Research

Renal Osteodystrophy in End Stage Renal Disease Patients in a Center in South East of Iran: A Cross-Sectional Study

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ABSTRACT

Background

Renal osteodystrophy is a set of metabolic bone disorders occurs in patients with chronic kidney disease.

Aim

This study aimed to investigate the causes of renal osteodystrophy in hemodialysis patients in Zabol, in south east of Iran.

Methods

A total of 60 patients with End Stage Renal disease (ESRD), aged between 11-85 years entered this cross-sectional study. Patients were evaluated through a questionnaire, for age, sex, marital status, education level, occupation, income –as personal factors- cause of kidney disease, co-morbidities –as disease related factors- duration of dialysis, the number of dialysis per week, number of visits by specialists and medications –as dialysis based subjects. Blood samples were taken for determination of serum calcium, phosphorus, alkaline phosphatase, creatinine, albumin, total protein, parathyroid hormone and blood sugar. Vitamin D level and PTH level were used to determine bone disease. Data were analyzed using SPSS 21 software.

Results

This study showed that 48 patients (80%) were diagnosed with renal osteodystrophy. About half of the patients (47%) had osteofibrosis, 7% and 26% of subjects had a dynamic bone disease and osteomalacia, respectively. There was no statistically significant relationship between the presence of renal osteodystrophy and age (P=0.7), gender (P=0.3), marital status (P=0.4), educational level (P=0.4), occupation (P=0.4), income (P=0.2), duration of dialysis (P=0.4), the number of dialysis per week (P=0.45), number of visits (P=0.7), underlying disease (P=0.35) and medications (P=0.3). Overall, PTH level was significantly higher in osteodystrophic patients comparing other ESRD patients (P<0.001).

Conclusions

The study found that the high prevalence of renal osteodystrophy in our patients is not due to the interventions that happen after starting hemodialysis.

Keywords

End Stage Renal disease, hemodialysis, Renal osteodystrophy

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List of Abbreviations

ESRD: End Stage Renal Disease; PTH: Parathyroid Hormone; CKD: Chronic Kidney Disease

Background

In patients with normal renal function, serum levels of phosphorus and calcium are maintained in the normal range, all by the help of parathyroid hormones (PTH) and calcitriol. Kidney has a major role in the regulation of normal serum levels of calcium and phosphorus and inability to follow the mineral homeostasis will occur with the progression of kidney failure [1-3].

Disorders of bone include those with high bone turnover with an increase in PTH, including osteoid cystic fibrosis (osteitis fibrosa cystica) to classical lesion secondary hyperparathyroidism, and those with low bone turnover with low or normal PTH (such as osteomalacia and adynamic bone disease) [3]. In some patients, histopathologic features of both diseases are evident. The term uremic combined osteodystrophy (mixed uremic osteodystrophy) describes a disease that combines the high and low bone turnover diseases [4]. Some studies reported a strong correlation between increased calcification of the coronary arteries and decreased bone marrow mineral density that was observed on Computed Tomography. Myocardial calcification can lead to arrhythmia or myocardial rupture. Deposition of calcium in the lungs causes restrictive lung diseases. Coronary calcium deposits are the most severe form of calcification [4].

Renal osteodystrophy in chronic kidney disease (CKD) patients causes several significant problems, including cardiovascular complications, the leading cause of mortality in chronic kidney disease [1,5]. There are many studies in the world reporting different results. Some studies showed that in patients who were on daily dialysis, phosphate control was better, and therefore the likelihood of metastatic calcification was less. Daily hemodialysis was effective in control of low bone turn over disease, as well [6]. Other studies found some affecting factors in renal osteodystrophy such as Hypertension, high levels of PTH [7], calcium level, Alkaline phosphatase, serum calcitonin [8,9] and duration of being under hemodialysis [10-12].

Objectives

As a previous study showed a high prevalence of renal osteodystrophy among our patients [13], we aimed to evaluate the relevant causes in our patients to plan strategies for preventing the complications.

Methods

In this cross-sectional study, all cases with ESRD (60 patients), aged between 11 and 85 years were studied in Imam Khomeini hospital in Zabol. Data about patients who entered the study were collected through a questionnaire, for the cause of kidney disease, age, sex, weight, occupation, disease duration, the amount of calcium and vitamin D supplements, the number of visits by in charge doctors, medicines, income and education, number of family members, and the presence of a similar sick patient in the family [7,11,14]. Blood samples were taken from patients for testing before dialysis for these elements: Calcium, phosphorus, alkaline phosphatase, creatinine, albumin, protein, parathyroid hormone and random blood sugar [15-19]. PTH level was used for diagnosis of bone disease. We considered PTH levels higher than 300pg/ml as high-turnover bone disease. Patients with low circulating PTH level (below 150pg/ml) were considered to have low bone turnover disease (osteomalacia or adynamic bone disease). Free plasma $1.25(OH)_2D$ concentrations level of vitamin D was used to differentiate adynamic bone disease from osteomalacia so that patients with low levels of vitamin D were diagnosed as osteomalacia.

■ Ethical issues

The research followed the tenets of the Declaration of Helsinki; informed consent was obtained; and the research was approved by the ethical committee of Zabol University of Medical Sciences (ethical code: ZBMU.1.REC.1395.1).

■ Statistical analysis

Data were analyzed using SPSS V.21 software. Chi-square test was used to compare the categorical variables and P-value less than 0.05 was considered statistically significant.

Results

We studied all 60 ESRD patients who were on hemodialysis. Mean (Standard Deviation) age of patients was 48.13 (17.35) years (minimum 11 years and maximum 85 years), 28 (46%) of which were male. Ten patients (16.7%) were single and others were married. About half (40%) of our patients were illiterate, 18 patients (30%) had

elementary level and the same portion had high school levels and more. About half of our patients (46.7%) were housekeepers; 8.3% were students; 8.3% were employees, 6.7% were businessman, 15% were unemployed and 15% had other jobs. Underlying diseases were hypertension (21.7%), diabetes (20%), polycystic kidney disease (8.3%), glomerulonephritis (6.7%) and in 26.6% of cases we did not detect any underling diseases.

About two third of our patients (65%) had around 30 USD monthly income, five patients (8.3%) had 30-100 USD and 16 patients (26.7%) had more than 100 USD income.

About one fifth (16.7% or 10 cases) of our patients were under 30 years old age, 33.3% (20 cases) were 30-49 years old, 38.3% (23 cases) were 50-69 years old and 11.7% (7 cases) were older than 70 years. Forty patients (66.7%) had no other patient in their family. 15 cases (25%) had one other patient in their family and five cases (8.3%) had two and more patients in their family. The study showed that of 60 patients with ESRD, 48 patients (80%) had renal osteodystrophy. About half of them (47%) had osteofibrosis, 7% and 26% of those surveyed adynamic bone disease and osteomalacia, respectively.

About One third (35%) of our patients were dialyzed two times a week and 65% (39 cases) underwent dialysis three times a week. Time span for dialysis was 1 year in 41.7%, two years in 23.30%, three years in 13.3%, four years in 5%, five years in 6.7%, six years in 1.7%, eight years in 1.7%, nine years in 3.30%, and ten years in 3.30% of patients.

Mean time duration for dialysis was 2.71 years in osteodystrophic patients and 2.58 years in non-osteodystrophic cases (P = 0.4). Mean duration of ESRD diagnosis was 2.88 years in osteodystrophic patients and 2.75 years in non-osteodystrophic cases (P = 0.3). In average, Patients who had osteodystrophy were visited 10 times a month while non-osteodystrophic cases had the chance to be visited by specialist 9 times a month (P = 0.7). Statistical analysis of data showed that age (P = 0.7), gender (P = 0.3), different marital statuses (P = 0.4), different educational levels (P=0.4), educational levels (P=0.4), income (P=0.2), number of dialysis per week (P = 0.45), medication (P = 0.3), different occupations (P = 0.4) and underlying diseases (P = 0.35) were not statistically differ between patients with and without osteodystrophy (Table 1).

On the mean concentrations of electrolytes such as calcium, phosphorus and some other laboratory parameters including albumin, total protein, creatinine, alkaline phosphatase, parathyroid hormone, blood sugar, vitamin D, hemoglobin, ferritin and ESR among patients with and without osteodystrophy are shown in Table 2. We found that the mean serum PTH levels were significantly higher in patients with renal osteodystrophy (P <0.001) than those

Table 1. The association between demographic status, number of dialysis per week and prevalence of renal osteodystrophy.

Variable	Number (%)	Osteodystrophy		P value
		Yes Num (%)	No Num (%)	
Sex				
Male	28 (46.7)	24 (50)	4 (33.3)	P=0.30
Female	32 (53.3)	24 (50	8 (66.7)	
Marital status				
Single	10 (16.7)	9 (18.8)	1 (8.3)	P=0.38
Married	50 (83.3)	29 (81.2)	11 (91.7)	
Education level				
Illiterate	24 (40)	19 (39.6)	5 (41.7)	P=0.39
Elementary school	18 (30)	15 (31.3)	3 (25)	
High school and higher levels	18 (30)	14 (29.2)	4 (33.3)	
Number of dialysis per week				
Two	21 (35)	16 (33.3)	5 (41.07)	P=0.45
Three	39 (65)	32 (66.7)	7 (58.3)	
Occupation status				
Unemployed	9 (15)	6 (12.5)	3 (25)	P=0.37
Employee	5 (8.3)	5 (10.4)	0 (0)	
Housekeeper	28 (46.7)	21 (43.8)	7 (58.3)	
Student	5 (8.3)	5 (10.4)	0 (0)	
Businessman	4 (6.7)	4 (8.3)	0 (0)	
Others	9 (15)	7 (14.6)	2 (16.7)	
Underlying diseases				
Hypertension	13 (21.7)	10 (20.8)	3 (25)	P=0.35
Diabetes	12 (20)	9 (18.8)	3 (25)	
Polycystic kidney disease	5 (8.3)	4 (8.3)	1 (8.3)	
Glomerulonephritis	4 (6.7)	2 (4.2)	2 (16.7)	
Urinary tract infection	10 (16.7)	9 (18.8)	1 (8.3)	
Undiagnosed	16 (26.6)	14 (29.2)	2 (16.7)	

Table 2. The association between blood elements and PTH levels with renal osteodystrophy.

Variable	Osteodystrophy		P value
	Yes Mean	No Mean	
Calcium	9.02	8.72	P=0.30
Phosphore	5.42	4.60	P=0.38
Albumin	4.14	4.15	P=0.39
Total protein	6.65	6.84	P=0.45
Creatinine	7.23	5.82	P=0.45
Alkaline phosphatase	544	411	P=0.35
PTH	455	233	P=0.001
Blood glucose	113	98	P=0.38
Vitamine D	22	25	P=0.39
Hemoglobin	16	18	P=0.45
Ferritin	566	540	P=0.45
ESR	45	36	P=0.35

Table 3. The association between drugs and prevalence of renal osteodystrophy.

Variable	Osteodystrophy		Total	P value
	Yes Mean	No Mean		
Calcium carbonate Yes (number/percent) No (number/percent)	 46 (95.8) 2 (4.2)	 11 (91.7) 1 (8.3)	 57 (95) 3 (5)	P=0.49
Vitamin D Yes (number/percent) No (number/percent)	 24 (50) 24 (50)	 3 (25) 9 (75)	 27 (45) 33 (55)	P=0.11
Folic Acid Yes (number/percent) No (number/percent)	 44 (91.7) 4 (8.3)	 10 (83.3) 2 (16.7)	 54 (90) 6 (10)	P=0.59
Erythropoietin Yes (number/percent) No (number/percent)	 45 (93.8) 3 (6.3)	 11 (91.7) 1 (8.3)	 56 (93.3) 4 (6.7)	P=1
Venofer Yes (number/percent) No (number/percent)	 42 (87.5) 6 (12.5)	 10 (83.3) 2 (16.7)	 52 (86.7) 8 (13.3)	P=0.65
Aspirin Yes (number/percent) No (number/percent)	 15 (31.3) 33 (68.8)	 5 (41.7) 7 (58.3)	 20 (33.3) 40 (66.7)	P=0.51
Vitamin B6 Yes (number/percent) No (number/percent)	 18 (37.5) 30 (62.5)	 5 (41.7) 7 (58.3)	 23 (38.3) 37 (61.7)	P=1
Vitamin E Yes (number/percent) No (number/percent)	 6 (12.5) 42 (87.5)	 3 (25) 9 (75)	 9 (15) 51 (85)	P=0.36
Vitamine B12 Yes (number/percent) No (number/percent)	 16 (33.3) 32 (66.7)	 3 (25) 9 (75)	 19 (31.7) 41 (68.3)	P=0.73
Metoral Yes (number/percent) No (number/percent) Total	 8 (16.7) 40 (83.3)	 1 (8.3) 11 (91.7)	 9 (15) 51 (85)	P=0.67
Carvedilol Yes (number/percent) No (number/percent)	 3 (6.3) 45 (93.8)	 0 (0) 12 (100)	 3 (5) 57 (95)	P=1
Nitrocantine Yes (number/percent) No (number/percent)	 7 (14.6) 41 (85.4)	 0 (0) 12 (100)	 7 (11.7) 53 (88.3)	P=0.32
Furosemide Yes (number/percent) No (number/percent)	 8 (16.7) 40 (83.3)	 2 (16.7) 10 (83.3)	 10 (16.7) 50 (83.3)	P=1
Atorvastatine Yes (number/percent) No (number/percent)	 10 (20.8) 38 (79.2)	 3 (25) 9 (75)	 13 (21.7) 47 (78.3)	P=0.71
Amlodipine Yes (number/percent) No (number/percent)	 12 (25) 36 (75)	 1 (8.3) 11 (91.7)	 13 (21.7) 47 (78.3)	P=0.43
Captopril Yes (number/percent) No (number/percent)	 10 (20.8) 38 (79.2)	 0 (0) 12 (100)	 10 (16.7) 50 (83.3)	P=0.18
Other drugs Yes (number/percent) No (number/percent)	 25 (52.1) 23 (47.9)	 5 (41.7) 7 (58.3)	 30 (50) 30 (50)	P=0.51

among patients without renal osteodystrophy (Table 2).

Drugs used by each of the participants in the study based on history and evidences in their files were determined. Data analysis did not show any statistically significant difference between the two groups regarding use of specific drugs (Table 3).

Discussion

Renal osteodystrophy is a set of metabolic bone disorders in patients with chronic kidney disease. In this disease, serum levels of calcium, phosphorus, PTH and vitamin D are altered and consequently bone turnover will be impaired. This study investigated the causes of renal osteodystrophy in 60 hemodialysis patients in Imam Khomeini Hospital in Zabol in 2013. The most common causes of kidney disease were: hypertension (22%), diabetes (20%), urinary tract infection (18%), polycystic kidney disease (8%), glomerulonephritis (7%) and idiopathic (25%). The mean duration of dialysis patients was 2.71 years.

The study showed that of 60 patients with ESRD studied 48 patients (80%) were diagnosed with renal osteodystrophy. About half of the patients had osteofibrosis, 7% and 26% of subjects suffered from adynamic bone disease and osteomalacia, respectively.

Several studies have reported the prevalence of renal osteodystrophy in different hospitals in Iran. Barzin [10], reported 56% of patients with ESRD are suffered from osteodystrophy in a hospital in Sari city. Bagheri [11] and Rahbar [20] reported 59% and 97% of mentioned cases in two different hospitals in Tehran city [10,11,20]. On the other hand there is similar studies have been conducted to determine osteodystrophy in other countries. Buargub and colleagues reported that 55.3% of their patients suffer from renal osteodystrophy in Libya [21]. Santoso [22] reported the prevalence of renal Osteodystrophy was about 79% in Indonesia [22]. Other studies were done in Thailand, Jordan, Czech Republic and Jordan showed the prevalence of osteodystrophy as 92.9%, 68.9%, 57% and 24.4%, respectively [7,23-25]. Nidal reported that secondary hyperparathyroidism is a common cause of bone disease in patients with CKD [7]. Buargub [8], showed the main causes of osteodystrophy were renal bone disease, hyper parathyroid bone disease and adynamic bone disease in Libya [21]. Bagheri [11] in a similar study on dialysis dependent patients in Iran has demonstrated the most common cause of osteodystrophy were adynamic bone disease, mixed uremic osteodystrophy and CKD related hyperparathyroidism [11].

Statistical data analysis showed that there was no significant statistical association between gender, marital status, educational level, occupation, and monthly income, number of dialysis per week and medications and developing renal osteodystrophy. Other studies have also reported that there is no link between these factors and the disease [26, 27]. The mean duration of dialysis in patients with and without renal osteodystrophy was 2.71 years and 2.58 years, respectively. There was no significant relationship between duration of dialysis and prevalence of renal osteodystrophy. However, Berzin and colleagues reported higher prevalence of renal osteodystrophy in patients who were under hemodialysis for a longer period of time. They divided patients into three groups based on duration of dialysis: less than a year (n = 11), 1 to 4 years (23 cases) and more than 4 years (n = 7). Prevalence of osteodystrophy in these groups was 45%, 52%, and 86%. This might be due to the limited number of patients in each group and is not reliable [10].

In this study, there was no statistically significant association between renal osteodystrophy and underlying disease causing ESRD but Nidal study in Jordan showed that patients with high blood pressure ($p < 0.04$) had statistically significant more severe bone disease. Radiological findings were used to determine the severity of bone disease [7]. Since the occupational exposure with different materials as well as exposure to sunlight in the workplace is different, we evaluated patients in terms of jobs in different categories. It was apparent that prevalence of renal osteodystrophy is not much different among these groups. Other studies have not examined this issue in these patients.

Serum calcium, phosphorus, albumin, creatinine, alkaline phosphatase, parathyroid hormone, blood sugar, vitamin D, hemoglobin, ferritin and ESR were measured in each patient [28-31]. In this study it was found that only parathyroid hormone serum level had statistically significant relationship with prevalence of osteodystrophy.

As well as genetic factors, nutrition, environmental conditions and age can also affect the incidence of the disease in different populations. The method used to diagnose renal osteodystrophy is also a significant factor in the prevalence of the disease. Currently, the best way to determine renal osteodystrophy with high accuracy and low false positive is bone biopsy. In this study, the serum levels of hormones (parathyroid hormone and vitamin D) were used for the diagnosis of renal osteodystrophy and it was one of the limitations of this study.

Conclusions

Although the research achieved its aims but there were some unavoidable limitations. Firstly because the target group limitation, the study was conducted only on a small sample size of patients which included all diagnosed patients with ESRD. Secondly using kidney biopsy, more specific data we could have reached to, but because of this method further complications and risks, we preferred to conduct our study rely on laboratory data.

In conclusion, although we failed to observe any relationship between the investigated factors and developing renal osteodystrophy, further longitudinal and multicenter studies with greater participants may reveal the main related factors of this disorder. It is also suggested to investigate other potential factors such as lifestyle, diet and environmental factors during the future studies.

Acknowledgements

We would like to thank the patients who participated in the study. The authors acknowledge Imam Khomeini hospital personals for their cooperation.

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