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SERUM CALCIUM LEVEL AND THE ASSOCIATED FACTORS ON REGULAR HEMODIALYSIS PATIENTS

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ABSTRACT

Chronic kidney disease-mineral bone disorder (CKD-MBD) is a chronic complication of regular hemodialysis (HD) patients. Previously, several study had found that serum calcium in regular hemodialysis patients can be low, normal or high level. However, there is a lack of data in our region. This study is a cross-sectional descriptive analytic study to obtain serum calcium level and the associated factors. Serum calcium were measured by calorimetric methods using Arsenazo III then it was classified into low, normal, and high serum calcium level according to Indonesian Society of Nephrology consensus. This study collected 100 patients who perfomed chronic hemodialysis at Sanjiwani Gianyar and Ari Canti hospital which consisted of male (67%) and female (33%). The mean age was 52.52 years with 44.6 months of mean dialysis vintage. Most of the subjects underwent hemodialysis twice a week (96 %) with total HD duration of 9 hours a week. Sixty six percent of the subjects used arterio-venous fistula for vascular access. This study showed that most chronic hemodialysis patients (60%) had low serum calcium level (<8.4 mg/dL). Linier regression test indicated that serum calcium is significantly influenced by serum phosphate, however, serum urea has less powerful effect to serum calcium concentration with r = -0.371 and r= -0.013 respectively with r^2= 0.313. This study obtained that most of the subjects had low serum calcium level and the serum calcium associated with serum phosphate and serum urea.

Keywords: CKD-MBD; Hemodialysis; Serum Calcium.

INTRODUCTION

Chronic Kidney Disease-Mineral Bone Disorder (CKD-MBD) is a chronic complication of patients who undergone regular hemodialysis (HD). There are calcium metabolism alteration that is initiated in early stages of CKD then worsen along with the progression of chronic kidney disease (CKD) (Hill Gallant & Spiegel, 2017; Hwang et al., 2015). The laboratory alterations in CKD-MBD is initiated by elevation of serum fibro-blast growth factor-23 (FGF23), serum phosphate, and para-thyroid hormone (PTH), followed by decrease in serum 1,25-dihydroxy-vitamin D and serum calcium concentra-tion (Bossola et al., 2015; Hill Gallant &

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Spiegel, 2017; Langman & Cannata-Andia, 2010). Patients with CKD-MBD also showed low absorption of calcium and decreased calcium excretion in urine, as well as exaggerated calcification of vascular, soft tissue, and heterogeneous bone disease. Mineral bone disorder is characterized by bone remodeling, this remodeling is associated with development of fractures and calcification of extra skeletal soft tissues and vascular (Hruska et al., 2017; KDIGO, 2009; Moorthi & Moe, 2011).

Chronic Kidney Disease stage 2 and 3 there is an increase in PTH and FGF-23, this leads to decreased levels of calcitriol which caused blood calcium and phosphorus levels appear to be normal to near-normal in early stage of CKD. In the end stage of CKD, the overwhelming compensatory mechanisms results in abnormalities that are involved in CKD-MBD (KDIGO, 2009; Li et al., 2021; Mahdavi et al., 2019; Moorthi & Moe, 2011).

Numerous cohort studies reported that mineral metabolism disorders are associated with cardiovascular disease, mortality, and fractures. The cardiovascular events, cardiovascular-related mortality, and the risk of fracture were caused by vascular calcification (Hill Gallant & Spiegel, 2017; Hwang et al., 2015; Langman & Cannata-Andia, 2010). Meanwhile, the underlying disease process that initiated the abnormalities were unclear and incompletely understood as well as lacking in definitive therapies.

Maintenance of calcium balance is important in treatment of CKD-MBD. Negative calcium balance may increase the risk of osteoporosis and fracture. Meanwhile positive calcium balance contributes to the increasing risk of extra skeletal calcification and cardiovascular events. Even if the positive or negative calcium balance separately is unproven as the initiating factor, the negative or positive calcium balance contributes to CKD-MBD progression in adults and it is necessary to monitor and control calcium balance in regular hemodialysis patients (Hill Gallant & Spiegel, 2017).

The purpose of this study is to examine serum calcium level and the associated factors in regular hemodialysis patients.

RESEARCH METHOD

This cross-sectional study collected 100 HD patients on the sample size measurement at Sanjiwani Gianyar and Ari Canti Hospital in Gianyar, Bali, Indonesia on July 2018. The selected subjects were regular hemodialysis patients aged 18 and older. This study excluded the subjects who were

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hospitalized at the time sample collection. All subjects have signed the informed consent.

The laboratory measurements were performed by trained laboratory staff. Subjects were required to fast for 12 hours prior to routine blood test i.e. serum creatinine, serum urea, profile lipid, fasting blood sugar, and complete blood count. Serum calcium level were measured by calorimetric method with Arsenazo III.

Data were analyzed using software and then presented in mean standard deviation (SD) (Raka Widiana, 2017). Kolmogorov-Smirnov was used to asses the data normality in this study. The relationship of serum calcium level and the associated factors were analyzed using regression linear test (Dahlan, 2014).

RESULTS

This study collected 100 regular HD patients that comprised of 67% male with the mean age 52.52 years as listed in table 1. Mean duration of hemodialysis had been for 44.60 months. The major etiologies of regular HD patients were Chronic Pyelonephritis (CPN) 30%, Diabetic Kidney Disease (DKD) 21%, Nephropathy Obstructive (18%) and Chronic Glomerulonephritis (CGN) 14%. Mean of serum calcium concentration and phosphate serum concentration were 8.43 ± 1.16 and 4.98± 1.62 respectively. All of the subjects were under the same hemodialysis treatment by nine hours a week according to PERNEFRI (an Indonesian Society of Nephrologist) recommendations. The baseline data were similar to the current data from the 10th report of Indonesian Renal Registry 2017 (PERNEFRI, 2018).

Table 1. Baseline Characteristics

Characteristics	Mean ± SD
Ages (years)	52.52 ± 12.81
Length of HD (month)	44.60 ± 32.23
QB (ml/min)	268.90 ± 22.60
Ultrafiltration (liter)	1.90 ± 0.89
Body Mass Index (kg/m2)	23.27 ± 4.62
Hemoglobin (g/dl)	10.79 ± 1.44
Blood Chemistry (mg/dL)	44.71 ± 13.80
BUN	
Serum Creatinine	10.04 ± 10.68
FBS	94.91 ± 31.64
Uric Acid	6.23 ± 1.92
Total Cholesterol	168.81 ± 43.91
Low Density Lipoprotein (LDL)	110.45 ± 39.86
Calcium serum	8.43 ± 1.16
Phosphate serum	4.98± 1.62

This study explored the serum calcium level of chronic hemodialysis patients by calorimetric method with Arsenazo III. Data of serum calcium were classified into three categories according to ISN classification (PERNEFRI, 2009). This study found that most of the subject showed low serum calcium level which is less than 8.4 mg/dL (60%). Normal calcium level

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(8.4-9.5 mg/dL) were found in 18% of subjects and high calcium level (>9.5%) were found in 22% of the subjects (table 2). This finding are useful for the medical treatment of chronic hemodialysis patients especially patients with low level of serum calcium. Calcium supplementation are given to these patients to control the calcium balance.

Table 2. Serum Calcium level Classifications

Serum Calcium level (mg/dL)	%
Low (<8.4)	60
Normal (8.4-9.5)	18
High (>9.5)	22

This study also determined of several factors that related to serum calcium concentration. We observed that serum calcium concentration had associated to serum phosphate concentration with r = -0.519; p = 0.000. This study also obtained that serum calcium concentration associated to BUN with r = 0.437; p= 0.015 with r^2 = 0,331 as listed in table 3. This finding explained that the serum calcium concentration was strongly associated with phosphate serum concentration meanwhile the serum calcium concentration lesser influenced by the BUN of chronic HD patients.

Table 3. Factors Related to Serum Calcium Concentrations.

Variables	Regression coefficient	*p*
Ages	-0.104	0.287
Duration of HD	-0.089	0.416
BMI	0.42	0.255
BUN	-0.437*	0.437*
SC	- 0.066	0.066
Uric Acid	-0.004	0.004
Phosphate	-0.371**	0.000**

DISCUSSION

Calcium balance is important in the body of health and disease. It is influence by the calsium absorption in the intestine and the excretion in the kidney, intestine and the sweat gland. The body of calcium store is in equilibrium over some extend time period, however in the chronic kidney disease there are a complex metabolic change in calcium metabolism that is change the calcium level in the body (Peacock, 2010). Hypocalcemia in CKD physiologically promotes by FGF 23 and deficient of 1,25-dihydroxyvitamin D3 (1,25(OH)-2D3) that is influence the absorption of intestinal calcium. The intestinal absorption of calcium is age related too. Therefore, a lower serum calcium level in this setting might indicate suboptimal supplementation of vitamin D, a pathophysiological role deficiency of vitamin D in CKD progression and indicate poor renal outcome (Janmaat et al., 2018; Lim et al., 2014). This subjects in this study have treated in accordance with the standard of hemodialysis by ISN with 9 hours a week of dialysis vintage. This study found that the mean age of chronic HD patients were 52.52 years, and most of HD patients were more than 45 years (77%). This characteristic of age were

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similar to current data from *Indonesian Renal Registry* report on 2017 that the most of subjects who had undergone chronic hemodialysis were in more than 45 years of age group (70.5%) (PERNEFRI, 2018). This finding explained that no difference in the absorption of calcium that is related to the age.

This study obtained that the mean serum calcium concentration was 8.43 ± 1.16 mg/dl. Most of the subjects had low serum calcium level (60%). This results was different with Bala dan Raquel study in Africa (2017) that obtained most of the serum calcium level were 63.8% in normal level (8.5-9.5 mg/dL). Indonesian Renal Registry report on 2017 also obtained most of serum calcium concentration were in normal level 8.4 -9.5mg/dl in 56% (PERNEFRI, 2018). However results of that study was similar to Hosseininejad et al (2018) data from Iran that found mean serum calcium concentrations in normal range (8.53±0.79). And this study was resembled to study in Japan by Inaguma, et al (2017) that obtained serum calcium concentration 58% <9.0 mg/dl, although the cut of point a little bit different with our study. It is necessary to evaluate because hypcalcemia associated to poor renal outcome and tend to progression of kidney disease (Janmaat et al., 2018; Lim et al., 2014; Ogata et al., 2021).

Several factors in this study had been tested by linier regression to serum calcium concentration. This study obtained that serum calcium concentration had significantly associated with phosphate concentration with r = - 0.519; p= 0.000, and BUN with = -0.13; p=0.015, and the r2 = 0.031that mean the serum calcium concentration 31 % was strongly influenced by phosphate concentration however the serum urea concentration less affected to the serum calcium level. The other factor did not significant influenced to serum calcium concentrations.

CONCLUSION

This study obtained that the most of serum calcium were in low level and the serum calcium concentration had significantly to serum phosphate concentration and weak negative correlations with BUN and serum creatinine concentrations.

We recommend to continue this study for detection of other biochemical abnormality, i.e. intact PTH and vitamin D concentrations, assessing of bone turnover, and detecting vascular calcification and as diagnosed of CKD-MBD according to KDIGO recommendations.

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