

## Serum Phosphate Level among Chronic Kidney Disease Patients on Chronic Dialysis

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The increase level of serum phosphate is common due to secretion failure of the kidney on chronic kidney disease patients (CKD). The study objective is to determine the level of serum phosphate among the CKD patient on chronic dialysis in Gianyar Bali. A prospective cross-sectional study conducted in 100 serum of the patients visiting dialysis clinic in Sanjiwani and Arisanti Hospital on October 2018. A three mL of blood was collected and the phosphate level was measured with spectrophotometer. Sixty-seven of 100 samples was male with mean age of 52.52 (SD±12.811). The most cause of CKD was chronic pyelonephritis. The mean of hemodialysis duration was 44.59 (SD± 32.40). Level of the phosphate more than normal limit found as high as 69% of the samples. There was a correlation between age ( $p=0.001$ ), gender ( $p=0.020$ ) and phosphate level, but no correlation between Body Mass Index, hemodialysis duration and phosphate level were observed, accounting for  $p=0.222$  and  $p=0.264$ , respectively. High finding of hyperphosphatemia that found in the study revealed the presentation of CKD-mineral and bone disorder in CKD patients. Correlation of age with higher phosphate level may relate with the deterioration of kidney function in elderly.

**Keywords:** CKD; Phosphate Level; Hemodialysis.

The propensity toward phosphate retention develops early in chronic kidney disease (CKD) due to the reduction in the filtered phosphate load. Normal serum phosphorus ranges between 3 mg/dl to 4.5 mg/dl. Overt hyperphosphatemia develops when the estimated glomerular filtration rate (eGFR) falls below 25-to 40 mL/min/1.73 m<sup>2</sup>.<sup>1-3</sup> At this point serum phosphorus levels start to rise and remain increasing as these patients reach end-stage kidney disease (ESRD, Stage 5).<sup>4</sup> Hyperphosphatemia has been associated

with increased mortality and morbidity.<sup>5,6</sup> Mechanisms underlying the physiologic response to phosphate retention are discussed elsewhere.<sup>3,5</sup> Hyperphosphatemia has been independently linked with calcification of the coronary arteries and aorta, left ventricular hypertrophy, as well as cardiovascular and all-cause mortality in the setting of End Stage Renal Disease (ESRD).<sup>1,5,6</sup>

Mechanism of normal serum phosphate maintenance by several methods such as absorption in the gut, reabsorption and excretion by the

kidney, and the flux between the extracellular and skeletal pools.<sup>7,8</sup> A complex system of crosstalk between the bone, intestine, kidney, between fibroblast growth factor 23 (FGF 23), vitamin D and parathyroid gland (parathyroid hormone or PTH) are the results of phosphate homeostasis coordination. Dysfunction of this system has serious clinical consequences in healthy individuals and those with conditions, such as CKD, in which hyperphosphatemia is associated with increased risks of cardiovascular morbidity and mortality.<sup>9</sup> The last half-century of renal research has helped define the contribution of the parathyroid hormone, calcitriol, fibroblast growth factor 23 in the regulation of phosphate.<sup>10</sup> Hyperphosphatemia is ordinarily asymptomatic, although pruritus and red irritated eyes reported on several patients with phosphate level greater than 1.8 mmol/L,<sup>11,12</sup> hence screening phosphate level recommended not only to provide the treatment to relief the symptoms but also alleviate the risk of cardiovascular events among chronic dialysis patients. Oral phosphate binders can be ameliorated the phosphate level due to dietary phosphate restriction, but the clinical outcome remain indeterminate.<sup>13</sup> Directing phosphate load remains the primary goal in the treatment of CKD. Control of hyperphosphatemia is an fundamental component of the routine care of long-lasting dialysis patients.<sup>14</sup> The Kidney Disease: Improving Global Outcomes (KDIGO) and Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines the importance of regular assessing and monitoring of serum phosphate and provide recommendations for phosphate levels.<sup>15</sup>

The current study assess the level of phosphate among chronic hemodialysis patients at hospitals in Gianyar, Bali.

## MATERIAL AND METHODS

### Ethical Consideration

Involvement of human subjects in this study have been reviewed by Institutional Review Board of Udayana University, Bali, Indonesia. All patients provided informed consent.

### Patients

One hundred patients who underwent routine dialysis at Sanjiwani and Arisanti Hospital Gianyar were enrolled to the study. End stage renal

disease was define with estimated GFR below 25- mL/min/1.73 m<sup>2</sup>.<sup>16</sup>

### Blood Collection and Serum Phosphate Measurement

We collected three mL of CKD patient's blood who underwent continuing hemodialysis after approving the informed consent. Measurement of the phosphate level was performed using the spectrophotometer methods, according to method described by previous study.<sup>17</sup> Measurement of serum phosphorus, creatinine, and other biomarkers was performed at the time of HD schedule in a fasting state. Phosphate level greater than 3.5 mg/dl define as high level of serum phosphate.<sup>18</sup>

### Statistical Analysis

Data were analysed using SPSS version 16.0. Data were presented as descriptive data. Continuous demographic, clinical, laboratory variables are presented as mean and SD or median when suitable. Categorical variables are expressed as proportions. The level of phosphate serum and others variables were compared using independent t-test. Correlation test used to associate between each variables and phosphate levels.

## RESULTS

The study recruited 100 CKD on dialysis in two hospitals in Gianyar Regency with end stage renal disease. Sixty-seven percent of the participant is male, mean age of 52.52 (SD±12.811). The predominant cause of CKD was PNC. The characteristic of the participant are listed on table 1.

**Table 1.** Characteristic of the participants

Variables	N=100
Age ,mean (SD)	52,52 ±12,811
Gender	
Male	67 (67%)
Female	33 (33%)
Etiology of CKD	
Chronic Pyelonephritis	30 (30%)
Diabetic Kidney Disease	21 (21%)
Obstructive nephropathy	18 (18%)
Chronic Glomeruli Nephritis	14 (14%)
Nephrotic syndrome	13 (13%)
Polycystic kidney	3 (3%)
Uric Acid Nephropathy	1 (1%)
Duration of HD, mean (SD)	44.59 ± 32.40

Greater levels of mean phosphate significantly found in male ( $p=0.02$ ; 95% CI 0.128-1.467). Higher mean body height and dry body weight in male were statistically significant, accounting for  $p=0.000$ ; 95% CI 6.488-11.749 and  $p=0.001$ ; 95% CI 3.440-13.522, respectively. There were no significantly difference of age, IMT, duration and frequency of HD between male and female.

Haemoglobin level was more than 10 mg/dl in all participants. The highest creatinine level was as high as 12.16 mg/dl. Hyperphosphatemia found in 69% of the participants. The difference mean each laboratory parameter between male and female participants were not significant. Detail laboratory-finding list in table 2.

There were correlation between phosphate levels and age ( $p=0.001$ ,  $r=-0.333$ ), as well as gender ( $p=0.020$ ,  $r= 0.276$ ). Older age had higher phosphate level. There were no correlation between duration of HD with level of phosphate.

**DISCUSSION**

Hyperphosphatemia is a clinical concern of the progressive stages of CKD. The role of

hyperphosphatemia in the pathogenesis of CKD-associated cardiovascular (CV) complications, including vascular calcification, and with increased all-cause and CV mortality has been pointed with extensive evidence.<sup>5,19,20</sup> High level of phosphate has been implicated in the substantial morbidity and mortality observed among people who receive chronic dialysis. The study found that mortality risk increased linearly with each following 0.5-mg/dl increase in serum phosphate levels.<sup>9</sup>

The current study objective is to evaluate level of phosphate serum among CKD on dialysis patients in Gianyar, Bali. The entire participants are on stage 5 of CKD. The study finding is in contrast with other study with 33% of the participants was on stage 3, 46% of stage 4 and 21% stage 5. 21% of the 22% of patients with phosphate levels outside of the target range, 19% had values above the upper limit, and 3% had values below the lower limit.<sup>21</sup> This result is discordant with the current study where 69% of the participant has phosphate level above normal limit. Another study found 43.18% of the participants had phosphate level more than 3.5 mg/dl. The discordant may relate with CKD stage 5 in all the current study participants that inversely with the previous study whereas 64.7% of

**Table 2.** Profile of CBC, BUN/SC, BG and Phosphate level among participants

Variable	N=100	
	Mean	CI
White blood cell	7.012 ± 2.054	6.611-7.426
Hemoglobin	11.571 ± 7.843	10.012-13.127
Platelet	204.641 ± 64.378	191.867-217.415
BUN	79.403 ± 38.516	71.760-87.045
SC	10.039 ± 10.681	7.920-12.159
Random blood glucose	94.907 ± 31.640	88.629-101.185
Phosphate	4.977 ± 1.623	4.655-5.299

**Table 3.** Correlation between ages, gender, IMT, duration of HD with phosphate level in Gianyar

Variable	R	Significant
Age	-0.333	0.001
Gender	0.276	0.020
IMT	0.123	0.222
Duration of HD	0.113	0.264

the participants had stage III CKD.<sup>9</sup> In our hospital, stage I-III CKD is not routinely visit the hospital.

This study found the higher phosphate level among the older participants. This finding inversely with another study which found patients with higher serum phosphate levels tended to be younger.<sup>9</sup> The discrepancy may relate with only CKD stage of the study. Older age has tend lower eGFR due to ageing process in elderly.<sup>22</sup> There will be macro-anatomical structural changes in elderly,

where older age companions with reduced cortical volume, larger medullary capacity until middle age, and larger and extra numerous renal cysts.<sup>22</sup>

The current study also found higher phosphate level among male than female. This finding support by another study where male with phosphate level greater than 3.5 mg/dl found as high as 95.36% of the participants. Whether male has more decrease kidney function than female, need further investigations or study.

Regulation of phosphate balance during CKD before loss of equilibrium occurs is complicated. Loss of calcitriol production capability is an important issue leading to a reduction in Ca absorption, hypocalcaemia and stimulation of parathyroid hormone (PTH) secretion. The rise in PTH levels reduces the section of the filtered phosphate load and preserves phosphate excretion at normal levels although the reduction in the filtered load of phosphorus due to the diminution in glomerular filtration.<sup>17</sup> Unfortunately, we did not evaluate the level of PTH in order to assess regulation of phosphate balance among the participants.

In conclusion we highlight hyperphosphatemia among CKD participant as a consequence of reduce function of the kidney. The data provide information on the hyperphosphatemia among CKD that will be useful for better management and understanding of CKD pathogenesis.

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