ORIGINAL ARTICLE

Title

Correlation between Dialysis Vintage and Vitamin D and Bone Mass Density on Patients with Chronic Kidney Disease Undergoing Hemodialysis In Zainoel Abidin Hospital

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*Received 23 September 2019, revised 26 March 2020, accepted 1 April 2020, published 20 April 2020***Abstract**

Background: Bone mineral disorders in chronic kidney disease (CKD-MBD) is one of the complications that occurs due to systemic disorders of minerals and bones in chronic kidney disease (CKD). This syndrome is one or a combination of laboratory abnormalities (phosphate, parathyroid hormone, and vitamin D), bone disorders (turnover, mineralization, volume, linear growth, and strength), and/or vascular calcification or other soft tissue. It is associated with high mortality and morbidity in CKD patients. To determine the relationship of vitamin D levels and bone mineral density (BMD) examination with the hemodialysis vintage in CKD patients undergoing hemodialysis at RSUD Dr. Zainoel Abidin.

Methods: This study is a cross-sectional study held in Zainoel Abidin Hospital, Banda Aceh, Indonesia, from January until May 2017. We include all patients who received twice-weekly hemodialysis for at least 3 months. Patients who received corticosteroids in the past 2 weeks, pregnant, suffering from endocrine disorders or malignancy, autoimmune diseases, and thalassemia, and menopausal women, were excluded. Laboratory examination and Bone Densitometry were performed before a single hemodialysis session. Data were analyzed using the Spearman Rank Correlation test.

Results: Thirty patients were analyzed from 196 hemodialysis patients. The proportion of patients that have vitamin D insufficiency was 56.6%. The proportion of patients that have with normal vitamin D was 43.3%. The proportion of patients that have osteoporosis was 30% and 56.6% were osteopenia based on bone densitometry examination. The magnitude of the Spearman Rank Correlation coefficient between vitamin D levels and the duration of hemodialysis in CKD patients is -0.552 with a p-value

0.002. The magnitude of the Spearman Rank Correlation coefficient between BMD and hemodialysis time in CKD patients is -0,397 with a p-value of less than 0.030.

Conclusion: There was a correlation between dialysis vintage with vitamin D levels and bone densitometry.

Keywords: vitamin D, bone mineral density, hemodialysis

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BACKGROUND

Chronic kidney disease (CKD) is associated with high mortality and morbidity because it can cause a variety of serious complications. Mineral Bone Disorder (CKD MBD) is a clinical syndrome that occurs due to systemic disorders in mineral and bone metabolism in CKD. This syndrome includes one or a combination of the following: laboratory abnormalities that occur due to impaired metabolism of calcium, phosphate, parathyroid hormone (PTH), and vitamin D, and bone disorders in terms of turnover, mineralization, volume, linear growth, and strength, vascular calcifications or other soft tissues. One example is renal osteodystrophy.¹

Research by Tjekyan et al in Palembang showed that 72.5% of 142 CKD patients have hyperphosphatemia.² Research by Yauri et al in Manado found that serum calcium levels decreased (< 8.3 mg / dL) in 51.21%

male subjects and 38.23% female CKD subjects. And serum phosphate levels increase (> 4.5 mg / dL) in 34 men out of a total of 41 subjects, whereas in women 27 out of a total of 34 subjects. The prevalence of patients with hypocalcemia ($\text{Ca} < 8.4$ mg / dl), hyperphosphatemia ($\text{P} > 4.6$ mg / dl), hyperparathyroidism (intact $\text{PTH} > 65$ pg / ml) will increase as the glomerular filtration rate decreases.

The purpose of this study was to determine the correlation of vitamin D levels and Bone Mineral Density (BMD) examination with the duration of hemodialysis in CKD patients undergoing hemodialysis at dr. ZainoelAbidin General Hospital.

METHODS

This study is a cross-sectional study from January until May 2017 in the hemodialysis unit at dr. Zainoel Abidin Hospital, Banda Aceh. The study was carried out according to the principles of the Declaration of Helsinki and was approved by the local ethics committee. Written informed consent was obtained from all participating patients.

We include all patients who received twice-weekly hemodialysis for at least 3 months. Patients who received corticosteroids in the past 2 weeks, pregnant, suffering from endocrine disorders, malignancy, autoimmune diseases and thalassemia, and menopausal women were excluded. The estimated size of the study sample using a sample size formula was 30 hemodialysis patients.

Measurement of vitamin D levels was carried out by the clinical laboratory improvement amendments (CLIA) method, by taking the patient's blood 5 ml before dialysis. Bone mineral density (BMD) examination was conducted at Prince Nayef Bin Abdul Azis Hospital - Syiah Kuala University (Darussalam). Spearman Rank Correlation was used to determine the correlation between vitamin D and BMD levels with hemodialysis vintage.

RESULTS

Thirty patients were analyzed from 196 hemodialysis patients. The proportion of patients that have vitamin D insufficiency was 56.6%. The proportion of patients that have with normal vitamin D was 43.3%. Most of the patients were male (60 %). Overall, most patients were aged between 41 and 50 years. Most of the patients were married. Most patients have normal BMI (36.7%), with details of 5 people (16.7%) have vitamin D insufficiency levels and 6 people (20.0%) with vitamin D levels normal according to Table 1.

The proportion of patients that have osteoporosis was 30% and 56.6% were osteopenia based on bone densitometry examination. The others were normal bone densitometry (13.3%). Of the 18 male subjects, 33.3% of them have osteopenia, while of the 12 female patients, 23.3% have osteopenia. Most of the patients were aged between 41-50 years (36.7%), with details of 6 BMD osteopenia, and 5 BMD osteoporosis. Majority of patients have BMI normoweight (Table 2).

Vitamin D levels are normally distributed, while the hemodialysis vintage data are not normally distributed (Table 3). So the correlation used is the Spearman rank correlation. The magnitude of the Spearman Rank Correlation coefficient between vitamin D levels and the duration of hemodialysis in CKD patients is -0.552 with a p-value 0.002. This shows that the relationship between vitamin D levels with hemodialysis duration is strong and significant. The magnitude of the Spearman Rank Correlation coefficient between BMD and hemodialysis time in CKD patients is -0,397 with a p-value of less than 0.030. This shows that the relationship between BMD and hemodialysis duration is strong and significant.

DISCUSSION

Chronic kidney disease (CKD) is associated with high mortality and morbidity because it can cause a variety of serious complications. Mineral Bone Disorder (CKD MBD), which is a clinical syndrome that occurs due to systemic disorders in mineral and bone metabolism in CKD. This syndrome includes one or a combination of the following: laboratory abnormalities that occur due to impaired metabolism of calcium, phosphate, parathyroid hormone (PTH), and vitamin D, bone disorders in terms of turnover, mineralization, volume, linear growth, and strength, vascular calcifications or other soft tissues. One example is renal osteodystrophy.¹

Chronic kidney disease is characterized by low levels of 25 (OH) vitamin D (calcidiol), low levels of 1.25 (OH) 2vitamin D (calcitriol), and calcitriol resistance.⁴ Valkovskystudy show that high prevalence of 25 (OH) vitamin D deficiency (96%) and a decrease in bone densitometry in patients undergoing hemodialysis.⁵

Risk factors for osteoporosis are age (≥ 65 years for women and ≥ 70 years for men), history of glucocorticoid therapy for more than 3 months, smoking, alcohol consumption, rheumatoid arthritis, and other autoimmune diseases, endocrine diseases (hyperthyroidism, hypothyroidism, Cushing's syndrome), CKD, and malignancy.⁶

Table 1. CharacteristicsOf Subjects

	Vitamin D					
	Insufficient		Normal		Total	
	N	%	N	%	N	%
Gender						
Male	8	26.7	10	33.3	18	60.0
Female	9	30.0	3	10.0	12	40.0
Age						
≤ 30 years	6	20.0	2	6.7	8	26.7
31 - 40 years	3	10.0	3	10.0	6	20.0
41 - 50 years	6	20.0	5	16.7	11	36.7
51 - 60 years	2	6.7	3	10.0	5	16.7
Marital status						
Single/Widower	5	16.7	2	6.7	7	23.3
Married	12	40.0	11	36.7	23	76.7
Body Mass Index						
Underweight	5	16.7	1	3.3	6	20.0
Normoweight	5	16.7	6	20.0	11	36.7
Overweight	4	13.3	4	13.3	8	26.7
Obese grade I	2	6.7	2	6.7	4	13.3
Obese grade II	1	3.3	0	0.0	1	3.3

Table 2. Subject's baseline characteristics according to bone densitometry

Table 2. Subject's baseline characteristics according to bone densitometry

Subject Characteristics	BMD							
	Osteoporosis		Osteopenia		Normal		Total	
	N	%	N	%	N	%	N	%
Gender								
Male	6	20.0	10	33.3	2	6.7	18	60.0
Female	3	10.0	7	23.3	2	6.7	12	40.0
Age								
≤ 30 years	2	6.7	6	20.0	0	0.0	8	26.7
31 - 40 years	0	0.0	4	13.3	2	6.7	6	20.0
41 - 50 years	5	16.7	6	20.0	0	0.0	11	36.7
51 - 60 years	2	6.7	1	3.3	2	6.7	5	16.7
Marital Status								
Single/Widower	2	6.7	5	16.7	0	0.0	7	23.3
Married	7	23.3	12	40.0	4	13.3	23	76.7
Body Mass Index								
Underweight	4	13.3	2	6.7	0	0.0	6	20.0
Normoweight	1	3.3	10	33.3	0	0.0	11	36.7
Overweight	3	10.0	2	6.7	3	10.0	8	26.7
Obese grade I	1	3.3	2	6.7	1	3.3	4	13.3
Obese grade II	0	0.0	1	3.3	0	0.0	1	3.3

Table 3. Test for normality of Vitamin D levels and duration of hemodialysis.

Variable	Shapiro-Wilk	p-value
Kadar vitamin D	0,950	0,174
Lama hemodialysis	0,801	< 0,001

Tabel 4. Spearman rank correlation test results.

Variable	N	Correlation Coefficient	p-value
Kadar vitamin D - Lama Hemodialysis	30	- 0,552	0,002
BMD - Lama Hemodialysis	30	- 0,397	0,030

The prevalence of osteoporosis in hemodialysis patients varies and depends on various factors, including the dialysis method, area examined for the bone scan, and gender.⁷ According to the study by Ebeling et al (2000), weight gain can increase osteoporosis risk. A study Hiiang et al(2009) showed weight loss and serum albumin are associated with low bone mass in patients undergoing hemodialysis. In women, estrogen deficiency before menopause is associated with a decrease in BMD. In men, testosterone deficiency is associated with decreased BMD. In CKD, estrogen has an important role in the development of bone mass in women who experience uremic.⁶

The KDIGO 2009 guideline did not recommend for patients with stage 3a to 5D CKD to undergo routine BMD examination, because BMD could not predict fracture risk as occurs in the general population, and BMD cannot determine the type of renal osteodystrophy. But KDIGO 2017 recommends patients with stage 3a to 5D CKD with the occurrence of GMT-CKD and/or risk factors for osteoporosis to have BMD to assess the risk of fracture if the results will influence the therapeutic decision. The updated reason is that there are many new prospective studies that low BMD results predict the incidence of fractures in patients with stage 3a to 5D CKD, and may influence the decision to do a bone biopsy.⁸

In patients with stage 3 to 5D CKD, KDIGO recommends that vitamin D levels be checked, and repeated for comparison of initial values and therapeutic interventions. KDIGO states that vitamin D deficiency and insufficiency can be corrected using recommended therapeutic strategies in the general population

Saafan FH's research and colleagues observed that 27% of hemodialysis patients had normal bone mineral density (BMD), 53% osteopenia, and 20% osteoporosis. There was also a significant negative correlation between BMD and the age of patients undergoing hemodialysis, body weight, body mass index, duration of hemodialysis, serum phosphorus, and serum iPTH.

There is a positive correlation between BMD and gender, height, and serum calcium.

Increased bone resorption and bone formation in patients with long periods of hemodialysis predispose patients to osteoporosis. Other risk factors that can predispose to increase the incidence of osteoporosis, such as acidosis. Adequate dialysis sessions will remove excessive phosphate and restore calcium balance, preventing bone resorption. Vitamin D increases calcium absorption and maintains the homeostasis of calcium

CONCLUSION

The study concludes that the levels of vitamin D and BMD have a statistically significant negative correlation with the duration of hemodialysis in CKD patients undergoing hemodialysis in RSUD dr. Zainoel Abidin Banda Aceh.

REFERENCES

1. Eknayan G, Lameire N, Eckardt K, Kasiske B, Wheeler D, et al. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Supp.* 2013 Jan;3(1);13-4.
2. Tjekyan RMS. Hubungan kepatuhan dan pola konsumsi obat pengikat fosfat terhadap kadar fosfat pada penyakit ginjal kronik stadium V. *MKS* 2015;47(2):97-104.
3. Yauri LF, Moeis ES, Pandelaki K. Gambaran hasil produk kalsium dan fosfor pada pasien penyakit ginjal kronik stadium V di ruang hemodial-

- isis RSUP Prof.DR.R.D.Kandou Manado. J eCI 2016;4(2):1-6.
4. Nigwekar SU, Tamez H, Thadhani RI. Vitamin D and chronic kidney disease-mineral bone disease (CKD-MBD). BoneKey Reports 3 2014;498:1-6.
 5. Valkovsky I, Olsanska R, Tvrdek J, et al. Evaluation of biochemical markers and bone mineral density in patients with chronic kidney disease stage 5D at the start of hemodialysis treatment. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2015;159(1):93-9.
 6. Saafan FH, Rashed AM, Awad AA, et al. Relation between hyperparathyroidism and osteoporosis in chronic renal failure patients with regular hemodialysis. J Am Sci. 2014;10(12):256-61.
 7. Omidvar B, Ghorbani A, Tamadon MR, et al. Relationship of bone density with serum parathyroid hormone in hemodialysis patients; a single-center study. J Parathyroid Dis. 2018;6(2):57-63.
 8. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int. 2017;7:1-59.