Articular and skeletal affection in regularly dialyzed patients with end-stage renal disease

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Background

Patients on regular hemodialysis (HD) are vulnerable to develop different articular and skeletal problems that interfere with life quality and affect morbidity and mortality in these patients. To, properly, overcome or even prevent the development of these complications, early detection, especially of the commonly affected parts, is required.

Aim

The aim was to detect articular and skeletal manifestations in patients with end-stage renal disease on regular HD, their relation to duration of dialysis, and which is more affected.

Patients and methods

A total of 50 patients (34 males and 16 females) with end-stage renal disease on regular HD, who were attendants of the dialysis unit of Internal Medicine Department at Al-Azhar University hospital, New Damietta, with duration of dialysis ranging between 3 and 15 years and age ranging from 26 to 70 years old were recruited for the study. They were classified into three groups: group I: mild, group II: moderate, and group III: severe joint affection. Full history taking, thorough clinical examination, especially for uremic and rheumatologic manifestations; laboratory investigations (inflammatory and metabolic markers); synovial fluid analysis and culture; and radiological investigations (radiography, dual-energy X-ray absorptiometry scan, ultrasound, computed tomography, and MRI of the affected parts) were done.

Results

There was a significant association between the duration of dialysis and the presence of joint affection. The most common affected joints were knee joints [n=23 patients (46%)] and shoulder joints [n=10 (20%)]. There was a statistically significant association between the severity of joints involvement and the prolonged duration of dialysis. The most common crystals present were the urate crystals (26%) followed by calcium pyrophosphate dihydrate (12%), and lastly oxalate crystals (8%). Carpal tunnel syndrome was diagnosed in 12 patients, with high significant association between the duration of dialysis and presence of carpal tunnel syndrome. There was increase in the level of parathyroid hormone with increase in the duration of renal dialysis. Moreover, 64% of patients had hyperparathyroid bone disease. The mean alkaline phosphatase level was increased in all groups of patients but was more in patients with severe joint affection. Serum albumin was maintained within normal level in HD patients. Radiological study of our HD patients showed that the most frequent radiological findings were signs of secondary hyperparathyroidism (subperiosteal resorption; acroosteolysis in the terminal tufts; pathological fracture, with two fractures in the spine, one in the neck of femur, and one fracture in the rib; and periarticular calcification, with one was found in the hand, and two were found in the pelvis). The incidence of these radiological findings increased with the increase of duration of HD. In addition, 18 patients had normal bone mineral density values, 18 patients had osteopenia, whereas 14 patients had osteoporosis.

Conclusion

The increased duration of dialysis is associated with increased incidence of articular and skeletal complications mainly renal osteodystrophy in the form of crystal-induced arthritis, osteoporosis, and periarticular calcification. Knee and shoulder joints, spine, neck of femur, wrist joints, and ribs are the main targets for complications and then for proper prophylaxis.

Introduction

The kidneys play a central role in mineral homeostasis. They maintain external balance of calcium, phosphorus, and magnesium. In addition, kidneys synthesize 1, 25-dihydroxyvitamin D3 and 24,25 di-hydroxy vitamin D3, and they serve as a target organ for the action of parathyroid hormone (PTH) and the clearance of PTH from the circulation. The kidneys also provide the major route for the elimination of certain substances (e.g. aluminum and B2-microglobulin) that can adversely affect mineral homeostasis and bone when retained in high concentration [1].

Chronic kidney disease (CKD) represented a worldwide public health problem, with increasing prevalence and adverse outcomes [including progressive loss of kidney function, that is, end-stage renal disease (ESRD), cardiovascular disease, and premature death] [2].

Articular and skeletal problems are still one of the important determinants of the life quality in patients with chronic renal failure, especially in patients maintained on hemodialysis (HD) [3,4].

Disturbances in mineral and bone metabolism are prevalent in CKD. These disturbances are an important cause of morbidity, decreased quality of life and extraskeletal calcification that have been associated with increased cardiovascular mortality. These disturbances have traditionally been termed renal osteodystrophy (ROD) and classified based on bone biopsy [5]. ROD had been used traditionally to describe the abnormalities in bone morphology that develop in CKD. It appears when the glomerular filtration rate falls below 60 ml/min [6].

The major disorders of bone disease in patients with CKD include causes related to the CKD itself that are characterized pathologically by high bone turnover with increased PTH levels (including osteitis fibrosa cystica and the classic lesion of secondary hyperparathyroidism) [7]. Another effect of CKD on musculoskeletal system is owing to causes related to HD itself, characterized pathologically by low bone turnover with low or normal PTH levels (adynamic bone disease and osteomalacia) [8].

Low-turnover bone disease can be grouped into two categories: adynamic bone disease and osteomalacia. In the latter condition, there is accumulation of unmineralized bone matrix that may be caused by vitamin D deficiency, excess aluminum deposition, or even metabolic acidosis [9]. In addition to bone histology and serum biomarkers, imaging has been an important component of evaluating bone disease in the past, and remains the main tool in assessing extraskeletal calcification in patients with CKD. In principle, the definition, evaluation, and classification of the mineral abnormalities and bone disease in CKD should include all three clinical components: serum biomarkers, non-invasive imaging, and bone abnormalities [10].

Aim

The aim of this study was to detect and evaluate the articular and skeletal affection in regularly dialyzed patients with ESRD, the commonly affected parts, and the relation to duration of dialysis.

Patients and methods

Study design

The present study included 50 patients (34 males and 16 females) already diagnosed as ESRD on regular HD and having articular and skeletal manifestations. They were attendants of the dialysis unit in Internal Medicine Department at Al-Azhar University Hospital, New Damietta. They were on regular HD three times weekly. The duration of HD ranged between 3 and 15 years.

Inclusion criteria

Patients with the following criteria were included in the study: (a) age above 18 years; (b) both sexes; and (c) patients on HD for at least 3 years.

Exclusion criteria

Patients on dialysis for acute renal failure were excluded from the study.

Ethical aspects

All patients gave their consent to be included in the study.

Study protocol

Evaluation of patients included full history taking with special attention to uremia symptoms (decreased or no urine output, fluid retention/edema of hands, feet or face,

nausea and/or vomiting, thirst, shortness of breath, and sleep interruption), articular and skeletal symptoms (pain, deformity, joint swelling, limited range of motion of joint, and myalgia), and thorough clinical examination. Pain was assessed by visual analog scale [11]. Muscle wasting (atrophy) was assessed if both sides are atrophied from grade 0 to grade 3 [12]. Joint swelling either bony or effusion was graded into grade from 0 to 3 [13]. Joint tenderness was assessed as the pain experienced by the patient when the joints are subjected to firm pressure over the articular margin, with the exception of the cervical spine, hip, and subtalar joints where tenderness is elicited by passive movement of the joint, and limitation of motion was graded for passive range of motion [14]. The assessment of the total severity of the clinical condition comprised the sum of the scores in each of the mentioned five criteria, giving each patient a total score for the severity of the clinical condition (maximum 16). Then blood samples were collected, and laboratory investigations for inflammatory and metabolic markers including erythrocytes sedimentation rate, C-reactive protein, complete blood count, rheumatoid factor, serum creatinine, blood urea, serum calcium, phosphorus, alkaline phosphatase (ALP), PTH, serum uric acid were done. Synovial fluid analysis was achieved by polarized light microscope and Alizarin red S staining. All fluids were cultured and stained by Gram stain. Leukocyte quantities were estimated on wet preparation. Radiological investigations in the form of radiography and dual-energy X-ray absorptiometry scan, ultrasound, computed tomography, and magnetic resonance imaging of the affected part were done [15]. Carpal tunnel syndrome (CTS) diagnosis was based on clinical assessment and electro diagnostic testing (electromyography and nerve conduction velocity). The dialysis machine used in HD was Fresenius 40008 B. machine (Fresenius Medical Care Deutschland, GmbH, 61346 Bad Homburg v.d.H., Germany).

Statistical methodology

Data were coded, tabulated, and statistically analyzed using statistical package for social sciences (SPSS) version 16 (SPSS Inc., Chicago, Illinois, USA). Parametric data were expressed as mean±SD, and nonparametric data were expressed as number and percentage of the total. Comparison between two means was done by unpaired Student's t-test and comparison between more than two means was done by one-way analysis of variance (F test), whereas comparison of two categorical variables was compared by χ^2-test. Measuring the mutual correspondence between two values was done using the Spearman correlation coefficient. P value less than 0.05 was considered significant.

Results

The present study was performed on 50 patients at Dialysis Unit of Nephrology Department in Al-Azhar University Hospital, New Damietta, and all had articular and musculoskeletal complaints. Patients were divided into three groups: group I included 18 patients who had mild affection of joints (score 1–5) and consisted of 12 males and six females; group II included 22 patients who had moderate affection of joints (score 6–10) and consisted of 15 males and seven females; and group III included 10 patients who had severe affection of joints (score 11–16) and consisted of seven males and three females. The mean age of these patients was 40.13±10.3 years, and the duration of dialysis period ranged from 4 to 13 years, with a mean duration of dialysis 13.52±9.3 years. There was a highly significant association between duration of dialysis and severity of joint involvement. But, there was no statistically significant difference between the sexes among different groups. There was a statistically significant increase of both diabetes and hypertension in group III when compared with group I or II. The joints of lower limb were affected more than those of upper limb, and the big joints were affected more than the small joints. The most common affected joints in the lower limbs were the knee joint (23 patients), whereas in the upper limbs, the shoulder joints were the most common affected joints (10 patients). Four patients had arthritis of the wrist joint. There was a highly statistically significant association between the severity of joints involvement and the number of joints affected (68.18% of patients in group II had oligoarticular, whereas only 20% of patients in group III had oligoarticular affection) (Table 1).

In the present work, there was a significant association between the duration of dialysis (years) and the number of joints involved (monoarticular had a duration of 4.59±2.29 years, the oligoarticular had 6.23±9.78 years, and polyarticular had a duration of 6.33±7.33 years). So, the number of joints involved increased with the increase of duration of dialysis. In the present work, there was a statistically significant association between pain, tenderness, swelling, movement restriction and atrophy grade with the severity of disease; group III had significantly higher grades of pain, tenderness, swelling, movement restriction, and atrophy (Table 2).

In the present study, CTS was reported in none in group I, compared with 50% of group II that elevated to 70% in group III. Thus, there was a significant association between disease severity and development

Table 1 Patients characteristics, disease duration, risk factors, and joint involvement in studied groups

Variables	Group I (*n*=18) [36 (%)]	Group II (*n*=22) [44 (%)]	Group III (*n*=10) [20 (%)]	Test	*P*
Age	48.5±9.45	53.7±9.45	52.4±14.9	3.11	0.047*
Duration	3.8±1.4	5.8±2.9	7.6±2.4	13.52	0.004*
Sex					
Male	12 (66.7)	15 (68.2)	7 (70.0)	0.03	0.98
Female	6 (33.3)	7 (31.8)	3 (30.0)		
DM	5 (27.7)	9 (40.9)	8 (80.0)	7.26	0.026*
HTN	7 (38.8)	12 (54.5)	9 (90.0)	6.84	0.033*
Joint involved					
Knee	9 (50.0)	10 (45.45)	4 (40.0)		
Shoulder	3 (16.7)	5 (22.7)	2 (20.0)		
Elbow	1 (5.6)	2 (9.1)	0 (0.0)		
Wrist	2 (11.1)	1 (4.5)	1 (10.0)		
Hip	1 (5.6)	1 (4.5)	1 (10.0)		
Ankle	0 (0.0)	1 (4.5)	0 (0.0)		
Small Joints of hand	1 (5.6)	1 (4.5)	1 (10.0)		
Subtalar	1 (5.6)	0 (0.0)	0 (0.0)		
Spine	0 (0.0)	1 (4.5)	1 (10.0)		
Severity of involvement					
Monoarticular	12 (66.7)	5 (27.7)	0 (0.0)	44.64	0.001*
Oligoarticular	5 (27.8)	15 (68.2)	2 (20.0)		
Polyarticular	1 (5.6)	2 (9.1)	8 (80.0)		

DM, diabetes mellitus; HTN, hypertension. *Statistical significance was defined as P ≤ 0.05.

Table 2 Variable grades of pain, tenderness, joint swelling, movement restriction, and muscle atrophy among the three different groups

Variables	Group I (*n*=18) [36 (%)]	Group II (*n*=22) [44 (%)]	Group III (*n*=10) [20 (%)]	Test	*P*
Pain grade					
1	5 (27.8)	5 (22.8)	0 (0.0)	97.40	<0.001*
2	9 (50.0)	15 (68.2)	1 (10.0)		
3	3 (16.7)	2 (9.1)	5 (50.0)		
4	1 (5.6)	0 (0.0)	4 (40.0)		
Tenderness grade					
0	0 (0.0)	0 (0.0)	0 (0.0)	85.97	<0.001*
1	14 (77.8)	4 (18.2)	0 (0.0)		
2	4 (22.2)	15 (68.2)	4 (40.0)		
3	0 (0.0)	3 (13.6)	5 (50.0)		
4	0 (0.0)	0 (0.0)	1 (10.0)		
Joint swelling grade					
0	3 (16.7)	3 (16.7)	0 (0.0)	53.06	<0.001*
1	10 (55.6)	6 (27.3)	0 (0.0)		
2	5 (27.8)	12 (54.5)	4 (40.0)		
3	0 (0.0)	1 (4.5)	6 (60.0)		
Grade of movement restriction					
0	0 (0.0)	1 (4.54)	0 (0.0)	64.98	<0.001*
1	12 (66.7)	3 (13.6)	0 (0.0)		
2	6 (33.3)	12 (54.5)	3 (30.0)		
3	0 (0.0)	6 (27.3)	5 (50.0)		
4	0 (0.0)	0 (0.0)	2 (20.0)		
Grade of atrophy					
0	16 (88.9)	17 (77.3)	3 (30.0)	28.16	<0.001*
1	2 (11.1)	5 (22.7)	6 (60.0)		
2	0 (0.0)	0 (0.0)	1 (10.0)		
3	0 (0.0)	0 (0.0)	0 (0.0)		

*Statistical significance was defined as P ≤ 0.05.

Figure 1
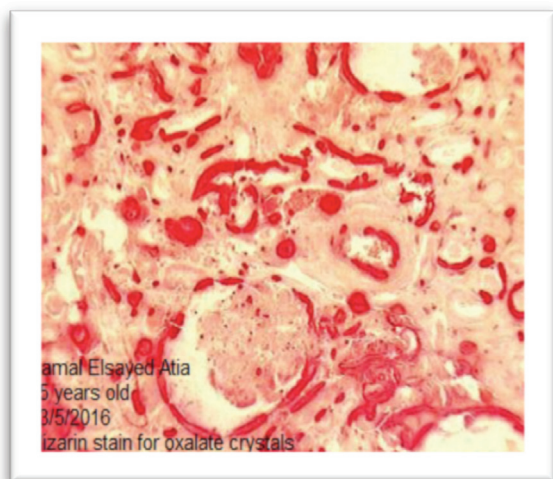
Alizarin stain for oxalate crystals.

Figure 2

Polarized light microscope for uric acid crystals.

of CTS. On the contrary, there was no statistical significance between the grade of joint affection and soft tissue affection.

In the present work, there was a statistically significant increase of calcium, PTH, ALP, serum uric acid, blood urea, serum creatinine, and serum albumin in group III (8.2±1.6, 644.3±248, 175±126.43, 11±1.87, 90.81±17.85, 10.91±1.33, and 3.9±0.13, respectively) when compared with group II (6.4±1.4, 567.81±300.4, 160±126.43, 9 ±1.53, 79.81±17.85, 8.91±1.33, and 3.87±0.13, respectively) or group I (7.1±1.27, 436.8±189.2, 142 ±126.43, 6±1.86, 60.81±17.85, 7.10±1.69, and 3.70 ±0.13, respectively). The most common crystals present were the urate crystals (26%) followed by calcium pyrophosphate dihydrate (12%), and lastly oxalate

Figure 3

Calcium pyrophosphate dihydrate (CPPD) crystals under polarized light microscope.

crystals (8%) (Figs 1–3). In addition, there was no significant difference between studied groups regarding the results of Alizarin examination (Table 3). In the present study, there was no significant association between the presence of crystals or results of Alizarin stain and the disease duration (Table 4).

In the present work, there was a significant correlation between the mean value of serum PTH and the dialysis period; meaning that the mean value of serum PTH increased with the increase of duration of dialysis. However, there was no significant correlation between serum calcium levels and duration of dialysis ($P<0.05$).

In group I, T score at lumbar spine revealed that nine (50%) patients had normal bone mineral density (BMD) values, five (27.77%) patients had osteopenia, whereas four (22.22%) patients had osteoporosis. Moreover, T score at femoral neck revealed that eight (44.44%) patients had normal BMD values, six (33.33%) patients had osteopenia, whereas four (22.22%) patients had osteoporosis, in comparison with healthy young adult of the same sex. In group II, T score at lumbar spine revealed that six (27.27%) patients had normal BMD values, 10 (45.45%) patients had osteopenia whereas six (27.27%) patients had osteoporosis. T score at femoral neck revealed that eight (36.36%) patients had normal BMD values, nine (40.90%) patients had osteopenia, whereas five (22.72%) patients had osteoporosis. In group III, T score at lumbar spine revealed that two (20%) patients had normal BMD values, three (30%) patients had osteopenia, whereas five (50%) patients had osteoporosis. Moreover, T score at

Table 3 The biochemical findings, fresh examination, and Alizarin staining of synovial fluid in the studied groups

	Group I (mean±SD)	Group II (mean±SD)	Group III (mean±SD)	P
Laboratory investigations				
Ca (mg/dl)	7.1±1.27	6.4±1.4	8.2±1.6	0.007*
P (mg/dl)	10.1±3.9	11.8±11.5	8.5±2.1	>0.05
PTH (pg/dl)	436.8±189.2	567.81±300.4	644.3±248	0.014*
Alkaline phosphatase	142±126.43	160±126.43	175±126.43	<0.001*
Serum uric acid	6±1.86	9±1.53	11±1.87	<0.001*
Blood urea	60.81±17.85	79.81±17.85	90.81±17.85	<0.001*
Serum Creatinine	7.10±1.69	8.91±1.33	10.91±1.33	<0.001*
Serum albumin	3.70±0.13	3.87±0.13	3.9±0.13	>0.05
Fresh examination of synovial fluid				
Negative	11 (61.1)	13 (59.1)	3 (30.0)	>0.05
CPPD	2 (11.1)	3 (13.6)	1 (10.0)	
Urate	4 (22.2)	5 (22.7)	4 (40.0)	
Oxalate	1 (5.6)	1 (4.5)	2 (20.0)	
Alizarin stain				
Negative	7 (32.4)	8 (31.1)	4 (40.0)	>0.05
Positive	11 (67.6)	14 (68.9)	6 (60.0)	

CPPD, calcium pyrophosphate dihydrate; PTH, parathyroid hormone. *Statistical significance was defined as $P \leq 0.05$.

Table 4 Association between results of synovial fluid examination and disease duration

	<5 years	5–10 years	>10 years	P value
Type of crystal in synovial fluid				
Negative	11 (61.1)	15 (62.5)	0 (0.0)	>0.05
CPPD	5 (27.8)	6 (25.0)	2 (25.0)	
Urate	1 (5.6)	2 (8.3)	5 (62.5)	
Oxalate	1 (5.6)	1 (4.1)	1 (12.5)	
Alizarin stain				
Negative	6 (33.3)	7 (31.8)	3 (30.0)	>0.05
Positive	12 (66.7)	15 (68.2)	7 (70.0)	

CPPD, calcium pyrophosphate dihydrate.

Table 5 Different values of dual-energy X-ray absorptiometry scan in studied groups at lumbar spine and femoral neck

BMD	Group I [n (%)]		Group II [n (%)]		Group III [n (%)]	
	At lumbar spine	At femoral neck	At lumbar spine	At femoral neck	At lumbar spine	At femoral neck
Normal (T score <−1)	9 (50)	8 (44.44)	6 (27.27)	8 (36.36)	2 (20)	2 (20)
Osteopenia (T score −1 to −2.5)	5 (27.77)	6 (33.33)	10 (45.45)	9 (40.90)	3 (30)	2 (20)
Osteoporosis (T score >−2.5)	4 (22.22)	4 (22.22)	6 (27.27)	5 (22.72)	5 (50)	6 (60)

BMD, bone mineral density.

femoral neck revealed that two (20%) patients had normal BMD values, two (20%) patients had osteopenia, whereas six (60%) patients had osteoporosis (Table 5).

In all groups, dual-energy X-ray absorptiometry showed that T score was normal in 18 (36%) patients, osteopenia was seen in 18 (36%) patients, and osteoporosis in 14 (28%) patients. Radiological features of ROD were presented in all patients in the form of subperiosteal resorption in 25 (50%) patients, where 16 of them were seen along the radial margin of middle phalanges, four of them were seen in the outer one third of the clavicle, and three of them were seen in symphysis pubis; acroosteolysis in the terminal tuft of 15 (30%) patients; pathological fracture in seven (14%) patients, with two fractures in the spine, one in the neck of femur, and one fracture in the rib; and periarticular calcification in three (6%) patients, with one of them found in the hand, and two were found in the pelvis.

Discussion

Our study was performed on 50 patients at Dialysis Unit of Internal Medicine Department in Al-Azhar

University Hospital, New Damietta. Their age ranged from 26 to 70 years old, and they were 34 males and 16 females. We found that there was a significant association between the duration of dialysis and the presence of joint complications, and these results coincide with that of Christopher et al. [16], who found that the incidence of dialysis-related arthropathy increased with the duration of dialysis therapy.

Our results showed that the most common affected joints were knee joints [n=23 patients (46%)] and shoulder joints [n=10 (20%)]. In agreement, Dougados et al. [10] found that knee joint was the most affected joint (57%), then shoulder joint (21%) and hip joint (14%). On the contrary, this did not coincide with Damian [17] who reviewed 97 HD patients, and regarding dialysis-related arthropathy, they found that the commonly affected joints were shoulders, hips, hands, and then knees.

In our study, there was a statistically significant association between the severity of joints involvement and the prolonged duration of dialysis; these results coincide with that found by Rodríguez-Henríquez et al. [18].

In the present study, CTS was diagnosed in 12 patients, and showed high significant association between the duration of dialysis and presence of CTS. These results are in contradiction to the study of Hoshino et al. [19] who estimated that 60–90% of HD patients developed CTS after 15 years of HD. This high incidence reported may be owing to the prolonged duration of dialysis of their patients as most of our patients were maintained on regular dialysis for period varied from 5 to 10 years, and all patients in their study and the study of Miyata et al. [20] had duration of dialysis of 15 years or more.

Regarding the biochemical markers in 50 HD patients, our results showed that 64% of patients had hyperparathyroid bone disease, and this is in agreement with Hazenberg [21] who found in a study conducted on 48 HD patients that 70% of them had hyperparathyroidism. Our study found that there was increase in the level of PTH with increase in the duration of renal dialysis, which indicates significant association between the level of serum PTH and the dialysis period. Our result is in agreement with Isaka et al. [22] who revealed that dialysis duration is the key determinant of severity of secondary hyperparathyroidism. However, our study is not in agreement with

Legendre et al. [23] who found no correlation between HD duration and increased PTH level. They explained this result by that most of their patients received vitamin D preparations.

In our study, which was done on 50 HD patients, the mean ALP was increased in all groups of patients but more in patients with severe joint affection, and this indicates significant association between increase in ALP level and prolonged duration of HD. This result is in parallel with Christopher et al. [16] who concluded from a study that measured bone markers in 43 HD patients that a positive correlation was found between HD duration and ALP level. Mason et al. [24] found that the increase in ALP isoenzyme is common in HD patients as a result of hepatic cirrhosis and cardiac failure.

Our result showed that serum albumin maintained within normal level in HD patients most probably owing to their good nutrition and is in agreement with Blumenkrantz et al. [25]. However, this result is not supported by Kaysen and Chin [26] and Rocco [27] who studied the effect of dialysis on nutritional parameters, and they found that some patients have low plasma albumin concentration despite adequate protein intake. However, Rocco [27] stated that hypoalbuminemia is a late manifestation of malnutrition and need a long time to be manifested as albumin has long half-life and large hepatic reserve.

Radiological study of our HD patients showed that the most frequent radiological findings were signs of secondary hyperparathyroidism in the form of subperiosteal resorption in 25 (50%) patients; acroosteolysis in the terminal tuft of 15 patients; pathological fracture reported in seven patients, with two fractures in the spine, one in the neck of femur, and one fracture in the rib; and periarticular calcification in three (6%) patients, with one of them found in the hand and two found in the pelvis. Our study showed highly significant difference between the radiological findings of the HD patients denoting that with prolonged duration of HD, there is increase in the incidence of radiological findings of ROD. Ureña et al. [28] stated that relative risk of fracture increases 6.4 times after 10 years of HD. Rolvien et al. [5] attributed periarticular calcification in HD patients to high serum phosphate that is not removed effectively by dialysis and to high doses of calcium carbonate used as phosphate binders.

As low values of BMD are the most important risk factor for fractures, Negri and Brandenburg [29] stated

that, in dialysis patients, the prevalence of osteoporosis is variable, and most of the studies are in line with reduced BMD in HD patients. Regarding BMD in our study, 18 patients had normal BMD values, 18 patients had osteopenia, whereas 14 patients had osteoporosis, denoting that the prevalence of osteoporosis increases with the duration of dialysis. However, this result is not supported by Gerakis *et al.* [30] and Ureña *et al.* [28] who conducted their study on 70 adult white HD patients, and they found no correlation between BMD and duration of HD.

Conclusion

The main articular and skeletal complications in dialyzed patients are ROD which includes crystal-induced arthritis, osteoporosis, and periarticular calcification. The lower limb joints were affected more than those of upper limb, the big joints were affected more than the small joints, and knee joints more than shoulder joints followed by wrist joints. Prevention is essential for optimizing skeletal health. Strategies should be directed at increasing peak bone mass, reducing risk factors for bone loss. Dietary phosphorus restriction is required to prevent hyperphosphatemia, secondary hyperparathyroidism, osteitis fibrosa cystica, and vascular calcification. Patients should be advised to consume adequate vitamin D (400–800 IU/day) and calcium (total 1500 mg/day). Weight-bearing exercise increases muscle strength and may stabilize or modestly increase bone density.

Conflicts of interest
There are no conflicts of interesting.

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