

## Original Research Article

# Hemodialysis duration and underweight as a risk factors of renal osteodystrophy (chronic kidney disease - mineral bone disorder) on regular hemodialysis patient

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### ABSTRACT

**Background:** Chronic kidney disease (CKD) is related to systemic disorders affecting multiple organs, including the bone, known as osteoporosis or renal osteodystrophy. Long duration of hemodialysis and underweight based on the Body Mass Index (BMI) is thought to be risk factors for renal osteodystrophy. This study aims to determine the risk factors in the form of hemodialysis duration and underweight in the incidence of renal osteodystrophy in patients with CKD stage 5.

**Methods:** This research is an analytic observational study with case and control group involving 26 patients. In each group, anamnesis, anthropometric examination and bone mass density (BMD) examination with DEXA were performed. Analysis using Chi-squared test, and an odds ratio (OR) calculation were performed to determine the effect of hemodialysis duration and underweight as risk factors for renal osteodystrophy in CKD patients

**Results:** There is a significant difference in the duration of hemodialysis ( $p=0.047$ , 95% CI=0.97-29.39) and underweight ( $p=0.011$ , 95% CI=1.39-141.49) between the CKD patient group. In addition, it was also found that the duration of HD (OR=5.33) and underweight (OR=14) were significant risk factors for renal osteodystrophy in CKD patients.

**Conclusions:** There is significant differences in the duration of hemodialysis and underweight between CKD patients with renal osteodystrophy and without renal osteodystrophy. Hemodialysis duration and underweight are also a significant risk factors for renal osteodystrophy in patients with CKD.

**Keywords:** Hemodialysis, Underweight, Renal osteodystrophy, Chronic kidney disease, Mineral bone disorder

### INTRODUCTION

Chronic Kidney Disease (CKD) is related to systemic disorders affecting multiple organs, one of which is bone, known as osteoporosis or renal osteodystrophy. Renal osteodystrophy is a silent health problem characterized by decreased bone density, decreased bone strength and a higher risk of fractures in the hip and spine. Deaths from osteoporosis-related diseases have profound effects on patients, their families and the social health system.<sup>1,2</sup>

Renal osteodystrophy patients who routinely underwent hemodialysis have low bone turnover, with prevalence of 58% on bone biopsy. This is likely due to increasing age, increasing diabetes mellitus sufferers, use of vitamin D analogues and calcium containing phosphate binders and differences in dialysis techniques.<sup>3</sup> Bone density examination can be done using a Dual Energy X-Ray Absorptiometry (DEXA) tool which measures Bone Mineral Density (BMD) in the spine and pelvis. This can be used as a guide in clinical evaluation of patients with

osteoporosis and a reference for determining treatment options to prevent further bone loss and prevention of fractures.<sup>4</sup>

There are many factors that suspected have an influence on the outcome of the bone density results of CKD patients, which is reflected in the results of BMD examinations who experience renal osteodystrophy.<sup>5</sup> Factors that are thought to be risk factors for renal osteodystrophy are long hemodialysis duration and underweight on the results of the Body Mass Index (BMI <18.5 Kg/m<sup>2</sup>).<sup>6,7</sup>

This study aims to determine the risk factors in the form of hemodialysis duration and underweight in the incidence of renal osteodystrophy in patients with CKD stage 5.

**METHODS**

This research is an analytic observational study with case and control group involving 26 patients with CKD, consist of 13 CKD patients with renal osteodystrophy as case group and 13 CKD patients without renal osteodystrophy as control group. This research was conducted at Hemodialysis Unit of Sanglah General Hospital Denpasar in January 2021. Renal osteodystrophy diagnosis is assessed with DEXA examination. The duration of hemodialysis information is gathered through anamnesis and anthropometric examination is done to measure the BMI.

The sample size in this study was determined by consecutive sampling in accordance with the inclusion and exclusion criteria to meet the number according to the requirements of the analysis. The sample size was calculated using case controls analytic comparative categorical unpaired for one measurement formulas. The inclusion criteria are CKD Stage 5 patients aged 30-75 years, underwent routine hemodialysis twice a week, cooperative with the examination, and sign informed consent. The exclusion criteria are had a history of fractures due to renal osteodystrophy, taking routine or long-term corticosteroid medication, and patients that have systemic diseases, hormonal diseases, malignancies, or congenital bone disorders.

Analysis using Chi-squared test, and an odds ratio (OR) calculation were performed to determine the effect of hemodialysis duration and underweight as risk factors for renal osteodystrophy in CKD patients. Statistical Package for Social Sciences (SPSS) for Windows version 26 program is used for data processing.

**RESULTS**

From the demographic data gathered, mean age of the patients with osteoporosis is 43 ± 11,23 years-old, while the non-osteoporosis group is 46,31 ± 10,74 years-old. There are 61,5% male on the osteoporosis group, and 92,3% on non- osteoporosis group. There are no significant difference of age, gender, and BMI between

two groups, with p-value of 0.45, 0.063, and 0.053 respectively (Table 1).

**Table 1: Research subject characteristic based on group.**

Variable	Group		P value
	Osteoporosis (n=13)	Without Osteoporosis (n=13)	
Age (years), mean±SD	43±11.23	46.31 ±10.74	0.45 <sup>a</sup>
Sex, number (%)			
Male	8 (61.5%)	12 (92.3%)	0.063 <sup>b</sup>
Female	5 (38.5%)	1 (7.7%)	
BMI (kg/m <sup>2</sup> ), mean±SD	19.68±2.95	22.54 ±4.13	0.053 <sup>a</sup>

IQR=interquartile range; BMI=body mass index; A=Independent Sample Student T-Test; B=Chi-Square Test

**Table 2: Result of chi-squared test for and hemodialysis duration and BMI in osteoporosis without osteoporosis group.**

Variable	Group		P value
	Osteoporosis (%) (n=13)	Without osteoporosis (%) (n=13)	
<b>Hemodialysis duration</b>			
≥2 years	10 (76.9)	5 (38.5)	0.047
<2 years	3 (23.1)	8 (61.5)	
<b>BMI</b>			
Underweight	7 (53.8)	1 (7.7)	0.011
Not underweight	6 (46.2)	12 (92.3)	

This study results shows that the duration of hemodialysis in the osteoporosis group was higher compared to the group without osteoporosis, with a statistically significant difference between the osteoporosis group and without osteoporosis (Table 2). Further analysis obtained an odds ratio (OR) of 5.33, so that patients who had undergone hemodialysis ≥ 2 years had 5.33 times the possibility of suffering from osteoporosis compared to populations who had a history of hemodialysis <2 years, with a range of 0.97 - 29.39 and p-value=0.045.

Body Mass Index in the osteoporosis group was lower compared to the group without osteoporosis group, with a statistically significant difference (Table 2). Further analysis obtained an odds ratio (OR) of 14, so that patients who were underweight (BMI <18.5) had a 14 times chance of suffering osteoporosis compared to not underweight populations, with a range of 1.39 - 141.49 and p value=0.025.

## DISCUSSION

Osteoporosis is a metabolic bone disease characterized by decreased bone mass density and architectural disturbances in normal bone. This condition reduced strength of the bones and increases the risk of pathological fractures.<sup>8</sup> In this study, it is found that patient with longer duration of hemodialysis have a higher risk to suffer osteoporosis. In general, there is a relationship between duration of hemodialysis and the incidence of osteoporosis in which the occurrence of osteoporosis in patients with chronic kidney disease is constituted by a complex mechanism. Decreased glomerular filtration rate initiates a cascade of metabolic disease, abnormal bone remodelling, leading to osteoporosis followed by decreased bone strength. Bone mineral disease in patients with chronic kidney disease is associated with secondary hyperparathyroidism.<sup>3,9</sup>

A study conducted by Brunerova et al examined the relationship between hemodialysis and osteoporosis. From 59 subjects who suffered from chronic kidney disease and underwent routine hemodialysis, there were 20 subjects (34%) with osteoporosis based on densitometric examination, laboratory test, and clinical assessment. In this study, it was also found that almost half of hemodialysis patients had severe micro-architectural bone defects as measured using a trabecular bone score.<sup>10</sup> A systematic review from the 8 studies presented that the average prevalence of osteopenia was of 45.91% and the average prevalence of osteoporosis was 23.29% in patients with chronic kidney disease. A higher prevalence rate is found in women and patients with a low body mass index, with the lumbar being the most susceptible to osteoporosis.<sup>11</sup> Berzin et al reported a higher prevalence of renal osteodystrophy in patients that had underwent hemodialysis for a longer duration. The patients divided into three groups based on the duration of hemodialysis, that is less than a year (11 cases), 1 to 4 years (23 cases) and more than 4 years (7 cases). The prevalence of osteodystrophy in this group was 45%, 52%, and 86%.

On the other hand, different results were obtained by Polymeris et al study that investigate the relationship between mineral density and metabolism in hemodialysis patients. This study resulted that the duration of hemodialysis did not significantly affect bone density.<sup>12</sup> Research by Balouche et al suggested that there was no significant relationship between the duration of hemodialysis in patients with the prevalence of renal osteodystrophy, where the mean duration of hemodialysis in patients with and without renal osteodystrophy was 2.71 years and 2.58 years.<sup>13</sup>

This study presents that underweight have a higher risk to suffer osteoporosis in patient with CKD on regular hemodialysis. In the CKD condition, there is a disruption in the removal of phosphorus in the body, this causes intoxication from accumulated phosphorus that decreases

appetite. in addition to reducing BMI, decreased appetite will also lead to reduced intake of other mineral substances such as calcium and magnesium, thus causing a decrease in BMD.<sup>14,15</sup> There is a correlation between body mass index and the incidence of renal osteodystrophy / osteoporosis which is associated with Malnutrition-Inflammation Syndrome (MIS). Apart from the presence of a mild but chronic inflammatory process, this syndrome is also associated with high level phosphorus, low BMI and low cholesterol level.<sup>16</sup>

A study conducted by Iseri et al that assess nutritional status of 426 CKD patients found that patients with well-maintained nutritional conditions had better BMD compared to malnourished patients. Randomized controlled trial of 210 patients in 12 hemodialysis units, found that patients with good nutrition achieving a better health-related quality of life (HRQOL) score compared to patients with malnutrition.<sup>16</sup>

This study has several limitations, including the small number of samples due to the difficulty of finding subjects with renal osteodystrophy who are willing to be examined for bone mineral density. In addition, there is a possibility of recording errors in the medical record related to the duration of hemodialysis which may lead to bias. In the future, we hoped that research can be carried out with a larger number of research subjects as well as better research methods and designs in order to get more conclusive results.

## CONCLUSION

In conclusion, there is significant differences in the duration of hemodialysis and underweight between CKD patients with renal osteodystrophy and without renal osteodystrophy. Hemodialysis duration and underweight are also become a significant risk factors for renal osteodystrophy in patients with CKD.

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