The Prevalence and Characteristics of Renal Osteodystrophy in Patients Undergoing Hemodialysis

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Abstract

Background - The reported prevalence of renal osteodystrophy among patients undergoing hemodialysis varied between studies. Different types of this condition were also reported but it was not yet determined if there are any differences in demographic data of patients with each type. Herein, this study was conducted to evaluate the prevalence of renal osteodystrophy in hemodialysis patients and to compare the characteristics of patients with each type of this complication.

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1. Introduction

Renal osteodystrophy associated with hyperparathyroidism and vitamin D deficiency are the common manifestations of chronic kidney disease (CKD) (1). Renal osteodystrophy is a set of metabolic bone disorders that affects people with CKD or end-stage renal disease (ESRD) undergoing hemodialysis. It can be either high turnover bone disease with increased PTH or low turnover one with low or normal PTH levels (2). Renal osteodystrophy can be divided into 4 types including 1) Osteitis fibrosa cystica, in which the bone turnover due to secondary hyperparathyroidism increases. 2) Adynamic bone disease, in which bone turnover is low. 3) Osteomalacia, in which low bone turnover is associated with increased non-mineral component of bone. 4) Osteodystrophy mixed uremic, in which high and low bone turnover features are obvious. In this disease, bone marrow fibrosis and non-mineralized osteoid matrix are increased (3).

Renal osteodystrophy causes multiple co-morbid conditions in ESRD patients such as cardiovascular issues, which are identified as the leading causes of death in CKD population (4). It can also lead to metastatic calcifications. Myocardial calcification can cause arrhythmia or a rupture of the myocardium in
some cases. Furthermore, the calcium deposition released into the lungs can cause obstructive lung diseases.

Calcium vascular deposition causes atherosclerosis, the most severe form of which is calciphylaxis. Sometimes the calcified masses form near the joints and can enlarge to 20 cm in diameter and 10 kg weight. The mass interacts with the joint activity and is sometimes infected. Bone pain and fracture, electroencephalogram changes, and muscle weakness are other complications of the disease (5). Several studies are conducted on the prevalence of renal osteodystrophy but their results varied possibly due to their methodological differences. There are also several factors affecting the prevalence of renal osteodystrophy. For example, bone volume is a function of age, gender, race, genetic factors, nutrition, endocrine disorders, mechanical stimuli, neurological function, and growth factors (4). On the other hand, the pattern of the prevalence of these disorders in the world is changing; in such an extent that the number of patients with osteitis fibrosa cystica is decreasing and the number of the ones with adynamic bone disease is increasing (6-9). Although there are some studies in Iran on the prevalence of renal osteodystrophy (10-12), different statistics were released for different cities. For example, the commonest type of renal osteodystrophy in patients undergoing hemodialysis in Tehran is adynamic bone disease (12), while in Zabul, osteitis fibrosa cystica has higher incidence (10).

Evaluation of the prevalence of these disorders in a variety of populations can guide physicians for better treatment of the patients. Therefore, the current multicenter study aimed to investigate the prevalence of renal osteodystrophy and compare the characteristics of its different types in patients undergoing hemodialysis.

[Abstract Continued…]

**Methods** - This is a cross-sectional study with 87 hemodialysis patients. They were divided into three groups according to PTH results: PTH>300pg/ml as high turnover bone disease or hyperparathyroidism, PTH ranged between 150-300pg/ml as normal and PTH<150pg/ml as patients with low turnover bone disease. Bone mineral densitometry (BMD) results from the spine and femoral neck were also recorded.

**Results**- Fifty-five patients (63%) were male with the mean age of 59 ± 14 years. Twenty-five (29%) patients had normal bone turnover; while 45 of them (52%) had high turnover, and 17 (19%) had low turnover types. A total of 72 patients (83%) had BMD results and 37 (51%) of them suffered from osteoporosis. Comparison of patients' characteristics with different types of renal osteodystrophy did not demonstrate any significant differences. Only the level of phosphorus and alkaline phosphatase and calcium phosphate product was significantly lower in patients with low turnover bone disease than in patients with high turnover type.

**Conclusion** - The high prevalence of bone disorders in hemodialysis patients indicate that appropriate interventions to prevent these complications are essential.

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2. Material and methods

In the current cross sectional study, patients who underwent hemodialysis for at least three months were included. Exclusion criteria were the presence of any other bone disorder such as multiple myeloma or bone tumors. Overall, 87 patients were assessed in this study. Demographic characteristics including age, gender and weight, kidney disease characteristics (cause of end-stage renal disease (ESRD), duration of ESRD, duration of dialysis, number of weekly dialysis sessions), history of kidney transplantation, use of calcium supplements, vitamin D, or its derivatives, and the results of calcium, phosphorus, alkaline phosphatase, PTH, vitamin D, albumin, hemoglobin, ferritin, ESR, and CRP tests were recorded for each subject in a checklist. Patients were divided into three groups based on PTH results: PTH > 300 pg/mL as subjects with high turnover and hyperparathyroidism, PTH 150-300 pg/mL as normal subjects, and PTH <150 pg/mL as subjects with bone disease and low turnover. Also, bone mineral densitometry (BMD) of the spine, femoral neck, or forearm bones was also recorded if available. T score ≤-2.5 in BMD of spine or femoral neck bones was considered as osteoporosis.

Data were analysed with SPSS version 22. Qualitative variables were expressed as frequency and percentage, and the quantitative variables were expressed as mean and standard deviation (SD). Chi-square and one-way ANOVA tests were used to compare the patient's characteristics and their laboratory results in terms of types of renal osteodystrophy and osteoporosis. To determine the relationship between body mass index (BMI) and BMD, Pearson correlation coefficient was used. P value <0.05 was considered as a significant level.

3. Results

Out of 87 patients enrolled in the current study, 54 patients (62%) were male and 33 (38%) female. The mean age of the patients was 59 ± 14 years ranged from 23 to 88. The mean weight of the patients was 70 ± 13 kg. The mean height of the patients was 164 ± 9 cm ranges. The mean BMI of the patients was 6.6 ± 6.6 kg/cm².

The most common causes of ESRD were diabetes or high blood pressure (each in 24 patients, 28%) and 14 patients (16%) had both diabetes and high blood pressure. Other causes of ESRD include glomerulonephritis in 4 (5%), polycystic kidney in 2 (2%), other causes in 10 (11%), and unknown causes in 9 patients (10%). The mean duration of ESRD and dialysis was 51 ± 43 months ranged 5 to 26. All patients were undergoing dialysis three sessions per week, and 7 patients (8%) had a previous history of kidney transplantation. Eleven patients (13%) received calcium supplements and 73 patients (84%) used supplements containing vitamin D or its derivatives. The test results of the patients are shown in Table 1.

Forty-five patients (52%) had high turnover bone disease, 25 patients (29%) had normal bone turnover, and 17 (19%) had low bone turnover. A total of 72 patients (83%) had femoral neck, spine, and forearm bones BMD (Table 2). Considering T score ≤-2.5 in each of the BMDs of the spine or femoral neck as osteoporosis, 72 patients had BMD, and 37 (51%) had osteoporosis.

There were no significant differences in the patients' characteristics including age, gender, height, weight, BMI, ESRD, duration of ESRD or dialysis, history of kidney transplantation, taking calcium supplements, vitamin D, or its derivatives between different types of renal osteodystrophy (Table 3). Levels of
phosphorus and alkaline phosphatase and calcium x phosphate were significantly lower in patients with low bone turnover than patients with high bone turnover (P = 0.016, P = 0.003, and P = 0.048, respectively). However, there was no significant difference between the types of renal osteodystrophy in terms of other test results (Table 4). There was no statistically significant difference between the types of renal osteodystrophy in terms of BMD as well as the prevalence of osteoporosis (Table 5). There was no significant association between BMI with BMD of femoral neck and forearm bones (P >0.05), but it had a significant direct correlation with T score of BMD of spine (r = 282, P = 0.043) and Z score of BMD of spine (r = 430, P = 0.001), in such an extent that with increasing BMI, these scores also increased (Table 6).

4. Discussion

The findings of the current study on 87 patients undergoing hemodialysis showed that 25 patients (29%) had normal bone turnover and 62 (71%) had renal osteodystrophy of with 45 patients (52%) had high bone turnover and 17 (19%) had low bone turnover. Thirty-seven of patients (51%) with BMD also had osteoporosis. There was no significant difference between patients’ characteristics in different types of renal osteodystrophy. Only the levels of phosphorous, alkaline phosphatase, and calcium phosphorous were significantly lower in patients with low bone turnover compared to the ones with high bone turnover.

Renal osteodystrophy and CKD-MBD are the systemic disorders of bone and minerals metabolism that manifests itself with one or a combination of the following symptoms: calcification of vessels or other soft tissues, disorders in serum concentrations and calcium, phosphorus, PTH, or vitamin D metabolism, bone disorders in bone regeneration, mineralization, volume, linear growth, or bone strength (13). As a result of bone disorders, the probability of bone fractures increases (14). The current study showed that 71% of the patients had renal osteodystrophy, most of them with high turnover rates. Sepehri et al., (2012) reported the prevalence of renal osteodystrophy in patients undergoing hemodialysis in Imam Khomeini Hospital of Zabol, Iran, as 80% that is slightly higher than that of the current study (10). Barzin et al., (1998) also evaluated the prevalence of renal osteodystrophy in patients undergoing hemodialysis in Hazrat Fatemeh (SA) Hospital in Sari, Iran, using radiographs and indicated that 56% of the patients had radiological changes in favour of osteodystrophy (15). Bagheri et al., (2006) examined the prevalence of renal osteodystrophy in patients undergoing hemodialysis in Tehran and indicated adynamic bone disease in 44% and secondary hyperparathyroidism in 15% of the cases. However, there was no significant difference between different groups in terms of age, gender, and hemoglobin and albumin levels; they finally indicated that adynamic bone disease the most common complication in patients with renal osteodystrophy (12). However, in the current study, PTH levels >450 ng/mL were considered secondary hyperparathyroidism. Rahimian et al., (2007) examined the frequency of hyperparathyroidism in 85 patients undergoing hemodialysis in Yazd and reported 36 (45%) cases of hyperparathyroidism (16). The results of abovementioned and the result studies indicate that renal osteodystrophy is common among hemodialysis patients. However, the current study failed to find a correlation between the duration of ESRD and dialysis with the type of renal osteodystrophy.

The prevalence of renal osteodystrophy in hemodialysis patients in other countries is also high, although the pattern of outbreak is different. In Singapore, a skeletal study showed renal bone disease in 24.4% of the patients undergoing hemodialysis (17). In the Czech Republic, the prevalence of renal osteodystrophy
in patients with uremia was 57% (18). In Thailand, adynamic bone disease was reported 41.1%, hyperparathyroidism 28.6%, mixed type 19.6%, mild lesions 4.5%, osteomalacia 3.6%, and osteosclerosis 1.8%. In addition, two cases of aluminium-related bone disease were found (7).

Bone biopsy reports in five different countries (Brazil, Uruguay, Argentina, Portugal, and Spain), reported that the prevalence of low-turnover osteomalacia and mixed uremic osteodystrophy in Brazil, Uruguay, and Argentina were higher than Portugal and Spain, while hyperparathyroid bone disease in Portugal and Spain was more common than the others (19). In Turkey, children with chronic renal failure who were undergoing peritoneal dialysis, high-turnover renal osteodystrophy was the most common bone disease (47%), followed by low-turnover bone disease (29%) and mixed renal osteodystrophy (24%) (20). A study in Poland on uremic children showed that the prevalence of adynamic bone disease was 27%, natural bone histology 37%, osteomalacia 2%, mixed lesions 10%, and hyperparathyroidism 24%, and there was no significant difference in the prevalence of different types of renal osteodystrophy between patients with peritoneal dialysis and the ones with hemodialysis (21). Santoso et al., (2003) in Indonesia using iPTH and radiographic parameters in 48 patients undergoing hemodialysis reported the highest prevalence of renal osteodystrophy in the cases with low bone turnover, and indicated differences between their results are those of previous studies (22). Khan and Iraniha (2009) in a review study examined the prevalence of renal osteodystrophy and their association with biochemical indices reported in different studies from 1985-2007. Of bone biopsy results of 1701 patients undergoing hemodialysis, 41% had hyperthyroid bone disease, 5% osteomalacia, 33% adynamic bone disease, 13.5% mixed osteodystrophy, and 5% were normal. In addition, of the 1316 patients with CKD not undergoing hemodialysis, 34% had hyperparathyroid bone disease, 19% osteomalacia, 8% adynamic bone disease, and 18% mixed osteodystrophy, and 20% were normal (23). Malluche et al., reviewed the prevalence of renal osteodystrophy in 603 adults (316 patients from the United States and 314 from Europe) with stage 5 CKD who underwent dialysis during 2003-2008 using bone biopsy and reported that white patients mostly had low bone turnover (62%), while blacks were often normal or had high bone turnover (68%) (24).

In general, the results of all studies show that renal osteodystrophy has a high prevalence in patients undergoing hemodialysis, although its pattern varies among populations and countries, and the reason can be attributed to sampling methods, duration of dialysis, nutritional and medication differences, and different criteria for the diagnosis of renal osteodystrophy. The current study results in agreement with those of other studies indicated that based on laboratory criteria, more than two-thirds of hemodialysis patients had renal osteodystrophy, and high turnover was more prevalent in the current study subjects. In addition, half of the patients with BMD had evidence of osteoporosis. The small sample size was one of the limitations of the current study, although the number of patients in most dialysis centers is few; hence, wider, multicenter studies with larger sample size can produce more generalized results. Other limitations of the study were the lack of bone biopsy and hand radiographs since they were not performed in many patients. There was no BMD in a number of patients. However, the relationship between BMD and PTH was one of the strengths of the current study.
5. Conclusion

The findings of the current study demonstrated that despite the treatment of kidney failure by hemodialysis, bone disorders such as renal osteodystrophy and osteoporosis are still common in such patients and appropriate measures and preventions should be taken to resolve such complications.

REFERENCES


