased mortality in predialysis CKD as well as patients on maintenance hemodialysis and in fact, in CKD patients without liver disease serum ALk-P can be elevated in high-turnover bone disease [65]. Some liver disease during the stage of kidney failure also lead to an elevated of ALk-P level are bile duct obstruction ,primary biliary cirrhosis, primary sclerosing cholangitis, drug induced cholestasis for example : anabolic steroids, adult bile ductopenia, metastatic liver disease [66,67]. Our study shows that serum calcium concentrations decrease in patients with dialysis compared with healthy control. This result agrees with other studies [68,69],those who explain present decrease in serum calcium level in dialysis patients may be due to chronic renal insufficiency is associated with hyperphosphatemia, the elevated serum phosphate levels directly depress serum calcium levels and thereby stimulate parathyroid gland activity. Patients with hemodialysis have a low level of calcium, and this is due to three reasons, the first of which is the low level of calcium in food. As for the second reason, due to kidney failure, the calcium is not reabsorbed, due to the damage that occurred along the nephrons responsible for filtering and the calcium reabsorption process [70,71]. The last reason is the low level of vitamin D in the active form, which is responsible for the absorption and reabsorption of calcium, due to the kidneys losing their function, an enzyme is not produced, 1-alpha hydroxylase responsible for converting vitamin D from the formula 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol (vitamin D3 or calciferol) the active formula [64].

Our study shows that serum phosphate concentrations increase in patients with dialysis compared with healthy control. [71,72] agreed with our result study in that patients with dialysis have a high level of phosphorus , because the kidney is principally responsible for phosphate homeostasis. The kidneys regulates serum phosphate by modulating urinary phosphate excretion, and this ability is lost in CRF. Similarly, [39,73] reported that hyperphosphatemia and hypocalcemia occur due to loss of vitamin D because of the damage in kidneys ,and vitamin D binding protein and when there is an impaired production of 1,25 dihydroxy cholecalciferol. Also, [74] reported that P ion excretion increased as a result of reduction in renal tubular

absorption of phosphate . Fibroblasts Growth Factor-23 FGF-23 a new protein that is responsible the phosphorus homeostasis in the blood [35]. Elevated serum phosphorus concentration is an established independent risk factor for increased mortality in patients with end stage renal disease (ESRD) requiring hemodialysis. Phosphorus retention in these patients is a major contributor to the development of secondary hyperparathyroidism, osteitis fibrosa and extraosseous calcification of both vascular and nonvascular tissues [64,75]. Patients with end-stage renal disease develop hyperphosphatemia because their dietary intake exceeds phosphorous elimination by intermittent thrice-weekly dialysis.Dietary restriction of phosphorus, although important, is difficult to accomplish since dialysis patients are encouraged to consume a relatively high protein diet in order to prevent protein malnutrition [76]. As because of the kidneys inability to perform the function in the filtering process and get rid of excess phosphorous in the blood due to damage to nephrons, there is a retention of phosphorus, and the percentage of phosphorus in the blood rises, and this in turn affects the parathyroid gland, which stimulates it to excrete the hormone parathyroid, which stimulates the bone cells to secrete FGF23, which helps to regulate the level of phosphorous in the blood and due to irregular phosphorous levels in the blood due to kidney failure and the continuous increase in phosphorus, which leads to a rise in the hormone parathayroid [77].

Our result in the present study showed an increase in the level of potassium in dialysis patients compared with healthy control. These consistent with other studies of [78,79] ,whom found that there is sever increase in $K^+$ level in patients with dialysis . The kidneys play a crucial role in potassium homeostasis, and the importance of their contribution to the maintenance of potassium balance is reflected by the high rates of potassium disorders in patients with decreased kidney function [80]. Indeed, individuals with chronic kidney disease (CKD) and those with end-stage renal disease (ESRD) can occur both hyperkalemia and hypokalemia; by of low kidney function or as a consequence of drugs such as Angiotensin Converting Enzyme inhibitors (ACEIs) or Angiotensin-Receptor Blockers (ARBs), whereas the latter is typically a consequence of diuretic administration [81]. The renal hyperkalemia can be attributed to a deficiency of aldosterone, the major hormonal regulator of renal potassium transport [82,83]. On the other hand there is no significant difference in Serum $Na^+$ concentrations between the patients with CRF and controls. This result of our study was in agreement with other study published by [84]. They explained normal level of serum $Na^+$ due to reduce $Na^+$ intake and humoral natriuretic

factor in chronic kidney failure which helps to increase sodium excretion and maintain normal $Na^+$ balance. In addition, also not forget the effect of permanent hemodialysis on maintenance of normal $Na^+$ concentration. As well as ,to fact that salt wasting is a common problem in advanced renal failure because of impaired tubular reabsorption of sodium [85] which may support our results . Also, there is significant difference in chloride concentrations between the patients with dialysis and controls, these results were agreement with [86], who explain there are hyperchloremia in dialysis patients. Chloride is the most important anion in the extracellular fluid compartment. It is regulated by oral intake, renal absorption and secretion. Chloride is usually associated with proportional changes in sodium concentration and is altered by the acid-base state of the animal. Chloride is the digestion of hydrochloric acid which is excreted from the gastric mucosa, and is absorbed into the intestine. Cl is regulated by the kidneys, the kidney plays an important role in the regulation of chloride concentration through a variety of transporters that are present along the nephron; it is filtered out by the glomeruli and is reabsorbed in the tubules, where it follows water and sodium [87]. Hyperchloremia is because they are either from more water loss than sodium and chloride during urine or hemodialysis due to a defect in renal nephrons, or from a high level of hydrochloric acid in the blood, and rarely given hydrochloric acid as a direct acid factor but it can be created from the metabolism of ammonium chloride Or positive amino acids such as lysine and arginine [88].

The present study showed an increase in the level of creatinine and urea in dialysis patients compared with healthy control. These consistent with other studies of [89,90]. Highly significant increase these parameters may result from decrease in filtration of creatinine as a result of a diminished glomerular filtration rate (GFR) [89]. The high level of serum uric acid related to the uric acid is reabsorbed and ousted by the proximal tubular cells. In this way, hyperuricemia might advance when uric acid production increases or secretion decreases, or both [91]. The albumin concentration in hemodialysis patients decreases primarily due to the increase in inflammation with a subsequent decrease in the rate of albumin synthesis along with the failure to regulate albumin degradation as occurs during protein restriction [92]. Dietary insufficiency of nitrogen is clearly related to albumin levels, but food additives were not significantly effective in correcting albumin deficiency, it may be that the relationship between nitrogen consumption and hypoalbuminemia in these patients with dialysis patients to reduce the

fractional metabolism rate of albumin when nitrogen intake is limited which makes these patients sensitive to nitrogen reduction [93].

## 5. Conclusions

There was severe deficiency in vitamin D in renal failure females patients undergoing hemodialysis. The results showed the occurrence of renal bone disease among hemodialysis patients. The most common pattern of bone disease is high bone turnover disease combined with very high PTH levels, followed by low bone turnover disease which combined with low PTH levels. These metabolic alternations may increase factor of bone fractures in patients.

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# دراسة بعض المؤشرات الحيوية لدى مرضى اناث الغسيل الكلوي

**المستخلص**

ان مرض العظام الكلوي هو أحد الاضطرابات الأيضية التي تظهر في مرضى الفشل الكلوي والذي يسبب الامراضية. الهدف هو دراسة المؤشرات الحيويه مع حصول الحثل العظمي ( امراض العظام) في مرضى الغسيل الكلوي. طريقة العمل : تم جمع 50 عينة لاناث مرضى الغسل الكلوي ( المداومين بالغسيل لمدة لاتقل عن سنه ) من مستشفى البصرة التعليمي / العراق و30 عينه من الإناث الأصحاء كمجموعة مقارنة . تم قياس مستويات كل من فيتامين D، وهرمون الغدة الجاردرقية PTH، وهرمون الأوستيوكالسين وبعض معايير المصل للعظام. النتائج: لوحظ انخفاض معنوي في مستوى فيتامين D في مصل اناث الغسيل الكلوي (12.770 نانوغرام / مل) مقارنه مع الاناث الاصحاء ( 20.816 نانوغرام /مل) . مستوى الأوستيوكالسين كان مرتفعا في المرضى (54.311 نانوغرام / مل) مقارنة بمجموعة الاصحاء. بشكل عام كان مستوى الـ PTH مرتفعاً عند اناث الغسيل الكلوي (262.211 بيكوغرام /مل) ولوحظ ايضا ارتفاع مستوى انزيم الفوسفاتيز القاعدي ALP (221.084 وحده دوليه/ لتر). وبالاعتمادا على مستويات PTH للمرضى اظهرت النتائج حصول امراض العظام الكلويه في مرضى الغسل الكلوي ل 30 انثى بنسبة 60% للنوع العالي الفقدان للكتلة العظميه تلاه النوع المنخفض الفقدان للكتلة العظميه في 20 انثى وبنسبة 40%. الاستنتاج: النقص في مستوى فيتامين D كان مترافق مع حدوث الحثل العظمي الكلوي في اناث مرضى الغسيل الكلوي .