The Role of Dexa Scan Application in Uremic Patients on Hemodialysis in Ibn-Sina Hemodialysis Center

Shakir Hameed Mohamed (FICMS)1, Yousif Naser Haded (MbChB, HMD)2, Ismail Ibrahim Latif (MbChB,PhD, HMD)3, Ahmed Methab Athab (PhD)4 and Nabeel Khalid Alwendi (FICMS)5

Abstract

Background: Chronic kidney disease is an international public health problem affecting 5–10% of the world population. As kidney function declines, there is a progressive deterioration in mineral homeostasis, with a disruption of normal serum and tissue concentrations of phosphorus and calcium.

Objective: To determine the effect on bone density by dexa scan and mineral derangement in chronic renal failure, by measuring calcium, phosphate, alkaline phosphatase and parathyroid serum,total serum protein and Albumin levels and to determine bone density by dexa scan of bones.

Patients and Methods: Cross sectional study was conducted in 75 patients with chronic renal failure. Blood was taken before dialysis session and measurements of serum calcium, phosphorus, serum alkaline phosphatase, protein and albumin levels, and dexa scan to measure the bone density in these patients.

Results: There was a significant correlation between Hypocalcemia and dexa scan results. Majority of patients had high serum phosphate levels (54.6%).and normal phosphate level in 40% while the hypophosphatemia result 5.33% and mean phosphate level is 2.24 mmol/l. Total serum protein mean is 61.51 , 37.33% of them had hypoproteinemia and 62.66 % of them had normal serum protein. There was a significant correlation between dexa scan and vit D level, calcium, alkaline phosphatase, female gender, smoking and body mass index.

Conclusion: The current study demonstrated that it can predict the chronic kidney diseases-Metabolic bone disorder from mineral levels before diagnosis by dexa scan.

Keywords: Metabolic bone disorder, dexa scan, chronic kidney disease.

Corresponding Author: ismail_6725@yahoo.com

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1,2,5 Baquba Teaching Hospital - Diyala-Iraq
3,4College of Medicine-University of Diyala-Diyala-Iraq

Introduction

Chronic kidney disease (CKD) is a worldwide public health problem, with increasing prevalence [1]. It is associated with a number of abnormalities in mineral metabolism such
as hypocalcemia, hyperphosphatemia and abnormalities in vitamin D metabolism that result in functional calcitriol deficiency[2,3,4]. The major consequences of disordered mineral metabolism in CKD are secondary hyperparathyroidism (SHPT), metabolic bone disease including renal osteodystrophy and vascular calcification[4,5,6]. These include parathyroid hormone (PTH), 25-hydroxyvitamin D (25(OH)D), 1,25-dihydroxyvitamin D (1,25(OH)2D), and other vitamin D metabolites, fibroblast growth factor-23 (FGF-23), and growth hormone. Beginning in CKD stage 3, the ability of the kidneys to appropriately excrete a phosphate load is diminished, leading to hyperphosphatemia, elevated PTH, and decreased 1,25(OH)2D with associated elevations in the levels of FGF-23. The conversion of 25(OH) D to 1,25(OH)2D is impaired, reducing intestinal calcium absorption and increasing PTH bone loss still remains an important problem due to post hemodialysis factors such as filter size and dialysate fluid type used, persistent HPT, and other metabolic and acid-base disturbances [7].

The therapeutic strategies for alleviation of post HD bone disease include, low dose of calcium, vitamin D, calcimimetic agents, bisphosphonates and, to a lesser extent, calcitonin, good nutrition and avoidance of analgesic and steroid[8].

Despite the knowledge of existence of mineral disorders after hemodialysis, this study was done to determine the severity of bone disease and mineral derangement in chronic renal failure, by measuring calcium, phosphate, alkaline phosphatase and parathyroid serum level, total serum protein and Albumin level and determine dexa scan of bones.

Patients and Methods

It is a cross-sectional descriptive study was conducted in Ibn- Sina hemodialysis Center at the Baquba teaching Hospital, Diayala/Iraq. HD patients of 20 years and above who have signed an informed consent. Enrollment was done from September 2016 to April 2017. Stud sample was 75 of HD patients on regular hemodialysis in ibn-sina dialysis center 51of them were males and 24 females aged between 20 and 78 years were studied and another 25 randomly chosen controlled normal peoples in the same territory was taken to compare results regarding dexa scan results[9].

Patients were those with ESRD on regular HD for 4 hours, three times a week, irrespective to etiology. All dexa scan were done within 2 hours before or after a dialysis session. Inclusion criteria: HD patients who are at least 3 months on HD programme and are on. Follow up at ISC hemodialysis in BTH. Patients who have a bone disorder for other reasons that may affect the results were excluded.

A printed questionnaire was used to collect data from recruited patients. Data consisted of Socio-demographic data including age, gender and dwell area. Information on smoking, alcohol intake, drugs. Medical history for possible etiology of kidney disease, time on dialysis program, since HD.
started and current medications were recorded.

**Laboratory Methods**

About 10 ml of blood was drawn before the session of hemodialysis in sterile plain tube for creatinine, urea, calcium, phosphate, total serum protein, vit D3, Alkaline phosphatase, albumin and intact PTH. The measurements of serum creatinine, albumin, calcium and phosphate were determined using automated clinical chemistry analyzer (cobas 400 plus) in IBN-Sina center laboratory, while serum PTH assays were performed in Baquba teaching hospital main laboratory using Enzyme Linked Immuno Sorbent Assay (ELISA) (Cobas e 411). According to the manufacturer instruction, (10-11) the results were analyzed after daily calibration using standard calibration methods and materials and tests assayed against controls. The glomerular filtration rate (GFR) was estimated using the MDRD formula [12] eGFR= 32788 \(\frac{\text{Serum Creatinine}}{1.154 \times \text{Age} - 0.203 \times \left[1.212 \text{ if Black}\right] \times \left[0.742 \text{ if Female}\right]}\) the formula was calculated using a free internet-based clinical equation calculator [13].

Total serum calcium was corrected for serum albumin using the equation: Corrected Calcium=Ca [40-measured serum albumin] x 0.02 + measured serum calcium. (A typical correction is that for every 1g/l that the albumin concentration is below 40g/l, the calcium concentration is 0.02mmol/l below what it would be if the albumin concentration was normal). All patients sent to Dxa scan unit in Baquba Teaching Hospital were weight, height, gender obtained and dxa scan is done for lumber spine and hip area.

**Dxa Technology**

A computer with specially designed proprietary software designed by each manufacturer completes the DXA "system." DXA measures bone mineral content (BMC, in grams) and bone area (BA, in square centimeters), then calculates "areal" BMD in g/cm2 by dividing BMC by BA. T-score, the value used for diagnosis of osteoporosis, is calculated by subtracting the mean BMD of a young-adult reference population from the patient's BMD and dividing by the standard deviation (SD) of young-adult population. Z-score, used to compare the patient's BMD to a population of peers, is calculated by subtracting the mean BMD of an age-, ethnicity-, and sex-matched reference population from the patient's BMD and dividing by the SD of the reference population. The mean BMD and SD of the reference populations used for these calculations is a critical variable in the determination of T-scores and Z-scores [20].

**Statistical analysis**

Data analysis was performed using SPSS version 20.0 software. DEXA scan for all patient and controlled were also done and T-score for hip and spine area measured were classified as normal, Osteopenia and osteoporosis. The relationship between bone biochemical parameters and dxa scan results was measured using Pearson correlation coefficient (r) and spearman s correlation coefficient, and linear regression coefficient (β). The levels of PTH, calcium and
phosphate were correlated with duration of
dialysis, age of the patients was compared
between groups using a nova test. All
statistical tests were performed at 5% level of
significance (95% confidence interval). The
findings were presented using table.

**Results**

**Table (1):** Socio-demographic characteristics of study sample

<table>
<thead>
<tr>
<th>Gender</th>
<th>BMI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>male</td>
<td>51(68%)</td>
<td>normal (23, 30.7%)</td>
</tr>
<tr>
<td>female</td>
<td>24(32%)</td>
<td>overweight (40, 54.7%)</td>
</tr>
<tr>
<td>age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>5 (6.7%)</td>
<td>residence (11, 14.7%)</td>
</tr>
<tr>
<td>30-39</td>
<td>11(14.7%)</td>
<td>rural (34, 45.3%)</td>
</tr>
<tr>
<td>40-49</td>
<td>12(16%)</td>
<td>urban (41, 54.7%)</td>
</tr>
<tr>
<td>50-59</td>
<td>27(36%)</td>
<td>socioeconomic state</td>
</tr>
<tr>
<td>60-69</td>
<td>17(22.7%)</td>
<td>low (22, 29.3%)</td>
</tr>
<tr>
<td>70-79</td>
<td>3(4%)</td>
<td>medium (48, 64%)</td>
</tr>
<tr>
<td>smoking</td>
<td>25(33.3%)</td>
<td>high (5, 6.7%)</td>
</tr>
<tr>
<td>alcohol</td>
<td>6(8%)</td>
<td></td>
</tr>
</tbody>
</table>

Most of our patients are male (58%) with
wide distribution of age at presentation but
most of them between 50-70 (58%) and
smokers constitute (33%) most of them are
overweight (54.7%) possibly fluid overload.

**Table (2):** Patients clinical characteristics

<table>
<thead>
<tr>
<th>Duration on dialysis (month)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>4-6</td>
<td>4(5.3%)</td>
</tr>
<tr>
<td>7-12</td>
<td>13(17.3%)</td>
</tr>
<tr>
<td>13-24</td>
<td>20(26.7%)</td>
</tr>
<tr>
<td>More than 24</td>
<td>38(50.7%)</td>
</tr>
</tbody>
</table>

More than (50%) are on HD for more than 2 years which indicate good survival rate.

**Table (3):** Patients Medical Status

<table>
<thead>
<tr>
<th>Disease</th>
<th>present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>19 (25.3%)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>26 (34.7%)</td>
</tr>
<tr>
<td>Genitourinary</td>
<td>15 (20%)</td>
</tr>
<tr>
<td>Polycystic disease</td>
<td>3 (3.3%)</td>
</tr>
<tr>
<td>Unknown cause</td>
<td>12 (16.7%)</td>
</tr>
</tbody>
</table>
Our result showed incidence of hypertension among patients (25.3%) as a primary cause, diabetes present as cause of uremia in (34.7%) genitourinary in (20%) polycystic disease in (3.3%) yet we cannot define the cause in (16.7%).

**Table (4): Patients history of drug intake**

<table>
<thead>
<tr>
<th>Drug history</th>
<th>present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ferro folic acid</td>
<td>75(100%)</td>
</tr>
<tr>
<td>Calcium carbonate</td>
<td>70(93%)</td>
</tr>
<tr>
<td>Calcitriol(one alfa)</td>
<td>70(93%)</td>
</tr>
<tr>
<td>Sevelamer</td>
<td>5(7%)</td>
</tr>
<tr>
<td>Epirax(erythropoietin)</td>
<td>75(100%)</td>
</tr>
</tbody>
</table>

Most of our patients are on regular treatment of calcium carbonate (93%) (100%) calcitriol (one alfa) (93%) and all of them receive erythropoietin supplement and iron.

**Table (5): Biochemical characteristics of the study sample**

<table>
<thead>
<tr>
<th></th>
<th>hypo</th>
<th>normal</th>
<th>hyper</th>
<th>mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTN</td>
<td>1(1.33%)</td>
<td>43(57.33%)</td>
<td>31(41.33%)</td>
<td>145.62 (+ 255.16)</td>
</tr>
<tr>
<td>Calcium</td>
<td>39(52%)</td>
<td>35(46.6%)</td>
<td>1(1.33%)</td>
<td>2.2 (+ 0.2)</td>
</tr>
<tr>
<td>Phosphate</td>
<td>4(5%)</td>
<td>30(40%)</td>
<td>41(55%)</td>
<td>2.4</td>
</tr>
<tr>
<td>Alk. Phosphatase</td>
<td>2(2.6%)</td>
<td>50(66.6%)</td>
<td>23(30.6%)</td>
<td>123.23</td>
</tr>
<tr>
<td>Vit D</td>
<td>73(97.3%)</td>
<td>2(2.66%)</td>
<td></td>
<td>38.3</td>
</tr>
<tr>
<td>Total serum protien</td>
<td>47(62.66%)</td>
<td>28(37%)</td>
<td></td>
<td>61.51</td>
</tr>
<tr>
<td>Serum albumen</td>
<td>56(74.66%)</td>
<td>19(25.33%)</td>
<td></td>
<td>30.11</td>
</tr>
</tbody>
</table>

Most of our patients have normal PTH (57.33%) and increase level of PTH in (41.33%). regarding calcium level majority have low calcium (52%) and normal calcium level in (46). phosphate are high in (55%) and normal in (40%). alk.phosph are normal in (66.6%) but elevated level present in only (30.6%). VIT D are low in almost all patients (97.3%), most of patients have low TSP and low Albumen (62.66%) (74.66%) respectively.

**Table (6): Deya scan results in study Sample**

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Osteopenia</th>
<th>Osteoporosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deya scan total</td>
<td>20 (26.66%)</td>
<td>35 (46.66%)</td>
<td>20 (26.66%)</td>
</tr>
<tr>
<td>Deya scan hip</td>
<td>27 (32%)</td>
<td>37 (49.33%)</td>
<td>11 (14.66%)</td>
</tr>
<tr>
<td>Deya scan spine</td>
<td>33 (44%)</td>
<td>25 (33.33%)</td>
<td>17 (22.66%)</td>
</tr>
</tbody>
</table>
Dexa scan showed that nearly half (46.66%) of patients have osteopenia and only quarter have osteoporosis (26.66%). There is very significant anova regression between mineral (biomarkers) and dexa scan result for future relation and dependable.

**Discussion**

The chronic kidney disease is a worldwide public health problem associated with high morbidity and mortality (14-15). Secondary hyperparathyroidism after HD has been reported even in the presence of excellent HD [16].

In this study, CKD on HD programme, calcium, phosphorus and PTH considerably normalized in majority of the patients. The mean ages of our patients 54.5yrs , the common age groups affected 50-59 y are 27(36%), then age group 60-69 y were 17(22.7%). there is significant correlation between age and hyper tension (p=.040) and with BMI(p=.000).

Our study is agree by a study done by Evenepoel et al and Kawarazaki et al 54.5 and 50.0 years respectively [17]. A study done by Sidney Klawansky, et al., showed that there are links between osteoporosis increased mortality, possibly reflecting links of low BMD with poor nutritional status and vascular calcification[19]. In our study, males made up the majority of the patients with 51 (68%) and females 24(32%) this goes with other study done in Africa (Nigeria, Senegal and Burkina Faso) have also reported a male preponderance among patients with ESRD [19]. In one study by M Asaka, H Iida, M FUJITA, K IZUMINO, M TAKATA, H SETO, and S SASAYAMA, female was inversely correlated with BMD with age, but not in male HD patients [20]. Which may be due to hormonal changes and exercise reduction with chronic diseases. Female gender has also been linked as an independent risk factor. This was negatively related with BMD, suggesting that the female skeleton is more vulnerable CKD_MBD changes than that of the male [21]. Regular weight-bearing, physical activity also had a beneficial effect on bone mass, while prolonged bed rest had a powerful negative impact on skeletal health [22]. This may explain difference between genders in BMD. The majority of patients in our study were overweight 41(54.6%), and 11 (14.6%) obese but only 23(30.66%) normal. This possibly because many patients have fluid overload and didn’t reach the dry weight The higher level of PTH mean was with overweight group also major reduction of vit D occur in over weight group and lowest in normal weight group for both 41.84(+13.93), 2.01(-+1.188) respectively. There is no significant Anova correlation between BMI with PTH, Ca, po4 and age but high significant with alkaline phosphatase and also significant person s correlation between BMI and sex which are similar to other studies results. There was a statistically significant relationship between increased age of the patients as well as duration of dialysis and a high PTH level (p<0.001) [18]. The study by Bess Dawson-Hughes et al., there is a positive correlation between body weight and BMD in the general population [23].
Similarly, several studies demonstrated that the body size relates with BMD also in CKD and ESRD patients [24; 25; 26]. A study done in Turkey among renal HD, low BMI values and decreased 25OH vitamin D levels were found to be a main risk factors for loss of bone mineral density[27]. Priyanka et al reported a positive correlation between BMI and bone mineral density in spine and femur. Longer CKD duration prior to HD showed greater loss of BMD in the femur[28]. In general body mass index associates with BMD or bone mass as measured by DEXA and the BMI is a predictor of BMD also in ESRD patients [29]. Thus, not surprisingly, body weight and BMI were primary responsible factors for BMD variation, osteoporosis and fractures (30.31). Almost half 39 (52%) of our study population had hypocalcemia ,we found no significant correlation between age group nor duration of dialysis with hypocalcemia.

We found significant correlation between hypocalcemia and estimated T_score and no with BMI. Only 1(1.33%) of our patients had hypercalcemia as it has been reported in other studies with hypercalcemia ranging from 3%- 21% [18,33, 34 , 35, 36]. In the early post HD period serum calcium has been reported to follow a biphasic pattern with an immediate post HD decline followed by a significant increase. All 100% patients were on calcium supplements regularly despite having different calcium level because our patient compliance is less than other population and a bad minded about hemodialysis programme and poor patients and nutritional and gastrointestinal complication of uremia. In this study vitamin D levels were low determined and thus a correlation with low serum calcium levels in this population could be ascertained (37,11).

In my study, nearly as half as 41 (54.6%) of renal HD patients had high serum phosphate Kawarazaki et al., reported hypophosphatemia among 15% of HD 12 month duration. Hypophosphatemia was associated with persistent HPT 12 months of HD The difference in the prevalence of hypophosphatemia might be due to the fact that in the study by Kawarazaki et al the mean PTH levels at 12 months duration of HD was higher 107 (71.0-205.3)pg./ml compared to a mean of 2.24(+1.44) (25.0-58.6)pg./ml at a median duration of ( 13-24) months HD in this study. The mean of serum phosphate in the early three months of dialysis was 2.300 mmol/l.

Serum phosphorus levels are usually elevated prior to renal dialysis and decreases rapidly following HD to within or below range for patients with normal kidney function in the first few post HD months (38,39). The results in my study were 73(97.33%) have vit D deficiency and 2(2.33%) of patient were normal. This study results are go with that done by Grahame J Elder (40) but not agree by study in japan by K Nakatsuka and Y Nishizawa. Vitamin D supplementation reduces serum PTH levels and improves bone strength. The results of our study, the dexa scan as a whole show 20 (26.66%) of patients with normal BMD, and 35(46.6%) with osteopenia BMD, and
20(26.66%) of them having osteoporotic BMD and no fractures in between but there is considerable difference in BMD between the hip area t-score and spine area t-score. Shows that 27(32%) were normal BMD 37(49.33%) had osteopenia and 11(14.66%) of them with osteoporosis. The osteopenia of hip associated with lower values of PTH, PO4, Ca while osteoporotic hip associated with highest elevation of PTH, ALP and po4 but with lowest most values of Ca, VIT D, total serum protein and albumin. There is significant correlation in anova table between hip t-score and PTH (p=.000) and with serum albumin (p=.000) while no significant correlation with PTH in Duncan test nor with albumin level. In spearman s rho there is very significant correlation between hip T-score and serum albumin (p=.004) and with alkaline phosphatase (p=.004) and also with total serum protein (p=.000) and no significant correlation with Ca or po4.

Conclusions
1-This study demonstrated that elevated serum PTH levels are present even after HD and are associated with many factors for bone diseases. It also showed presence of low PTH levels though the prevalence is lower than those reported in the CKD counterpart. This may indicate continuing presence of a dynamic bone disease if PTH levels are used as surrogate markers for bone turnover.
2-Hypocalcemia was present in almost half of HD as opposed to hypercalcemia reported in other studies. This may be as a result of higher prevalence of a dynamic bone disease in our CKD patients. Hypocalcemia was associated with relatively older patients and was not correlated with duration of dialysis.
3-Nearly half of our patients had serum phosphorus levels within reference ranges.
4-There is great predictable value can be obtained from mineral analysis for patient with mineral and bone diseases and used as a good indicator for follow up of them without need to do dexa scan and can be depended on these biochemical markers as screening tests to evaluate the bone mineral diseases especially when dexa scan is not available in some peripheral hospitals or areas.

References
The Role of Dexa Scan Application in Uremic Patients on Hemodialysis in Ibn-Sina Hemodialysis Center

Shakir Hameed Mohamed

17. M Asaka, H Iida, M FUJITA, K IZUMINO, M TAKATA, H SETO, and S SASAYAMA. Total and regional bone


