



Proportions of hyperphosphatemia in different stages of chronic kidney disease



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ABSTRACT

Introduction: In chronic kidney disease (CKD) patients, calcium and phosphate homeostasis disorders occur. Decreased kidney function will result in decreased phosphate excretion. In stage 3b CKD, the kidneys are no longer able to compensate for the phosphate load sufficiently and hyperphosphatemia is resulted.

Objectives: This research aimed to figure out the proportions of hyperphosphatemic patients at different levels of glomerular filtration rate in CKD.

Patients and Methods: An observational study with a cross-sectional approach involving 80 CKD subjects, distributed into stage 3 (n = 20), stage 4 (n = 20), stage 5 non-dialysis (n = 20) and stage 5 dialysis CKD subjects (n = 20), at Wahidin Sudirohusodo hospital and Unhas hospital, Makassar, from April through August 2021. Phosphate concentrations were measured using ELISA (enzyme-linked immunosorbent assay) kit (Immutoptics). A result of the statistical test would be significant if $P < 0.05$.

Results: The average phosphate concentrations at stage 3, stage 4, stage 5 non-dialysis and stage 5 dialysis were 4.14 ± 1.85 mg/dL, 4.17 ± 1.12 mg/dL, 6.43 ± 3.09 mg/dL and 5.42 ± 3.09 mg/dL, respectively. Based on the average phosphate concentration by CKD stage, stage 3 was not significantly different from stage 4 ($P = 0.969$), however there was a significant difference between stage 3 and stage 5 non-dialysis ($P = 0.004$) and also between stage 4 and stage 5 non-dialysis ($P = 0.005$). The proportions of hyperphosphatemic patients (serum phosphate >4.5 mg/dL) with stage 3, stage 4, stage 5 non-dialysis and stage 5 dialysis CKD were 15% (n = 3), 20% (n = 4), 75% (n = 15) and 43.3% (n = 9), respectively.

Conclusion: The proportion of hyperphosphatemic subjects increased with the decline in the kidney function. Dialysis process reduces phosphate levels and the proportion of patients with hyperphosphatemia.

Implication for health policy/practice/research/medical education:

In this study, it was found that phosphate levels and the proportion of hyperphosphatemia increased along with decreased kidney function. It is necessary to measure phosphate levels in chronic kidney disease with eGFR (estimated glomerular filtration rate) <60 mL/min/1.73 m² and therapy should be conducted, if hyperphosphatemia is found.

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Introduction

Chronic kidney disease (CKD) is a global health problem with a bad prognosis and high cost (1). In the USA, over 20 million adults were reported as suffering from this disease. In the UK, the prevalence of stage 3 to 5 CKD had touched 1.7 million adults, with the annual stage 5 CKD prevalence reaching 100 per one million in population (2). Based on the Indonesian Renal Registry (IRR)'s 2018 data, there were 66433 new patients with CKD in Indonesia (1-3).

In CKD patients, calcium and phosphate homeostasis disorders occur (4). Decreased kidney function will result in decreased phosphate excretion. The body will respond through an increase in the synthesis and secretion of fibroblast growth factor-23 (FGF-23) from the bones, functioning in promoting phosphate excretion (4-5). In stage 3b CKD, the phosphate concentration starts to rise, showing that the compensatory mechanism is no longer sufficient to maintain the phosphate balance and to

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prevent hyperphosphatemia (6). Numerous studies, such as those by Kritmetapak et al (7), Liu et al (8), Gutierrez et al (9) and Isakova et al (10), reported that phosphate concentration would increase with the decrease in glomerular filtration rate.

Objectives

In this observational study, we aimed to determine the proportions of hyperphosphatemic patients at different levels of glomerular filtration rate in CKD.

Patients and Methods

Study design

An observational study with a cross-sectional approach at Wahidin Sudirohusodo hospital and Hasanuddin university hospital, Makassar.

Research Subject

The subjects of this research were criteria-meeting stage 3–5 CKD patients receiving or not receiving hemodialysis therapy and undergoing outpatient or inpatient treatments at RSWS since 2021. The inclusion criteria were the patients being aged 18–65 years and not receiving a phosphate-lowering therapy.

Data analysis

The analytical method consisted of descriptive methods and statistical tests. The statistical tests used were Kruskal-Wallis, Mann-Whitney U and Spearman's rho test. The results of the statistical test were considered significant if the *P* value was <0.05. Data were analyzed using SPSS version 25.

Results

This study included 80 CKD subjects, consisting of 42 males (52.5%) and 38 females (47.5%). The age range was 18–65 years and the age average was 48.28 ± 12.65 years. The phosphate concentration range was 1.5–15 mg/dL and the average phosphate concentration was 5.04 ± 2.58 mg/dL. The effect of diet in this study was not analysed. Our study showed that the average phosphate concentrations in stage 3, stage 4, stage 5 non-dialysis and stage 5 dialysis CKD were 4.14 ± 1.85 mg/dL, 4.17 ± 1.12 , 6.43 ± 3.09 mg/dL and 5.42 ± 3.09 mg/dL, respectively (Table 1), suggesting an increase of phosphate concentration for each increase of CKD stage. The greater the CKD degree of severity resulted to the significantly higher the phosphate concentration ($P=0.007$).

Furthermore, we found the proportions of hyperphosphatemia (serum phosphate >4.5 mg/dL) in stage 3, stage 4, stage 5 non-dialysis and stage 5 dialysis CKD were 15% ($n = 3$), 20% ($n = 20$), 75% ($n=15$) and 43.3% ($n = 9$; Table 2), respectively, suggesting that the proportion of hyperphosphatemia increased with the increase of CKD stage and decreased in stage 5 dialysis due to the dialysis process. There were significant

Table 1. Average phosphate concentration by CKD stage

Stage	Phosphate Concentration			P value*
	N	Mean + SD (mg/dL)	95% CI	
3	20	4.14 ± 1.85	3.27–5.00	0.007
4	20	4.17 ± 1.12	3.64–4.69	
5 Non-dialysis	20	6.43 ± 3.09	4.98–7.87	
5 Dialysis	20	5.42 ± 3.09	3.97–6.87	

* Kruskal–Wallis test.

Table 2. The proportions of hyperphosphatemia in different CKD stages

CKD stage	No. (%)	Phosphorous group		Total
		> 4.5	≤4.5	
3	No. (%)	3 (15)	17 (85)	20 (100.0)
4	No. (%)	4 (20)	16 (80)	20 (100.0)
5 Non-dialysis	No. (%)	15 (75)	5 (25)	20 (100.0)
5 Dialysis	No. (%)	9 (43.3)	11 (56.7)	20 (100.0)
Total	No. (%)	31 (43.3)	49 (56.7)	80 (100.0)

difference between stage 3 and stage 5 non-dialysis ($P < 0.001$), between stage 3 and stage 5 dialysis ($P = 0.038$) and between stage 4 and stage 5 non-dialysis ($P < 0.001$).

Discussion

In this study, it was shown an increase in phosphate concentration for each increase of CKD stage. The higher the CKD degree of severity led to the significantly higher the phosphate concentration ($P=0.007$). This finding is in line with the research by Kritmetapak et al (7), Caravaca et al (11) and Liu et al (8), which found that the higher the CKD stage the higher the phosphate concentration.

The proportion of subjects with hyperphosphatemia went up with the increase in CKD stage and went otherwise in stage 5 dialysis due to the dialysis process. This finding mirrors the research by Gutierrez et al (9), Chartsrisak et al (12) and Isakova et al (10), according to which hyperphosphatemia rises with the increase in CKD stage ($P=0.001$) and the decrease in glomerular filtration rate. In early-stage CKD, the phosphate metabolism is disturbed, however the serum phosphate concentration usually is maintained at the normal range as a result from the compensation for fibroblast growth factor-23 while hyperphosphatemia increases to the final stage of the kidney disease (13–14). The prevalence of hyperphosphatemia in CKD patients is elevated with the lowering of kidney function. Serum phosphate concentration increase occurs after the CKD progression, showing that the mechanism of phosphate homeostatic compensation remains effective to stage 3a of CKD (15). In advanced-stage CKD (stage 3b), when glomerular filtration rate drops to <45 mL/minute/1.73 m², the kidneys will no longer be able to compensate for the phosphate load sufficiently and hyperphosphatemia is resulted (16).

Conclusion

The proportion of hyperphosphatemia increased with the decrease in the kidney function.

Limitations of the study

In our observational study, we did not assess phosphate intake in study patients.

Authors' contribution

AI, HR and SB were the principal investigators of the study. HK, FS, NAD and AS were included in preparing the concept and design. HR and SB revisited the manuscript and critically evaluated the intellectual contents. All authors participated in preparing the final draft of the manuscript, revised the manuscript and critically evaluated the intellectual contents. All authors have read and approved the content of the manuscript and confirmed the accuracy or integrity of any part of the work.

Conflicts of interest

The authors declare no competing interests.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The Ethics Committee of Hasanuddin University of Medical Sciences approved this study (Recommendation Letter No. 59BIUN 4.6.4.5.31/PP36/2421, under protocol number UH2O12O7OI). Accordingly, written informed consent was taken from all participants before any intervention. Additionally, ethical issues (including plagiarism, data fabrication and double publication) were completely observed by the authors.

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