Prevalence of Renal Osteodystrophy and its Related Factors among Patients with End-Stage Renal Disease Undergoing Hemodialysis: Single Center Experience from Kermanshah, Iran

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ABSTRACT

Objectives: The current study aimed to determine the prevalence of Renal Osteodystrophy (ROD) and its related factors in a group consisting of End-Stage Renal Disease (ESRD) patients undergoing maintenance hemodialysis. ***Methods:*** One hundred twenty –eight ESRD patients (52 men & 76 women) with a mean age of 59.3 years old undergoing maintenance hemodialysis at Imam Reza Referral Hospital, were included in this cross-sectional study. Thereafter, serum parathyroid hormone (PTH) levels were measured, and the range of 150 to 300 pg/mL was determined as the desirable range for the values. Values lower or higher than this range were used to determine ROD. Furthermore, this study investigated the association of ROD with clinical and laboratory variables (age at the onset of renal failure, hemodialysis sessions per week, clinical symptoms associated with renal osteodystrophy, and serum calcium and phosphate levels). ***Results:*** ROD was diagnosed in 93 patients (72.7%) out of 128 patients studied. Of them, 53 (41.4%) patients had PTH levels above 300 pg/mL (high bone turnover, HTO group) and 40 patients (31.3%) had PTH levels below 150 pg/mL (low bone turnover, LTO group). No statistically significant difference was detected in terms of ROD-related clinical findings (P=0.11), age at the time of ESRD diagnosis (P=0.2), and number of hemodialysis sessions per week (P=0.2). Hyperphosphatemia (52 patients, 57.1%) was more prevalent in ROD group compared with 11 patients (31.4%) included in the group without ROD (P=0.004). ***Conclusion:*** The prevalence rate of ROD in this study was found to be significant, and it was largely consistent with the rate reported in the research previously performed in some Asian countries. Hyperphosphatemia were laboratory variables closely related to ROD.

Keywords: End-Stage Renal Disease; Renal Osteodystrophy; Parathyroid Hormone (PTH); Hemodialysis.

Introduction

Renal osteodystrophy (ROD) refers to bone disorders resulted from or associated with chronic kidney disease (CKD) and its associated metabolic disorders. ROD initiates when the renal function starts to deteriorate.[1] The association between bone disorders and renal failure was firstly reported in the mid-19th century. Until 1950s, it was believed that CKD is complicated by concomitant hyperparathyroidism.[2] CKD-Mineral and Bone Disorder (CKD-MBD) is a broader clinical syndrome developing as a systemic abnormality of mineral and bone metabolism due to CKD. Accordingly, it is characterized by disturbance in bone and mineral metabolism and/or extra-skeletal calcification. It is alleged that the term ROD can be used solely to describe bone disorders associated with kidney disease.[3] Thus, ROD can be considered as a part of the CKD-MBD.[3,4] By considering the operation as the direct consequence of electrolyte abnormalities and endocrine disorders represented by high serum phosphate levels and low or normal serum calcium levels, ROD can lead to the elevated secretion of PTH by the parathyroid glands and of fibroblast growth factor 23 (FGF-23) by osteoblast and osteocytes, in order to normalize serum calcium and phosphate levels.[1,5] it was found that ROD is associated with bone pain, and the increased incidence of fractures and bone deformities, myopathy, muscle pain, and tendon rupture.[3,4] The prevalence rate of ROD in developing countries ranges from 33.3% in Egypt to 81% in Brazil.[6] This disorder can be divided into two categories in terms of bone metabolic status. High bone turnover (HTO) group is characterized by the increased serum PTH level, and low bone turnover (LTO) group is characterized by normal or the decreased serum PTH levels. HTO is osteitis fibrosa cystica whose clinical manifestations are pain and fragility of bones. On the other hand, LTO can be grouped into two categories, named adynamic bone disease and osteomalacia.[7] There is an evidence that despite the decreased HTO type of ROD, LTO type of ROD (especially adynamic bone disease) follows an increasing trend. Correspondingly, this change in epidemiology of ROD is hypothesized to be related to the newly-introduced treatments as well as higher rate of access to hemodialysis worldwide.[1] LTO is associated with the reduced bone volume and mineralization, which can be engendered by the suppression of PTH

production, chronic inflammation or both of them. PTH suppression can be caused by taking vitamin D supplements or excessive exposure to calcium in the form of calcium phosphate binders as well as high calcium hemodialysis solutions. Notably, Adynamic bone disease complications are as follows: the increased incidence of bone fracture, bone pain, and having an association with the increased cardiovascular calcification.[2,7] Although in a guideline entitled Kidney Disease Outcome Quality Initiative (KDOQI) published by the National Kidney Foundation, normal range of serum PTH level has been regarded from 150 to 300 pg/mL.[8] There is still an unfortunate absence of multiple randomized controlled trials (RCTs) with the ability of determining an optimal PTH level for patients with CKD.[4] Even though bone biopsy is considered as the gold-standard method for the diagnosis of ROD, it is an invasive procedure, so it cannot be routinely used to determine the prevalence of ROD. Serum PTH levels are regarded as an acceptable alternative to bone biopsy in diagnosing ROD and categorizing its subtypes, namely LTO and HTO.[9] However, the novel recommendation in this regard is that the treatment should not be solely based on the elevated level of PTH[4]. Since its development, ROD has played an effective role in the quality of life among CKD patients. The current research aimed to determine the prevalence of ROD among hemodialysis patients. Such a prevalence is highly dependent on health care level and the adequacy of dialysis in a medical community.

Several studied have been previously performed to determine the prevalence of ROD in different parts of the world. Accordingly, the prevalence of ROD has been studied using various methods such as bone biopsy, radiography, and measurement of chemical biomarkers. One of the most important reasons underpinning such a discrepancy in the prevalence of ROD is a wide variety of ROD diagnosis methodologies. The following part of this research mainly intended to determine the prevalence of ROD in a sample comprised of ESRD-afflicted patients, to investigate the relevant factors.

METHODS

In the present cross-sectional research, the study population were all patients with ESRD who underwent maintenance hemodialysis at Imam Reza Referral Hospital of Kermanshah, Iran in 2018. Those participants who the researchers could get access to their medical records, were included in this study. This referral hospital provides tertiary-level medical services. The hospital also operates as the main hemodialysis center in Kermanshah province and fulfills the medical

needs of at least 2 million people. The exclusion criteria included bone diseases prior to the development of ESRD, incomplete medical record information, irregular referrals of the patients for hemodialysis, and the patient's affliction with a dialysis duration of less than 3 months. Considering the study design and previous studies indicating a prevalence of 72% for ROD among the hemodialysis patients residing in Sanandaj province, Iran [10], and confidence level of 95% and accuracy of 8%, according to the formula $n = \frac{\left(z_{1-\frac{\alpha}{2}}\right)^2 (p)(1-p)}{(d)^2}$ the required sample size (taking into account 10% dropout) was determined to be 133 patients. Finally, 128 patients from the study population who met inclusion criteria based on their medical records were selected using the available method and then entered the study and their information were analyzed.

To obtain the required information, a data collection form was designed by the researchers, and the data were then documented. This form included demographic information (age, gender, and weight at the last visit), clinical variables (underlying causes of ESRD including hypertension, diabetes mellitus, recurrent urinary tract infections, obstructive uropathy, congenital anomalies, and vesicoureteral reflux), duration of CKD, duration of hemodialysis, weekly hemodialysis sessions, age at the time of the onset of renal failure, age at the time of the onset of hemodialysis, calcium supplements, erythropoietin usage, and phosphate binder. As well, clinical symptoms related to ROD, including bone pain and sensory disturbances (paresthesia), were recorded.

Furthermore, serum biochemical variables documented in the medical records were gathered. These variables included levels of calcium after the correction based on serum albumin levels (normal range: 8.4 to 10.2 mg/dL), phosphate (normal range: 3.5 to 5.5 mg/dL), PTH, and alkaline phosphatase. Thereafter, in order to record the serum PTH level, the last recorded value in the medical records was extracted. The patients' serum PTH was measured every three months at the hemodialysis center of the study hospital. Given the date obtained from the last assessment of the serum PTH level, other biochemical variables measured concomitantly were extracted. Appropriate hormone levels for CKD patients were considered to be between 150 and 300 pg/mL. Serum PTH levels higher than 300 pg/mL were considered as HTO type of ROD, and values lower than 150 pg/mL were considered as LTO type of ROD.

This research was conducted in terms of the Declaration of Helsinki. The Ethics Committee of Kermanshah University of Medical Sciences approved the present research. Moreover, the

institutional ethical committee at Kermanshah University of Medical Sciences approved all the study's protocols (IR.KUMS. REC.1394.403). Accordingly, written informed consent was obtained from all the participants before the study and data collection was then started. The present article was derived from M.D thesis of Medical University of Kermanshah, Iran (Thesis#96035).

Frequency and percentage indices were used to report categorical variables. For continuous variables, mean and standard deviation (SD) were used. To determine the association between the ROD and the laboratory and clinical variables, the Chi-squared test was used. All the statistical analyses were performed by SPSS software (ver. 20.0). The statistical significance level was set at 0.05.

RESULTS

A total of one hundred twenty-eight ESRD patients (52 men and 76 women) with a mean (±SD) age of 59.31 (±14.27) years old (range: 23-87 years old) and a mean (±SD) weight of 66.34 (±10.79) kg were included in the current study. The mean (±SD) age of ESRD diagnosis was 48.73 (±16.76) years old. Table 1 presents ESRD causes and ROD clinical findings in 128 ESRD patients included in this study who were receiving maintenance hemodialysis. As observed, hypertension was the most common etiology for ESRD among these patients. In addition, bone pain was the most common symptom reported in about one-third of the patients.

Table 1: Clinical and laboratory characteristics of 128 end-stage renal disease (ESRD) patients.

Characteristics	Category	Frequency	Percentage
ESRD causes	Hypertension	67	52.3
	Diabetes mellitus	16	12.5
	DM + HTN	17	13.3
	Congenital urinary tract abnormalities[a]	9	7.0
	Autoimmune disorders	6	4.7
	Acute renal injury	8	6.3
	Obstructive uropathy	5	3.9
ROD symptoms/signs	Bone pain	41	32
	Paresthesia	9	7
	Numbness	3	2.3
	Combination of clinical findings	58	45.3
	None	17	13.4

[a] *These abnormalities included vesicoureteral reflux, polycystic kidney disease, and renal dysplasia; ESRD :end-stage renal disease.*

Table 2 summarizes the laboratory findings of the studied population. As seen, hypocalcemia was more common than hypercalcemia, and hyperphosphatemia was more common than hypophosphatemia. Furthermore, all the patients whose alkaline phosphate level was measured, regardless of their PTH level, had high alkaline phosphate levels.

Table 2: Laboratory findings in 128 end-stage renal disease (ESRD) patients.

Characteristics	Category	Frequency	Percentage
Corrected calcium levels,	Hypocalcemia (< 8.4 mg/dL)	48	37.5
	Normocalcemia (8.4 to 10.2 mg/dL)	72	56.3
	Hypercalcemia (> 10.2 mg/dL)	8	6.3
Phosphate	Hypophosphatemia (< 3.5 mg/dl)	9	7
	Normal (3.5 to 5.5 mg/dL)	54	42.2
	Hyperphosphatemia (> 5.5 mg/dL)	63	49.2
	Missing	2	1.6
Alkaline phosphatase	> 92	122	95.3
	Missing	6	4.7
Albumin	<3.5	10	7.8
	3.5-5.5	114	89.1
	>5.5	3	2.3
	Missing	1	0.8
ROD	No	35	27.3
	LTO	40	31.3
	HTO	53	41.4

ESRD: end-stage renal disease; ROD: renal osteodystrophy. HTO :High bone turnover; LTO: low bone turnover.

Mean (±SD) hemodialysis duration was 6.25 (±7.53) years (ranged from 0.25 to 7.5 years). Mean (±SD) weekly hemodialysis session was 2.9 (±0.33) sessions (ranged from 1 to 3 sessions per week). Mean (±SD) age at the hemodialysis onset was 53.63 (±15.41) years old (ranged from 12 to 84 years). Of 128 patients included in this study, ROD was diagnosed in 93 patients (72.7%). In this category, 53 patients (41.4%) had serum PTH levels higher than 300 pg/mL (HTO type of ROD) and 40 patients (31.3%) had serum PTH levels lower than 150 pg/mL (LTO type of ROD). Notably, serum PTH levels were desirable (i.e., 150 to 300 pg/mL) in 35 patients (27.3%).

Table 3 presents a comparison of variables between the two patient groups, namely with and without ROD. As shown, no statistically significant difference was observed in terms of ROD-related clinical findings (P=0.11), age at the time of ESRD diagnosis (P=0.2), number of hemodialysis sessions per week (P=0.2), and the patients' ages (P=0.161). However, a statistically significant difference was found regarding serum phosphate levels between the two groups. It was observed that Hyperphosphatemia (52 patients, 57.1%) was more prevalent in the ROD group compared with 11 patients (31.4%) in the group without ROD (P= 0.004). Accordingly, this means that the prevalence of hyperphosphatemia among the patients with ROD was more than one and a half times higher than in the patients without ROD.

Although no significant relationship was observed between serum calcium levels and ROD, almost half of the patients with ROD had (47 patients, 50.5 %) normal calcium levels (P= 0.093).

Table 3: Comparison of the studied variables between two groups of 128 end-stage renal disease (ESRD) patients with and without ROD.

Variables	Category	ESRD with ROD n(%)	ESRD without ROD n(%)	Total N	X^2	*p*-value
Age at ESRD diagnosis, year	< 20	10 (10.8)	1 (2.9)	11	4.65	0.20
	21-40	18 (19.4)	5(14.3)	23		
	41-60	47 (50.5)	17 (48.6)	64		
	61-80	18 (19.4)	12 (34.3)	30		
Hemodialysis sessions, per week	≤ 2	7 (7.5)	5 (14.3)	12	1.37	0.20
	3 ≤	86 (92.5)	30 (85.7)	116		
ROD symptoms / signs	No	13 (14.0)	4 (11.4)	17	11.62	0.11
	Yes[a]	80 (86.0)	31 (88.6)	111		
Corrected calcium levels, mg/dL	< 8.4	40 (43.0)	8 (22.9)	48	4.75	0.093
	8.4 to 10.2	47 (50.5)	25 (71.4)	72		
	> 10.2	6 (6.5)	2 (5.7)	8		
Serum phosphate, mg/dL	< 3.5	3 (3.3)	6 (17.1)	9	10.96	0.004
	3.5 to 5.5	36 (39.6)	18 (51.4)	54		
	> 5.5	52 (57.1)	11 (31.4)	63		
Age, year	20-40	14(15.1)	4(11.4)	18	3.647	0.161
	41-60	38(40.9)	9(25.7)	47		
	> 60	41(44.1)	22(62.9)	63		

ESRD: end-stage renal disease; ROD: renal osteodystrophy.[a] Symptoms of ROD comprised bone pain, paresthesia, and numbness alone or in combination; Percentages are presented vertically

Table 4 presents a comparisons of the variables between the two groups of the ROD patients (HTO vs. LTO groups). Hypocalcemia was more common (29 patients, 54.7%) in the HTO group compared to the LTO group (11 patients, 27.5%); P= 0.002.

Table 4: Comparison of the studied variables between two groups of 93 end-stage renal disease (ESRD) patients with high bone turnover (HTO) and low bone turnover (LTO) renal osteodystrophy (ROD).

Variables	Category	HTO ROD n(%)	LTO ROD n(%)	Total N	X^2	p-value
Age at ESRD diagnosis, year	< 20	6 (11.3)	4 (10.0)	10	1.89	0.59
	21-40	8 (15.1)	10 (25.0)	18		
	41-60	27 (50.9)	20 (50.0)	47		
	61-80	12 (22.6)	6 (15.0)	18		
Hemodialysis sessions, per week	≤ 2	2 (3.8)	5 (12.5)	7	2.5	0.12
	3	51 (96.2)	35 (87.5)	86		
Corrected calcium levels, mg/dL	< 8.4	29 (54.7)	11 (27.5)	40	12.55	0.002
	8.4 to 10.2	24 (45.3)	23 (57.5)	47		
	> 10.2	0 (0.0)	6 (15.0)	6		
Serum phosphate, mg/dL	< 3.5	1 (1.9)	2 (5.1)	3	2.30	0.32
	3.5 to 5.5	18 (34.6)	18 (46.2)	36		
	> 5.5	33 (63.5)	19 (48.7)	52		
Age, year	20-40	8(15.1)	6(15.0)	14	0.026	0.987
	41-60	22(41.5)	16(40.0)	38		
	> 60	23(43.4)	18(45.0)	41		

ESRD: end-stage renal disease; ROD= renal osteodystrophy; Percentages are presented vertically.

Additionally, the results of the association between the patients' dialysis sessions number and their calcium and phosphate levels showed that there was a statistically significant relationship between the number of dialysis sessions and the patients' blood calcium levels. More than half of the patients with dialysis sessions performed for three or more times per week, have normal blood calcium (Table 5).

Table 5: Comparison of the number of dialysis sessions of patients with their calcium and phosphate levels.

Variables	Category	Hemodialysis sessions, per week ≤ 2 n(%)	Hemodialysis sessions, per week ≥3 n(%)	Total N	X^2	p-value
Corrected calcium levels, mg/dL	< 8.4	3(25.0)	45(38.8)	48	16.59	<0.0001
	8.4 to 10.2	5(41.7)	67(57.8)	72		
	> 10.2	4(33.3)	4(3.4)	8		
Serum phosphate, mg/dL	< 3.5	1(8.3)	8(7.0)	9	0.031	0.985
	3.5 to 5.5	5(41.7)	49(43.0)	54		
	> 5.5	6(50.0)	57(50.0)	63		

Percentages are presented vertically

Table 6 shows the results of the investigation of the association among the level of PTH, the serum calcium and phosphate levels, and the patients' involvement with ROD. Accordingly, a statistically significant relationship was found between phosphate and calcium levels and PTH levels. This means that the patients' blood phosphate and ROD increase with PTH levels increasing, but this relationship has been reported reversely for calcium levels.

Table 6: Comparison of the level of PTH of patients with their calcium and phosphate levels.

Variables	Category	Serum PTH 150mg/dl n(%)	Serum PTH 150-300mg/dl n(%)	Serum PTH >300mg/dl n(%)	Total N	X^2	p-value
Corrected calcium levels, mg/dL	< 8.4	10(25.0)	8(22.9)	30(56.6)	48	20.14	<0.0001
	8.4 to 10.2	24(60.0)	25(71.4)	23(43.4)	72		
	> 10.2	6(15.0)	2(5.7)	0(0.0)	8		
Serum phosphate, mg/dL	< 3.5	2(5.1)	6(17.1)	1(1.9)	9	14.26	0.007
	3.5 to 5.5	19(48.7)	18(51.4)	17(32.7)	54		
	> 5.5	18(46.2)	11(31.4)	34(65.4)	63		
ROD	ESRD with ROD	40(100)	0(0.0)	53(100)	93	128.00	<0.0001
	ESRD without ROD	0(0.0)	35(100)	0(0.0)	35		

PTH: parathyroid hormone; ROD= renal osteodystrophy; Percentages are presented vertically.

DISCUSSION

ROD as a constellation of metabolic bone abnormalities in chronic kidney disease is accompanied with the alternation in serum levels of PTH, calcium, phosphorus, and vitamin D, which consequently lead to bone turnover impairment.[11,12] Since the low prevalence of ROD is an aftermath of the standard medical care level and adequacy of dialysis, and given that its high prevalence negatively affects the patient's quality of life, the current research intended to

determine the prevalence of ROD among the patients undergoing hemodialysis in Imam Reza Referral Hospital of Kermanshah, Iran. Moreover, this study aimed to compare the obtained rate with those of other similar studies. According to the results of the current research, hypertension was found as the most common cause of ESRD. Although the prevalence rate of ROD was 72.7% (HTO 41.4%), the impact of the factors, including etiology of renal failure, demographic factors, quality of treatment and hemodialysis frequency, and laboratory factors and nutrition led to significant discrepancies in prevalence, type, and nature of ROD in various studies.[7,11] In a systematic review presented in 2015, the approximate prevalence rate of secondary hyperparathyroidism (SHPT) (PTH>300) was reported to be about 30-50%, in such a way that the prevalence of SHPT in CKD patients across Europe and Australia ranged from 30 to 49%. In addition, the prevalence rate among the American patients (Canada, US) was estimated to be 54%. In Asia, the SHPT prevalence rate was 28% in India and 11.5% in Japan.[11]

In another study conducted in Pakistan in 2016, 89% of the studied patients had ROD, and the most common type was SHPT in 32% of the patients followed by the mixed type of ROD in 27% of the patients as well as a dynamic bone disease in 23%. More importantly, the results of the above-mentioned research was almost in consistent with our findings.[12]

In studying ROD among the patients afflicted with CKD, it is of importance to measure the 25-OH vitamin D level, which was not available in our study.[12,13] Due to the same absence, it was impossible to distinguish adynamic bone disease from osteomalacia in the LTO group of ROD. Herein, serum PTH measurement was performed for ROD diagnosis. However, there was a debate in the literature regarding the accuracy of this measurement in the diagnosis of ROD.[4] Herbert et al. in 2009 referred to the inability of PTH measurements to reliably diagnose bone turnover, and then suggested to perform more measurements of some other markers reflecting the effects of bone turnover, rather than measuring PTH as a single effector. As well, they represented that the common clinical practice of measuring alkaline phosphatase does not increase the predictive value of the classification rule for diagnosing bone turnover abnormalities in CKD patients.[14] For instance, in a previous study performed in Libya, 103 patients on hemodialysis were included, and intact PTH (iPTH) was used to categorize the enrolled patients.[13] As a result, ROD was diagnosed in about half of the patients (55.3%). In this research, adynamic bone disease (diagnosed by iPTH levels less than 60 pg/mL) was reported in 28 cases and hyperparathyroid bone disease was found in 29 cases. Since the diagnosis of ROD in the

above-mentioned study was done based on the iPTH levels, so the accuracy of PTH was obtained as higher than that of iPTH levels.[15] Therefore, the lower prevalence of ROD in this study can be partially justified.

Same as the above-mentioned research, in another prospective research performed in India[16] on 462 patients with CKD‐mineral and bone disorder (CKD‐MBD), SHPT was found among 82.7% of the patients using iPTH.

In a multicenter study in 2002 [17], 683 patients with a mean age of 61 years old and a mean duration of dialysis of 72 months were selected from 29 dialysis centers in southern Italy. Overall, 25.4% of the patients had hyperparathyroidism (iPTH > 400 pg/mL) and only 19.5% of them had iPTH levels within the normal range (i.e., 100-250 pg/mL). In addition, it was reported that both oversupression of the parathyroid gland and hyperparathyroidism were common among the patients, albeit the first one was more common.

In this study, hypocalcemia (37.5%) was found to be more common than hypercalcemia (6.3%), and hyperphosphatemia (49.2%) was more common than hypophosphatemia (7%). This finding is consistent with the nature of chronic kidney disease and also with the result of an Indonesian study that reported hypocalcemia in 61% of patients.[18] The development of ROD begins too early during the course of CKD. The three important pathogenic mechanisms include the reduced calciferol production (GFR <below 90 ml/minimum/1.73 m2), hyperphosphatemia (GFR < 35-30 ml/minimum/1.73 m2), and hypocalcemia occurring relatively early during the course of CKD.[9,19] In recent years, due to the extensive consumption of calcium-containing agents in patients, the pathogenic role of hypocalcemia in the development of ROD has remained in the background.[19]

A study investigating the relationship between the studied variables with ROD in the current article indicated an important relationship between phosphate levels and ROD. Although we found no relationship between calcium levels and ROD, about half of the patients with ROD were reported to have normal serum calcium. Accordingly, this may indicate a weaker link between calcium levels' disorders and renal ROD, in contrast with that was previously reported. However, our results may have been influenced by medications or hemodialysis. Contrary to what was explored regarding calcium, the statistical relationship between ROD prevalence and blood phosphate level was found to be strongly important, and the prevalence of

hyperphosphatemia among the patients with ROD was more than one and a half times that of those patients without ROD. It can be concluded that hypocalcemia was more common (29 patients, 54.7%) in the HTO group compared to the LTO group (11 patients, 27.5%). Buargub et al. in their study performed in 2006 reported higher serum calcium level in LTO patients.[13]

Since the association between PTH and ROD has been established in previous studies, the results show that there is a strong statistically significant relationship between PTH levels and calcium and phosphate levels. Similar to the findings of our study, a significant relationship was also found between blood phosphorus levels and iPTH in a research performed by Vikrant et al.[16]

Additionally, the results of our study underline that there is no significant relationship among age; the number of hemodialysis sessions per week; and the prevalence of ROD, LTO, and HTO.

Despite the inability to find a relationship between phosphate levels and the number of dialysis sessions per week, the current research explored the normal calcium levels in 57.8% of the patient with more frequent hemodialysis sessions per week (>=3time per week). While this finding is reasonable, a more important point is that almost 38.8% of the patients with more frequent hemodialysis sessions per week were afflicted with hypocalcemia. However, to improve this situation, we need to comply with effective nursing considerations within the dialysis process, in order to optimize hemodialysis machines using high-efficiency dialyzer, proper phosphate binder, and nutritional advice, for better controlling phosphate.

Contrary to our study, Daugirdas et al. in their study in 2012 found that blood phosphorus levels were significantly lower in patients undergoing six hemodialysis sessions per week than in those undergoing three sessions per week.[20]

Pain is a multidimensional sensation with psychological and physical components, which is associated with significant activity limitations in work and psychological problems. In this regard, ROD is a painful syndrome with multifactorial etiology, one of the most common complications in which is musculoskeletal pain.[9,21]

Bone pain was reported the most common complaint of the patients in this study (%32). This finding is consistent with those of some other studies. In a research performed on 95 hemodialysis patients in Turkey (2013), 51.6% of cases experienced moderate to severe level of bone pain. Chronic bone pain was found to be significantly associated with PTH levels.[21] In

another study conducted on 100 hemodialysis patients with at least three months of dialysis initiation in Turkey, 51% of patients complained of chronic bone pain. Likewise, this study found a relationship between chronic bone pain and PTH levels.[22] The discrepancy between these results and those of our study may be due to the differences in bone pain assessment methods used.

In our study, to perform the pain assessment, the patients were asked whether they felt any pain or not, and no standard pain classification scale was used regarding the pain duration and severity. This can be regarded as another limitation of the present research.

Although bone fractures, especially hip fractures, had been reported more commonly among hemodialysis patients with ROD [5], the incidence of fractures was not assessed in the current study as it has a cross-sectional design. As well, our study has some limitations. Firstly, and most importantly, we did not perform a bone biopsy to demonstrate the type of renal osteodystrophy histologically in our patients. Secondly, we did not measure serum vitamin25-OH vitamin D to rule out pure osteomalacia from the patients with ROD (LTO). In addition, the pain detection method, as it was mentioned earlier, can be considered as another limitation that should be referred to in this part as well.

CONCLUSION

The prevalence of ROD estimated in the present study among the patients undergoing maintenance hemodialysis was somewhat close to those of the similar studies with similar reference serum PTH levels, patients' mean age, and hemodialysis mean duration, especially in other regions of Iran. Accordingly, the results clearly showed that the prevalence of ROD was high at our Referral Hospital. Correspondingly, this high rate highlights the fact that patients need to be more closely monitored by physicians and to make them informed of the side effects of osteodystrophy as well as its impact on their quality of life. As it is necessary to differentiate two types of ROD, particularly LTO, it is advised to measure vitamin D levels regularly along with other laboratory variables that are extensively applicable for patient's monitoring.

Disclosure

The authors declared no competing interests.

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