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Original Article

Evaluation of cardiovascular, bone mineral, and hematological disorders in chronic hemodialysis patients

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ABSTRACT

Aims: The prevalence of cardiovascular diseases, bone mineral disorders, and anemia in patients undergoing continuous hemodialysis is higher than in the normal population. In addition, due to the ongoing renal parenchymal loss in these patients, there is continuous deterioration in bone mineral metabolism. Anemia, a leading hematological disorder, is considered to be one of the most important and frequent complications leading to compromised quality of life. In this study, we aimed to investigate cardiovascular, bone mineral, and hematological disorders in patients undergoing continuous hemodialysis.

Methods: Clinical data of 56 patients receiving continuous hemodialysis at Yüzüncü Yıl University Faculty of Medicine Hospital Nephrology Clinic Dialysis Unit between 01.07.2021 and 01.07.2022 were evaluated retrospectively. Echocardiography), dual-energy X-Ray absorptiometry and laboratory parameters were evaluated for each patient. Demographic characteristics and medications were recorded. Due to the retrospective nature of the study, the sample size was not calculated.

Results: The study included 56 patients undergoing hemodialysis, comprising 26 (46.4%) men and 30 (53.6%) women. Mean duration of hemodialysis was 5.55±5.09 years. Moreover, 92.9% of the patients were receiving medications, with the most common medications including erythropoiesis-stimulating agents (69.6%), phosphorus binders (48.2%), iron supplements (28.6%), active vitamin D supplements (37.5%), and cinacalcet (12.5%). Cardiovascular diseases were detected in 60.7% of the patients, osteoporosis in 41.1%, and anemia in 78.6%.

Conclusion: Cardiovascular disease, bone mineral disorders, and hematological disorders are commonly seen in hemodialysis patients. Hemodialysis patients should be regularly evaluated for complications.

Keywords: Hemodialysis, cardiovascular diseases, osteoporosis, anemia, erythropoiesis-stimulating agent

INTRODUCTION

Chronic kidney disease (CKD) is a common disease with high morbidity and mortality, typically resulting from irreversible damage to kidney function. The overall prevalence of CKD is 10-15%.[1] Renal replacement therapy is recommended for patients with end-stage kidney damage. Hemodialysis is the most common form of renal replacement therapy. End-stage kidney disease is closely associated with cardiovascular diseases (CVD), alterations in bone mineral metabolism, and anemia.[2]

In this study, we aimed to investigate the prevalence of CVD, bone mineral disorders, hematological disorders, and ongoing therapies as well as gender-based differences in patients receiving continuous hemodialysis treatment.

METHODS

Study Design

The study was initiated after obtaining an ethical approval from Van Yüzüncü Yıl Non-interventional Clinical Researches Ethics Committee (Date: 12.05.2023, Decision No: 2023/05-10). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Clinical data of 56 patients (30 female and 26 male) that received hemodialysis between July 2021 and December 2022 were retrieved from local databases. Echocardiography (Echo), Dual-energy X-Ray absorptiometry (DEXA), and laboratory parameters were evaluated for each patient. Demographic characteristics and medications were recorded.

Statistical Analysis

Data were analyzed using SPSS for Windows version 26.0 (Armonk, IBM Corp.). Descriptives were expressed as mean, median, standard deviation (SD), minimum, maximum, frequencies (n), and percentages (%). Normal distribution of variables was assessed using Kolmogorov-Smirnov test. Continuous variables with normal distribution were compared between two independent groups using independent samples T test and Mann-Whitney U Test. Categorical variables were compared using Pearson's Chi-squared test and Fisher's exact test. A p-value of <0.05 was considered significant.

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RESULTS

The 56 patients comprised 30 (53.6%) women and 26 (46.4%) men. Mean laboratory values were as follows: urea 134.64±32.42 mg/dl, creatinine 8.59±2.51 mg/dl, hemoglobin 10.82±1.96 g/dl, hematocrit 33.87±5.95%, calcium 8.12±0.68 mg/dl, parathyroid hormone 403.44±282.15 PG/ml, phosphorus 4.79±1.58 mg/dl, and ferritin 966.11±1161.49 ml/NG (Table 1).

Table 1. Laboratory parameters

	Mean	SD	Median	Min-max
Urea (mg/dl)	134.64	32.42	133.3	58.2-224.8
Creatinine (mg/dl)	8.59	2.51	8.7	3.9-17.2
Hemoglobin (g/dl)	10.82	1.96	10.9	5.6-15.1
Hematocrit (%)	33.87	5.95	34.3	19.2-46.4
Calcium (mg/dl)	8.12	0.68	8.1	5.9-10.1
Phosphor (mg/dl)	4.79	1.58	4.9	1.5-11.4
Parathormone (PG/ml)	403.44	282.15	360	21.6-1146.3
Ferritin (ml/NG)	966.11	1161.49	567.6	22-6235.3

SD: Standard deviation, Min: Minimum, Max: Maximum

Table 2 presents the duration of hemodialysis and medications used for each patient. Mean duration of hemodialysis was 5.55±5.09 (range, 0.2-22) years. Moreover, 92.9% of the patients were receiving medications, with the most common medications including erythropoiesis-stimulating agents (ESA) (69.6%), phosphorus binders (48.2%), iron supplements (28.6%), active vitamin D supplements (37.5%), and cinacalcet (12.5%).

Table 3 presents the laboratory parameters of the patients. Mean hemoglobin level was significantly higher in men than in women (11.42±1.83 vs. 10.27±1.95 g/dl; p<0.05). Similarly, mean hematocrit level was higher in men than in women (35.65±5.53% vs. 32.33±5.96%; p<0.05). Nevertheless, no significant difference was found between the two genders with regard to other parameters (p>0.05).

Table 2. Hemodialysis duration and medication use

		Mean	SD	Median	min-max
Hemodialysis duration (years)		5.55	5.09	4	0.2-22
		n			%
Medication use	Yes	52			92.9
	No	4			7.1
ESA		39			69.6
Iron		16			28.6
Phosphorus binders		27			48.2
Active vitamin D		21			37.5
Calcimimetic		7			12.5
Total		56			100

SD: Standard deviation, Min: Minimum, Max: Maximum, ESA: Erythropoiesis-stimulating agents

Of all patients, 78.6% (n=44) had anemia, 60.7% (n=34) had CVD, and 41.1% (n=23) had osteoporosis. Mean duration of hemodialysis was 6 years in men as opposed to 4 years in women. Among male patients, 22 had anemia, 21 had osteoporosis, and 15 had CVD, while 22 female patients had anemia, 19 had CVD, and 12 had osteoporosis. As for medications, 18 of the men were using ESA, 12 were using phosphorus binders, 8 were using iron supplements, and 12 were using active vitamin D supplements, whereas 21 of the women were using ESA, 15 were using phosphorus binders, 8 were using iron, and 9 were using vitamin D (Table 4). No significant difference was found between the duration of hemodialysis and CVD, osteoporosis, anemia, and medication use (p>0.05).

Table 5 presents the medication rates for CVD, osteoporosis, and anemia. No significant difference was found between patients with and without CVD and between patients with and without osteoporosis with regard to medication use (p>0.05 for both). Of the patients with anemia, 81.8% were using ESA, 45.5% were using vitamin D, and 4.5% were using cinacalcet. Moreover, there was a significant difference

Table 3. Laboratory parameters according to genders

	Gender	Mean	SD	Median	min-max	t[a]/Z[b]	p
Urea (mg/dl)	Male	132.9	32.01	128.2	75.9-224.8	-0.370a	0.713
	Female	136.14	33.24	138.6	58.2-200		
Creatinine (mg/dl)	Male	9.15	3	9.2	4.2-17.2	1.564a	0.124
	Female	8.11	1.92	8.2	3.9-12.1		
Hemoglobin (g/dl)	Male	11.42	1.83	11.4	5.6-15.1	-2.361b	0.018*
	Female	10.27	1.95	10.4	6.2-13.5		
Hematocrit (%)	Male	35.65	5.53	36.3	19.2-45.4	2.149a	0.036*
	Female	32.33	5.96	32.6	20.9-46.4		
Calcium (mg/dl)	Male	8.22	0.55	8.3	7.3-9.5	1.032a	0.307
	Female	8.03	0.77	8.1	5.9-10.1		
Phosphor (mg/dl)	Male	4.73	1.4	5	1.5-7.1	-0.223a	0.824
	Female	4.83	1.75	4.7	1.6-11.4		
Parathormone (PG/ml)	Male	441.03	294.85	371	21.6-1146.3	-1.082b	0.279
	Female	372.12	272.12	278.8	32.2-985.2		
Ferritin (ml/NG)	Male	1012.53	1354.76	452.7	27.5-6235.3	-0.526b	0.599
	Female	925.88	986.26	603.2	22-4758.6		

SD: Standard deviation, Min: Minimum, Max: Maximum

Tablo 4. Prevalence of cardiovascular diseases, osteoporosis, and anemia and medication use

		Gender					
		Male		Female			
		Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	Z	p
Hemodialysis duration (years)		6.30±5.98	4 (0.3-22)	4.87±4.13	3 (0.2-12)	-0.777	0.437
		n	%	n	%	X^2	p
CVD	Yes	15	57.7	19	63.3	0.186a	0.666
	No	11	42.3	11	36.7		
Osteoporosis	Yes	11	42.3	12	40	0.031a	0.861
	No	15	57.7	18	60		
Anemia	Yes	22	84.6	22	73.3	1.053a	0.305
	No	4	15.4	8	26.7		
Medication	Yes	25	96.2	27	90	0.138b	0.651
	No	1	3.8	3	10		
Medications							
ESA		18	69.2	21	70	0.004a	0.950
Phosphorus binders		12	46.2	15	50	0.083a	0.774
Iron		8	30.8	8	26.7	0.115a	0.735
Vitamin D		12	46.2	9	30	1.221a	0.213
Cinacalcet		4	15.4	3	10	0.041b	0.693

a: Pearson's Chi-square test, b: Fisher's exact test, Note: p-values in bold indicate statistically significant difference (p<0.05). SD: Standard deviation, CVD: Cardiovascular diseases, ESA: Erythropoiesis-stimulating agents

Table 5. Statistical comparison of medications by the prevalence of cardiovascular diseases. osteoporosis. and anemia

	Cardiovascular diseases					
	Yes (n=34)		No (n=22)			
Medications	**n**	**%**	**n**	**%**	**X2**	**p**
ESA	25	73.5	14	63.6	0.618a	0.432
Phosphorus binders	17	50	10	45.5	0.111a	0.740
Iron	9	26.5	7	31.8	0.187a	0.765
Vitamin D	10	29.4	11	50	2.416a	0.161
Cinacalcet	4	11.8	3	13.6	0.042b	0.837
	Osteoporosis					
	Yes (n=23)		No (n=33)			
ESA	14	60.9	25	75.8	1.421a	0.233
Phosphorus binders	11	47.8	16	48.5	0.002a	0.961
Iron	5	21.7	11	33.3	0.893a	0.345
Vitamin D	9	39.1	12	36.4	0.044a	0.833
Cinacalcet	5	21.7	2	6.1	3.024b	0.110
	Anemia					
	Yes (n=44)		No (n=12)			
ESA	36	81.8	3	25	11.835b	0.000*
Phosphorus binders	22	50	5	41.7	0.262a	0.609
Iron	15	34.1	1	8.3	1.933b	0.147
Vitamin D	20	45.5	1	8.3	4.073b	0.021*
Cinacalcet	2	4.5	5	41.7	8.727b	0.003*

a: Pearson's Chi-square test. b: Fisher's exact test. Note: p-values in bold indicate statistically significant difference (p<0.05). ESA: Erythropoiesis-stimulating agents

between patients with and without anemia (p<0.05). The rates of ESA and vitamin D supplement use were higher in patients with anemia, while the rate of cinacalcet use was higher in patients without anemia. Nevertheless, there was no significant difference between these two groups with regard to the use of iron supplements and phosphorus binders (p>0.05).

DISCUSSION

The 56 patients comprised 30 women and 26 men. Among all patients, 78.6% of them had anemia, 60.7% of them had CVD, and 41.1% had osteoporosis. It is known that the prevalence of CVD, bone mineral disorders, and anemia is higher in patients receiving hemodialysis than in the normal

population. Additionally, it is also known that the prevalence of CVD in the hemodialysis population increases in parallel with the increasing frequency of general risk factors for atherosclerosis, particularly including hypertension and diabetes.

It has been shown that a decrease in the estimated glomerular filtration rate (eGFR) is associated with an increased risk of CVD and mortality. Additionally, creatinine levels, which are markers of kidney function, may serve as an indicator of CVD-related mortality, and individuals diagnosed with heart failure have been reported to have more than twice the risk of developing CKD.[3]

The Turkish Public Health Journal, in its 2015 publication, evaluated the studies conducted between 1997 and 2007 and reported that the prevalence of CVD in the normal population aged ≥30 years varied between 4.4-10.9%, with 5.1-17.4% in men and 3.7-8.3% in women.[4] In our study, as consistent with the literature, the prevalence of CVD in men and women receiving hemodialysis was approximately 5-6 times higher than the prevalence in the normal population.

Osteoporosis is a skeletal disorder characterized by deterioration of bone strength, leading to an increased risk of fractures. CKD is an independent risk factor for osteoporosis.[5] The 2017 KDIGO (kidney disease: improving outcomes) guidelines recommend screening with DEXA in patients with CKD, which is a risk factor for osteoporosis (KDIGO, 2017). Osteoporosis is defined as a femoral neck T score of ≤-2.5 standard deviation (SD). In the Third National Health and Nutrition Examination Survey (NHANES III), osteoporosis was twice as common in participants with a glomerular filtration rate (GFR) of <60 ml/min compared to those with a GFR of >60 ml/min. Of note, the prevalence of osteoporosis in patients with stage 3-5 CKD in the Kashmir Valley was reported as 31.8%.[6] According to a study conducted by Festuccia et al.[7] in 2017, the prevalence of osteoporosis in patients with CKD was determined to be approximately 53%. A study conducted at Akdeniz University Faculty of Medicine in 2021 evaluated 74 patients that were receiving hemodialysis and peritoneal dialysis. The authors detected osteoporosis in 13 (35.1%) out of 37 patients receiving peritoneal dialysis and in 19 out of 37 patients (51.4%) receiving hemodialysis.[8] In our study, in line with the literature, osteoporosis was detected in 41.1% of the patients.

Anemia is a leading and frequent complication leading to compromised quality of life in CKD patients.

According to the World Health Organization (WHO), anemia is defined as a hemoglobin level below 12 g/dl in women and below 13 g/dl in men. The most common form of anemia in chronic kidney disease (CKD) is anemia caused by insufficient erythrocyte production due to erythropoietin deficiency. The prevalence of anemia increases with the progression of CKD stages (8.4% in stage 1, 53.4% in stage 5).[9]

A study conducted by Altun et al.[10] evaluated 244 hemodialysis patients and reported the mean hemoglobin as 10.9 g/dl.

When using the WHO's anemia definitions, anemia is detected in 87% of patients with a GFR below 25 ml/min who have not yet started dialysis.[11]

In the CREDIT (chronic renal disease in Turkiye) study conducted in Turkiye, the prevalence of anemia was determined as 12.8% in CKD stage 3, 33.3% in stage 4, and 66.7% in stage 5.[12] In our study, the prevalence of anemia in patients undergoing hemodialysis was 78.6% and the mean hemoglobin value of all patients was found to be 10.82±1.96 g/dl. Moreover, a significant difference was found between the two genders with regard to hemoglobin level ($p<0.05$). These findings were found to be consistent with those reported in the literature.

According to the Social Security Institution Communiqué on Healthcare Practices implemented in Turkiye, an ESA treatment can only be initiated in patients with hemoglobin <10 g/dl, transferrin saturation ≥20%, and/or ferritin ≥100 µg/L and the target hemoglobin value in treatment should be 11-12 g/dl.[13] The 2014 Summary Report published by the Turkish Society of Nephrology Registry demonstrated that 24.04% of hemodialysis patients had previously used ESA but were not currently using it, while 5.36% had never used ESA before and the remaining 70.6% of the patients were currently using ESA.[14] In our study, 69.6% of the patients had a history of ESA use and a significant difference was found between the patients with and without anemia in terms of ESA use ($p<0.05$).

Our study was limited since it was a single-center study and had a relatively small number of patients. Further randomized controlled studies with large numbers of hemodialysis patients are needed to substantiate our findings. We also believe that our findings will shed light on future studies.

Limitations

The most significant limitation of this study is the failure of some patients to attend their scheduled appointments or adhere to regular hemodialysis treatment, which resulted in missing blood test data.

CONCLUSION

Our study clearly showed that the frequency of CVD, osteoporosis, and anemia is higher in hemodialysis patients. Accordingly, hemodialysis patients should be evaluated through a multidisciplinary approach. In these patients, cardiovascular examinations should be performed and bone mineral density should be evaluated at certain intervals, and monthly hemodialysis visits should be made.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Van Yüzüncü Yıl Non-interventional Clinical Researches Ethics Committee (Date: 12.05.2023, Decision No: 2023/05-10).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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