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Protein and Phosphate Intakes are Associated with Hyperphosphatemia in Hemodialysis Patients at Sanglah Hospital, Bali, Indonesia

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Abstract

Increased chronic kidney disease (CKD) mortality rate is significantly associated with increased blood phosphate levels. Hyperphosphatemia control is one of the main focuses in the management of hemodialysis (HD) patients. A high protein diet has been suggested to prevent malnutrition in hemodialysis patients. However, a high protein and phosphorus diet has the risk of increasing the phosphate level in the blood circulation, leading to a higher mortality rate of hemodialysis patients. This study aimed to prove that the level of protein and phosphate intake is associated with hyperphosphatemia in CKD patients with routine HD. This was cross-sectional analytical study conducted from September to October 2020 on 66 CKD patients who underwent hemodialysis. Subject characteristics and phosphorus and protein intake data were obtained from a questionnaire food recall adapted from the Food and Agriculture Organization of the United Nations. Data consumption patterns were processed using the nutritional survey software to obtain the nutritional values. Data were analyzed using the Chi-Square test to identify the relationship and risk between hyperphosphatemia and diet protein, phosphorus, and protein-phosphorus ratio. The confidence level in this study was 95%. There was a significant relationship between protein and phosphorus intake in hyperphosphatemia in CKD patients. The risk factors for hyperphosphatemia were high phosphorus intake (p=0.018; OR=3.886;95% CI: 1.212–12.460) and adequate protein intake (p=0.035; OR=3.674; 95% CI: 1.049-12.865). This study showed no significant relationship between phosphorus-protein ratio, protein-phosphorus ratio, and hyperphosphatemia incidence. In conclusion, high protein intake and excessive phosphorus intake provide a significant relationship to the incidence of hyperphosphatemia in CKD patients undergoing routine hemodialysis.

Keywords: Chronic kidney disease, hemodialysis, hyperphosphatemia, phosphorus intake, protein intake

Introduction

Chronic kidney disease (CKD) has been recognized as a worldwide health problem. Significant population growth, aging and changes in other epidemiological trends is the cause of the increased incidence of CKD.[1] The prevalence of CKD based on global estimates is 13.4% (11.7–15.1%), followed by the need for renal replacement therapy estimated between 4,902–7,083 million.[2] CKD needs to be handled holistically and optimally to prevent unwanted fatal events.[3–5] Hemodialysis (HD) is a treatment option as the management of the terminal phase. The hemostasis condition of CKD patients with HD is significantly different from CKD patients without HD.[6]

Mortality rates, physical health outcomes and symptoms appeared to be worse in CKD patients who did not perform HD.[7,8] In the CKD with HD, cardiovascular disease is one of the leading causes of death. Cardiovascular disease in CKD patients with HD is associated with decreased renal function that lead to systemic hyperphosphatemia; high levels of phosphorus in the blood. [6,9]

Control of hyperphosphatemia is one of the main components focused on managing CKD

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patients undergoing routine HD processes, which is also associated with the amount of protein intake. [6]

A high-protein diet is recommended by the *National Kidney Foundation; Kidney Disease Outcomes Quality Initiative* (NKF K/DOQI) for CKD patients with HD, but a high protein diet will negatively affect the phosphate control process. The cause of hyperphosphatemia is due to an increase in phosphorus as a result of a high protein diet. Previous studies have shown that high protein intake in CKD patients causes hyperphosphatemia due to decreased kidney conditions. The glomerular filtration rate (GFR) decreases so that the mineral metabolism is disrupted, then phosphate excretion is reduced.[6,9] In addition to protein, phosphorus intake from other sources also needs to be considered.

Another study states that choosing foods with a low protein-phosphorus ratio is one of important consideration, so that protein levels are still be achieved but phosphorus levels in the blood also be maintained.[10] The incidence of hyperphosphatemia in CKD patients with HD can also be influenced by other factors, such as age, gender, GFR values, or comorbidities.[11,12] This study aims to assess whether the level of protein and phosphate intake can be used as a determinant of hyperphosphatemia in PKG patients on routine hemodialysis.

Methods

This research was conducted for 1 month from September 2020 to October 2020 at the Hemodialysis Installation of the Sanglah General Hospital, Bali. This study is an analytic observational study, using cross-sectional analytical design study.

This research method was carried out by taking a random sample in patients who matched the inclusion criteria that have been diagnosed with CKD Stage 5 with Regular HD in the period August 2020 at Sanglah Hospital. The sample selection was carried out using the stratified proportional random sampling technique, sampling was carried out proportionally from each HD unit until the minimum number of samples was reached. The sample size was calculated using *an observational cross-sectional analytical*, the minimum sample required was 66 samples. The inclusion criteria used were willingness to participate in the study with informed consent. Patients aged 18–65 years were diagnosed with CKD Stage 5 who had routinely undergone at least 2 months of regular hemodialysis. Some of the exclusion criteria were; no inpatient treatment in the last 3 months from the start of the study, incomplete medical records, patients with sepsis, malignancy, chronic liver disease, HIV infection, pulmonary tuberculosis, dementia, history of parathyroidectomy or total thyroidectomy.

Variable depending on the research is the level of phosphorus in the blood. The independent variables of this study were phosphorus intake, protein intake, and protein- phosphorus ratio. The basic characteristics of the subjects included age, gender, long history of HD, nutritional status, etiology of CKD. A questionnaire food recall adapted from the Food and Agriculture Organization of the United Nations was used to obtain the protein-phosphorus ratio, protein and phosphorus intake data. Nutri survey software is used to analyze consumption pattern data. Data on protein consumption patterns will be converted in grams per kilogram of body weight per day, and phosphorus intake in milligrams per day.

Furthermore, the intake needs of each person per day will be assessed based on the subject's body weight. Data on age, gender, long history of HD, nutritional status, etiology of CKD were obtained based on medical records and history taking to confirm data in medical records. Phosphorus levels in the blood are obtained through the results of blood tests in the laboratory before HD.

The food recall's[13] interviews were conducted twice a week during the hemodialysis schedule to see phosphorus and protein intake. Filling out the questionnaire was assisted by nutritionist. Protein intake is said to be adequate (high) if ≥1.2 grams/kgBW/day and inadequate (low) intake if <1.2 grams/kgBW/day. Meanwhile, phosphorus intake is said to be sufficient if it is 17 milligrams/kgBW and the excessive intake if it is more than 17 milligrams/kg BW. Intake with a low protein- phosphorus ratio if 5 milligrams/dl, and high if >5 milligrams/dL. It is calculated by averaging the amount of protein and phosphorus intake from each meal or drink in grams (gr). [14] Hyperphosphatemia is a condition when the level of phosphorus in the blood is >5 mg/dL. If levels 5 mg/dL is said to be normal. Phosphorus levels in the blood or called serum phosphorus are measured in pre-HD.[14]

Analysis of research data using SPSS 21-version. Univariate analysis was carried out to identify the distribution of the frequency and percentage of the data on the characteristics of

the subject, namely age, gender, long history of HD, nutritional status and etiology of CKD. The bivariate analysis method uses Chi-Square test which aims to find the relationship and risk between hyperphosphatemia and diet protein, phosphorus and protein-phosphorus ratio. Probability is considered statistically significant if the p value <0.05 is obtained with 95% confidence.

This study has been reviewed by the research ethics commission of the Faculty of Medicine, Udayana University/Sanglah General Hospital Denpasar and has been approved with permit number 2482/UN.14.2.2.VII.14/LT/2020.

Results

From 66 subjects were successfully collected in this study. The data shows 73%, there are more males than females as listed in Table 1, productive age (29%), and more in the good nutrition category (46%).

The results of the analysis showed that 74% of the subjects had hyperphosphatemia and the majority were classified as having adequate protein intake (54%) according to Table 2, most of the phosphorus intakes were classified as the excessive intake (70%), and most of the protein ratio and phosphorus is the low ratio (70%).

This study obtained 2 variables that significantly related, the intake of protein and the phosphate to phosphorus levels in the blood as listed in Table 3. In contrast to the protein-phosphorus ratio variable which showed no significant results. The next stage was carried out with risk analysis on 2 variables that had a significant relationship with the condition of hyperphosphatemia. There was an increase in the incidence of hyperphosphatemia 3.9 times

Table 1 Characteristics Subjects

Characteristics	Total	%
Gender		
Male	48	73
Female	18	27
Age (years)		
20–30	4	6
31–40	9	14
41–50	17	26
51–60	19	29
61–70	14	21
>70	3	4
Status Category Nutrional		
Over nutrition	28	42
Good nutrition	30	46
Undernourished	8	12
Length of HD (months)		
4–24	8	12
25–48	16	24
49–72	17	26
>72	25	38
Etiology of		
DKD	11	17
PNC	51	77
Other	4	6

DKD: diabetic kidney disease; PNC: chronic pyelonephritis

Table 2 Distribution of Protein Intake, Phosphorus Intake, Protein-Phosphorus Ratio, and Blood Phosphorus Levels

Characteristics	Total	%
Protein intake		
Adequate (≥1.2 g/kgBW/day)	30	46
Inadequate (<1,2 g/kgBW/day)	36	54
Phosphorus intake		
Sufficient (≤17 mg/kgBW)	20	30
Excessive (>17 mg/kgBW)	46	70
Protein-phosphorus ratio		
Low (≤5 mg/dL)	46	70
High (>5 mg/dL)	20	30
Blood phosphorus level		
Normal	17	26
Hyperphosphatemia	49	74

more often in subjects with high phosphorus intake than in subjects with normal phosphorus intake. In subjects with adequate protein intake, hyperphosphatemia also experienced an increased risk of 3.7 times compared to the inadequate protein intake group.

Discussion

In this study, the phosphorus levels in the subjects' blood were mostly classified as high category. This finding is supported by other studies conducted in several cities in Indonesia such as Jakarta, Semarang, Manado, and Palembang which all stated that more than 50% of research subjects had hyperphosphatemia.[15–18] This fact can be influenced because of similarities in diet, race, and decreased renal function that lead to systemic hyperphosphatemia in CKD patient with HD. Chronic kidney disease can lead to imbalances in mineral regulation, primarily causing hyperphosphatemia. Hyperphosphatemia conditions must be treated

Table 3 The Variable Relationship and Risk to Hyper Phosphate Level Condition

Characteristics	Category Blood Phosphorus Level				Total		OR (p)	CI 95%
	Hyperphosph-Atemia		Normal					
	n	%	n	%	n	%		
Protein intake								
Adequate (≥1.2 g/kgBW.day)	26 23	39.4	4	6.1	30	45.5	3.674 (0.035)	1.049–12.865
Inadequate (<1,2g/kgBW/day)		34.8	13	19.7	36	54.5		
Phosphorus intake								
Sufficient (≤17 mg/kgBW)	11	16.7	9	13.6	20	30.3	3.886 (0.018)	1.212–12.460
Excessive (>17 mg/kgBW)	38	57.6	8	12.1	46	69.7		
Phosphorus-protein ratio								
Low (≤5mg/dL)	33	50	13	19.7	46	69.7	1.576 (0.352)	0.443–5.61
High (>5mg/dL)	16	24.2	4	6.1	20	30.3		

immediately because it can cause bone disease called mineral and bone disorders in chronic kidney disease and also as risk factor for the cardiovascular disease.[14,19] Many studies have reported that the mortality rate of chronic kidney disease is significantly increasing due to an increase in phosphate levels in the blood.[20,21]

Phosphorus intake in most of the research subjects was excessive. This study showed that excess phosphorus and adequate protein intake had a significant relationship to the incidence of hyperphosphatemia, although the author was aware that the confidence interval is quite wide. In this study found that adequate (high) protein intake can increase the risk of hyperphosphatemia 3.7 times compared to inadequate (low) protein intake. A high intake of phosphorus also increases the risk of hyperphosphatemia by 3.9 times compared to a lower intake of phosphorus. The results of this study are in line with several other studies that reported a significant relationship between high intake of protein and phosphorus to the incidence of hyperphosphatemia.[9,22] Previous research has shown that there was a significant association between protein intake (p=0.037; RP=2.78), phosphate intake (p=0.005; RP=3.54), phosphate-protein ratio (p=0.045; RP=3.85), and blood phosphate level in CKD patients on routine HD.[16] Several studies have also stated that high protein intake, which is more than 1.2 g/kg BW per day in CKD patients plays a role in the occurrence of renal hemodynamic imbalances that will damage tissues and reduce kidney function.[23]

Modification of nutrition is an important point in the treatment of CKD because it is needed to improve the quality of life, reduce morbidity and mortality, and hinder the disease's progression. One of them is modifying the intake of protein and phosphorus. This modification depends on the stage of CKD and the type of dialysis being undertaken. The recommended daily protein intake for CKD patients undergoing routine hemodialysis is 1.2 grams/kg BW, phosphorus intake not more than 17 milligrams/kg/day or a maximum of 900 mg per day.[24] Previous studies have shown that a low protein diet in patients with CKD can significantly improve the anemia, reduce cardiovascular risk associated with uremia, control blood pressure, inhibit the progression of CKD, but increase the risk of malnutrition.[25,26]

Until now, a low protein diet in CKD patients with HD is still a debate, because it can cause protein malnutrition which can certainly worsen the patient's condition. The selection of protein intake is certainly an important point in modifying the diet of CKD patients. Selection of a good type of protein intake can be done by calculating the protein- phosphorus ratio. This ratio is obtained by comparing the content of protein with the phosphorus on protein foods consumed. Previous studies have stated that eating foods with high phosphorus levels or a high protein- phosphorus ratio causes hyperphosphatemia, increasing the risk of mortality in CKD patients with HD.[9,10] The ratio of phosphorus-protein in animal protein is lower, namely ±11 milligrams of phosphorus per gram of protein, while vegetable protein contains ±20 milligrams of phosphorus per gram of protein. Selection of protein intake by paying attention to the ratio of low phosphorus levels in addition to controlling serum phosphate in the blood can also prevent malnutrition. Fish and egg whites have a low protein-phosphorus ratio. Chicken liver, cow's milk, soy milk, cheese, nuts, and seeds have a high protein- phosphorus ratio.[10] The subjects in this study still chose foods with a high protein- phosphorus ratio such as green beans, chicken liver, milk and their products for daily consumption.

This study did not find a significant relationship between the protein- phosphorus ratio and the state of hyperphosphatemia in this study, but this result is different from other studies that have reported a significant relationship between these two variables.[15] Studies from the United States reported that CKD patients on hemodialysis who eat foods with low protein levels and low protein- phosphorus ratios tend to have lower blood serum phosphorus, which can increase life expectancy. [10]

This study has limitations for instance, the data taken in this study using the food recall method is strongly influenced by memory and interpretation of how much food is consumed in 24 hours. Apart from these limitations, this study also did not find other factors such as (parathyroid hormone and vitamin D metabolites) that have been shown to be associated with hyperphosphatemia in CKD undergoing regular hemodialysis. So that further research is recommended to assess these limitations.

In conclusion, the high protein intake and excessive phosphorus intake provide a relationship to the incidence of hyperphosphatemia in CKD patients undergoing routine hemodialysis. So that the intake of protein and phosphorus can be a determinant of

hyperphosphatemia in hemodialysis patients for further research.

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