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Original Research Article

A comparative analysis of serum phosphorus levels and mineral metabolic markers in non-dialysis and dialysis chronic kidney disease patient: a cross-sectional study

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ABSTRACT

Background: Chronic kidney disease is a major public health problem worldwide. As kidney function declines, it leads to several metabolic abnormalities including dysregulation of mineral metabolism. It is also reported that hyperphosphatemia in patients with advanced kidney disease is associated with an increased risk of mortality and cardiovascular events, and is higher in dialysis-dependent chronic kidney disease (CKD) patients compared to non-dialysis CKD. However, data in the Indian context is limited. Objectives were to evaluate and compare serum phosphorus levels and associated factors in non-dialysis and dialysis CKD patients. Also, the impact of dietary phosphate restriction and the use of phosphate binders on serum phosphorus is analysed.
Methods: A cross-sectional study was conducted at a tertiary care hospital in Kolkata, India, with 100 CKD patients: 50 non-dialysis CKD patients and 50 dialysis-dependent CKD patients. Relevant demographic, clinical and laboratory parameters including serum phosphorus, calcium, parathyroid hormone (PTH), alkaline phosphatase, albumin and estimated glomerular filtration rate (eGFR) were collected. Data was analyzed using appropriate statistical tests.
Results: Mean serum phosphorus was significantly higher in the dialysis CKD group (6.12±0.34 mg/dl) compared to the non-dialysis CKD group (4.56±0.80 mg/dl). Serum calcium and PTH were also higher while eGFR and albumin were lower in the dialysis CKD group. Serum phosphorus levels increased with advancing CKD stages in the non-dialysis group. Phosphate binder helped phosphorus control in dialysis CKD patients.
Conclusions: Our study is in confluence with other reports and dietary phosphate restriction and the use of phosphate binders help optimize phosphorus levels in CKD patients.

Keywords: Chronic kidney disease, Dialysis, Phosphorus, Serum, GFR, Calcium

INTRODUCTION

Hyperphosphatemia is defined as an elevated serum phosphate level above the normal range of 2.5-4.5 mg/dL and is a common complication in patients with CKD.[1] As the kidneys lose their ability to effectively excrete dietary and endogenous phosphate from the body due to decreasing glomerular filtration rate (GFR), serum phosphate levels begin to rise.[2] Hyperphosphatemia in CKD can have serious consequences. It is associated with an increased risk of cardiovascular disease and mortality. Several studies have shown a strong independent association between elevated serum phosphate and all-cause and cardiovascular mortality in both dialysis-

dependent and non-dialysis-dependent CKD populations.[2] High serum phosphate levels are also closely associated with the development and progression of renal osteodystrophy and soft tissue calcification in CKD patients through the mechanism of CKD-mineral and bone disorder (CKD-MBD).[1] This condition causes significant morbidity from fractures, bone pain, and vascular calcification.[2,3]

The KDIGO guidelines recommend maintaining serum phosphate levels within normal limits at all stages of chronic kidney disease to prevent complications.[1] However, achieving optimal phosphate control in clinical practice remains challenging due to several factors. Dietary restrictions alone are often not sufficient to control hyperphosphatemia as chronic kidney disease progresses because the capacity of the kidneys to excrete dietary phosphates decreases.[2] Adherence to phosphate binder medications can also be poor due to the high pill load and side effects such as gastrointestinal complaints.[3] Newer treatment strategies are needed to better manage hyperphosphatemia, particularly in the early pre-dialysis stages of CKD before complications occur.[1]

Rationale for the study

This study aimed to evaluate the prevalence and determinants of hyperphosphatemia in non-dialysis CKD and dialysis patients. Understanding the burden of hyperphosphatemia and the factors associated with elevated phosphate levels could help identify opportunities to improve current management practices. Specifically, the objectives of this study were to: Determine the graded prevalence of hyperphosphatemia (defined as serum phosphate >4.5 mg/dl), 3-5 CKD patients not requiring dialysis.[2,3] To analyze the association between serum phosphate levels and the stage of CKD, markers of mineral bone diseases such as PTH and alkaline phosphatase, use of phosphate binders, and dietary restrictions.[1] To identify patient characteristics that may independently predict higher serum phosphate concentrations.

It was expected that determining the true extent of hyperphosphatemia in the pre-dialysis CKD population using a cross-sectional study design would provide valuable insights. It could serve as a guide for the development of optimized treatment strategies aimed at phosphate control in earlier stages of kidney disease. This may help mitigate complications and reduce the growing burden of CKD-MBD on patients and the healthcare system.[1] The study results would add to the existing literature on hyperphosphatemia in CKD by providing local prevalence data and determinants of elevated phosphate levels in the Indian population. This information could be helpful to physicians in risk-stratifying patients and tailoring management approaches to individual needs.[1,2] It may also help identify potential barriers to phosphate control that need to be addressed through interventions in the education or health system.[1-3]

In summary, given the significant adverse consequences associated with hyperphosphatemia and the challenges in its treatment, this study aimed to provide comprehensive assessment of the burden and predictors of elevated serum phosphate levels in dialysis-naïve CKD patients using a cross-sectional observational study design. The results were expected to guide strategies to optimize phosphate control in early stages of kidney disease.

METHODS

A cross-sectional study was carried out with a sample size of (n=100) participants, for 18 months from 1st July 2018 to 31st December 2019, with 50 patient's non-dialysis CKD patients (ND CKD group) and 50 patient's dialysis CKD patients in the emergency ward at the department of nephrology, Apollo Gleneagles hospitals, Calcutta.

Inclusion criteria

All patients of CKD, in the age group of 18-65 years, who are not on dialysis and patients who are on dialysis were included in study.

Exclusion criteria

Age <18 or >65 years; patient refusal to participate in study; patients who are post-transplantation, patients who had received previous dialysis for more than 12 months were excluded.

All CKD patients who are not on dialysis and CKD patients on dialysis were screened with a fasting serum inorganic phosphorus level and the clinical history was taken to determine whether they were on dietary restriction/phosphate binders or both.

Statistical analysis

Data was summarized as mean ± standard deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. Paired t tests were a form of blocking and had greater power than unpaired tests. A chi-squared test ($\chi 2$ test) is any statistical hypothesis test wherein the sampling distribution of the test statistic is chi-squared distribution when the null hypothesis is true. Without other qualifications, the 'chi-squared test' often is used as short for Pearson's chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate. Explicit expressions that can be used to carry out various t-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a t distribution under the null hypothesis is given. Also, appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

Once a t is determined, a p can be found using a table of values from the student's t distribution. If the calculated p below threshold chosen for statistical significance (usually 0.05,), then the null hypothesis is rejected in favour of alternative hypothesis. P≤0.05 considered statistically significant.

Ethical consideration

Ethical approval for this study was granted by the Apollo Gleangles hospital, Calcutta (IEC/2018/DNB/07/19) dated 18 June 2020. Informed consent was obtained from all participants before data collection. Confidentiality and anonymity of participant data were ensured. The study was conducted according to the ethical guidelines of the committee to ensure the protection of human subjects.

RESULTS

In our study of 100 patients (with 50 CKD and 50 non-CKD patients), 17 patients (17%) were aged 31-40 years, 27 patients (27.0%) were aged 41-50 years, 48 patients (48.0%) were aged 51-60 years, and 8 patients (8%) were aged 61-70 years. In terms of gender, 31 patients (31%) were female and 69 patients (69%) were male and as presented as Tables 1 and 2 below.

Table 1 Distribution of age among participants.

Age (in years)	Frequency	Percentage (%)
31-40	17	17
41-50	27	27
51-60	48	48
61-70	8	8
Total	100	100

Table 2: Distribution of gender among participants.

Gender	Frequency	Percentage (%)
Female	31	31
Male	69	69
Total	100	100

Table 3 and 4 summarizes clinical features and baseline routine biochemical testing. Fifty patients (50%) had dialysis-dependent CKD (Dialysis CKD), while the other 50 patients (50%) had non-dialysis-dependent CKD (ND CKD). Regarding CKD stage, 5 patients (5%) were in stage IIIA, 16 patients (16%) were in stage IIIB, 15 patients (15%) were in stage IV, and 64 patients (64%) were in stage V.

Sixty-six patients (66%) had a history of dietary phosphorus restriction, and 58 patients (58%) had been using phosphate binders. Serum calcium levels were low in 74 patients (74%) and normal in 26 patients (26%). Serum phosphorus levels were high in 71 patients (71%) and normal in 29 patients (29%).

Mean (±SD) serum phosphorus level was 5.3420±0.9906 mg/dl. Mean (±SD) serum calcium level 7.7128±1.0029 mg/dl. Mean (±SD) serum PTH level 550.34±120.611 pg/ml. Mean (±SD) blood urea nitrogen level 69.76±10.4089 mg/dl. Mean (±SD) serum creatinine level 6.453±1.1466 mg/dl. Mean (±SD) eGFR 19.68±11.74 ml/min/1.73 m^2.

Table 3: A comprehensive snapshot of CKD patients and associated factors.

		N	Percentage (%)
Groups	Dialysis CKD	50	50
	Non-dialysis CKD	50	50
Stage	IIIA	5	5
	IIIB	16	16
	IV	15	15
	V	64	64
History of dietary restriction	No	34	34
	Yes	66	66
Phosphate binder use	No	42	42
	Yes	58	58
Serum calcium level	Low	74	74
	Normal	26	26
Serum phosphorus level	High	71	71
	Normal	29	29

Table 4: In-depth analysis of key clinical outcomes in CKD patients.

Clinical outcomes	Mean ± SD
Serum phosphorus	5.34±0.99
Serum calcium	7.71±1.00
Serum PTH	550.34±120.61
Blood urea nitrogen	69.76±10.40
Serum creatinine	6.453±1.14
Estimated GFR	19.68±11.74

Table 5: Biochemical parameters

Biochemical components	Dialysis CKD	Non-dialysis CKD	P value
Serum phosphorous	6.120± 0.33	4.564± 0.79	<0.0001
Serum calcium	7.069± 0.47	8.357± 0.98	
Serum PTH	622.64± 59.91	478.04± 123.02	
Blood urea nitrogen	73.44± 6.88	66.08± 11.99	
Serum creatnine	7.138± 0.25	5.768± 1.27	
Estimated GFR	12.22± 1.694	27.14± 12.73	

Table 6: Analysis of associations in chronic kidney disease.

Variables assessed for association	Chi-square value	P value	Odds ratio	Significance
Age in years vs group	0.1792	0.9809		Not significant
Gender vs group	0.0468	0.8288	1.0980 (95% CI: 0.4703, 2.5637)	Not significant
Stage vs group	56.25	<0.0001	-	Significant
History of dietary restriction vs group	8.7344	0.0031	3.6923 (95% CI: 1.5198, 8.9706)	Significant
Phosphate binder use vs group	8.046	0.0045	0.3056 (95% CI: 0.1329, 0.7024)	Significant
Serum phosphorus level vs group	40.84	<0.0001	-	Significant
Serum calcium level vs group	35.13	<0.0001	-	Significant

Table 7: Biochemical profiling across CKD stages: a comprehensive analysis of serum phosphorus, calcium, PTH, BUN, creatinine, and eGFR

Biochemical components	IIIA	IIIB	IV	V	P value
Serum phosphorous	3.84±0.28	3.86±0.21	4.50±0.27	5.69±0.22	<0.0001
Serum calcium	9.38±0.19	9.23±0.19	8.29±0.33	7.04±0.5	
Serum PTH	319.40±48.55	373.37±61.28	503.13	627.42±48.91	
Blood urea nitrogen	53.90±7.39	54.25±5.89	75.00±6.52	74.42±6.52	
Serum creatnine	4.12±0.39	4.86±1.25	6.28±0.69	6.84±0.42	
Estimated GFR	47±3.16	38.75±3.19	21.66±3.81	12.64±1.44	

Table 8: Associations in chronic kidney disease: examination of age, gender, dietary restriction, phosphate binder use, and biochemical parameters across disease stages.

Variables assessed for association	Chi-square value	P value	Odds ratio	Significance
Age in years vs stage	11.6	0.2363	-	Not significant
Gender vs stage	6.352	0.0957	-	Not significant
History of dietary restriction vs stage	11.4323	0.0096	-	Significant
Phosphate binder use vs stage	9.302	0.0255	-	Significant
Serum phosphorus level vs stage	81.8682	<0.0001	-	Significant
Serum calcium level vs stage	82.675	<0.0001	-	Significant
History of dietary restriction vs phosphate binder use	0.0143	0.9046	0.9500 (95% CI=0.4103, 2.1995)	Not significant
Phosphate binder use vs serum phosphorus level	12.1921	0.0004	0.2020 (95% CI=0.0794, 0.5140)	Significant
History of dietary restriction vs serum phosphorus level	10.1852	0.0014	6.7167 (95% CI=1.8603, 24.2504)	Significant

Table 5 shows key biochemical parameters measured in two groups of patients with chronic kidney disease-dialysis patients and non-dialysis patients.

Serum phosphorus was significantly higher in the dialysis group, with a mean of 6.12±0.33 mg/dl compared to 4.56±0.79 mg/dL in the non-dialysis group (p<0.0001). This suggests that renal replacement therapy may be less effective than functional kidneys in phosphorus control. Serum PTH and BUN were also increased in dialysis patients, with mean values of 622.64±59.91 pg/ml and 73.44±6.88 mg/dl, respectively, as opposed to 478.04±123.02 pg/ml and 66.08±11.99 mg/dl in non-dialysis patients. The higher concentrations of these uremic toxins in chronic kidney disease requiring dialysis reinforce the inability of current renal replacement methods to fully correct mineral and waste abnormalities that occur with advanced renal function loss. As expected, serum creatinine and eGFR showed more impaired renal function in dialysis patients, who had a creatinine value of 7.14±0.25 mg/dl and an eGFR of 12.22±1.69 ml/min/1.73 m^2 compared to 5.77±1.27 mg/dl and 27.14±12.73 ml/min/1.73 m^2 in non-dialysis CKD.

Analysis of associations in chronic kidney disease: exploring age, gender, disease stage, dietary restriction, phosphate binder use, and biochemical parameters.

The analysis revealed that age in years had no significant association with patient groups (chi-square=0.1792,

p=0.9809). Likewise, gender did not show a statistically significant association with the groups (chi-square=0.0468, p=0.8288, odds ratio=1.0980, 95% CI=0.4703, 2.5637). In contrast, stage of chronic kidney disease emerged as a highly significant factor (chi-square=56.25, p<0.0001), indicating a strong association with patient groups. In particular, history of dietary restrictions (chi-square=8.7344, p=0.0031, odds ratio=3.6923, 95% CI=1.5198, 8.9706), use of phosphate binders (chi-square=8.046, p=0.0045, odds ratio=0.3056, 95% CI=0.1329, 0.7024), serum phosphate level (chi-square=40.84, p<0.0001) and serum calcium level (chi-square=35.13, p<0.0001) were all identified as significant variables associated with the patient groups. These results overall highlight the importance of markers of mineral metabolism, particularly the stage of chronic kidney disease, dietary restrictions, the use of phosphate binders as well as the Serum phosphorus and calcium levels, in distinguishing between non-dialysis patients and dialysis patients with chronic kidney disease.

When examining the associations between various variables and the stages of CKD, several important findings emerged. Age in years and gender showed no statistically significant association with CKD stages, as indicated by chi-square values of 11.6 (p=0.2363) and 6.352 (p=0.0957), respectively. Consequently, odds ratios were not applicable for these comparisons, so both variables were not significant predictors of the CKD stage. Conversely, a notable association was observed between the history of dietary restrictions and the CKD stage, with a chi-square value of 11.4323 and a p=0.0096, indicating this variable as significant in predicting CKD stage marks. Similarly, the use of phosphate binders showed a significant association with the CKD stage, with a chi square value of 9.302 and a p=0.0255. Furthermore, serum phosphate and serum calcium levels showed a highly significant association with the CKD stage, supported by chi-square values of 81.8682 and 82.675, both yielding p values less than 0.0001. Beyond the association with the CKD stage, specific relationships between dietary restrictions, phosphate binder use, and serum phosphate levels were examined. Analysis revealed that history of dietary restrictions was not significantly associated with phosphate binder use (chi-square=0.0143, p=0.9046, odds ratio=0.9500, 95% CI=0.4103, 2, 1995). In contrast, the use of phosphate binders showed a significant association with serum pH.

DISCUSSION

We have conducted a hospital-based cross-sectional observational study from July 1, 2018 to December 31, 2019, among patients with CKD not receiving dialysis treatment and those undergoing dialysis. CKD patients who attended outpatient clinics, hospitalized, or visited the emergency ward at the department of nephrology, Apollo Gleneagles hospitals, Calcutta were also part of the study. A total of 100 patients were recruited for this study and divided into two groups. Group 1:50 CKD patients in the ND group; group 2:50 CKD patients on dialysis. All 100 CKD patients were screened for fasting serum inorganic phosphorus levels and clinical history was taken to determine whether they were taking dietary restriction or phosphate binders or both. The study patients were 30 years and older. We found that 17 (17%) patients were 31-40 years old, 27 (27%) patients were 41-50 years old, 48 (48%) patients were 51-60 years old, and 8 (8%) patients were 61 years old-70 years old. The patients are evenly distributed across all age groups. In our study, approximately 56% were over 50 years of age and older.[4,5]

In our study, 69% were men, compared to 55% of men in the study by Fang et al.[6] Our study results suggest that with increasing age, the incidence of CKD increases, which may be due to less attention being paid to medical examinations or to personal health. The staged distribution of subjects in our study revealed that more than half (64%) were at stage V, followed by 16% at stage IIIB and 15% at stage IV. Subgroup analysis revealed that all patients (n=50, 100.0%) in the dialysis CKD group were stage V. While in the ND group, 5 (10.0%) patients were in stage IIIA, 16 (32.0%) patients were in stage IIIA, while 15 (30.0%) patients were in stage IIIB were in stage IV and 14 (28.0%) patients were in stage V. This association between CKD stage and study group was found to be statistically significant (p=0.0001).

CKD patients may be particularly vulnerable to the effects of high phosphorus intake. In the present study, the majority of 66 (66%) patients had a history of dietary restrictions and 58 (58%) patients had the use of phosphate binders. Subgroup analysis revealed that approximately 26 (52.0%) patients in the CKD dialysis group had a history of dietary phosphate restriction. In the chronic renal failure group, 40 (80%) patients had a history of dietary phosphate restriction. This association between history of dietary phosphate restriction and study group was found to be statistically significant (p=0.003). The results of our study are consistent with the results of Cannata-Andía et al on dietary phosphate restrictions.[7] Reducing phosphate intake is one of the widely accepted strategies to help control hyperphosphatemia in CKD patients.[8] Our study patients reporting a significant proportion of dietary restrictions suggest that physicians were effective in recommending KDIGO strategies in the study setting.

We found that in group IIIA, 5 (100.0%) patients had a history of dietary phosphate restriction. In stage IIIB, 15 (93.8%) patients had a history of dietary phosphate restriction. In group IV, 13 (86.7%) patients had a history of dietary phosphate restriction. In group V, 7 (50%) patients had a history of dietary phosphate restriction. The association between history of dietary phosphate restriction and stage was statistically significant (p=0.0096). Our study produces statistically significant data on phosphate restriction in patients with CKD, which is comparable to the study by Toussaint et al to match.[9]

Comparing the CKD patients in the dialysis group and the ND group in our study revealed that 36 (72%) and 22 (44%) patients used phosphate binders, respectively. This association between phosphate binder use and group was statistically significant (p=0.0045). Our result is slightly higher than in a study by Bhandari et al 192 in the USA, in which 27% of patients in the ND-CKD group used phosphate binders (27%).[10] However, there is no clear evidence as to whether the use of phosphorus binders in chronic kidney disease improves survival or not. However, the high proportion in our study compared to real-world evidence from the US could potentially be due to the fact that our study setting is a tertiary care setting and is based on evidence from a single center.

Approximately 5 (31.3%) patients experienced the use of phosphate binders in stage IIIB. In group IV, 7 (46.7%) patients used phosphate binders and in group V, 10 (71.4%) patients used phosphate binders. The association between phosphate binder use and CKD stage was statistically significant (p=0.0255). As the stage progresses, the use of phosphate binders also increases. Our study suggests that a good proportion of CKD patients were prescribed phosphate binders. Barreto et al noted in a review that hyperphosphatemia is a common complication in CKD patients, especially those requiring RRT.[8]

Among patients who used phosphate binders in our study, 38 (65.5%) patients also reported a history of dietary phosphate restriction. Our study confirmed the studies of Chan et al, Suki et al, which focused on dietary restrictions along with phosphate binders. We did not find a strong association between history of dietary phosphate restriction and use of phosphate binders, which was not statistically significant (p=0.9046).[11,12] This could be due to the different intestinal absorption pattern of phosphate. In addition, the removal of phosphate by dialysis may vary depending on the treatment. The effectiveness of binder therapy can vary twofold in patients.[13]

The serum calcium level in our study revealed that 74 (74.0%) of the patients were at a low level and only 26 (26.0%) of the patients had a normal serum calcium level. Group-wise analysis revealed that all patients in the CKD dialysis group, 50 (100.0%) patients, had low serum calcium levels. In the ND-CKD group, 24 (48.0%) patients had low serum calcium levels and 26 (52.0%) patients had normal serum calcium levels. The association between serum calcium level and group was found to be statistically significant (p<0.0001). These results are consistent with those of Jahan et al 183. We observed significantly decreased serum calcium levels in patients with early-stage chronic kidney disease compared with controls (p<0.001). In the CKD dialysis group, the mean (SD) serum calcium value of the patients was 7.07±0.47. In the ND CKD group, the mean ± S.D. The serum calcium level of the patients was 8.40±0.98. The difference in mean serum calcium was statistically significant in the ND-CKD group (p<0.0001). A study by Kim et al reported a serum calcium level of 9.1±0.7 mg/dL, which is slightly higher than our results. This could possibly be due to SHPT in our study.[14] Therefore, early detection and treatment of biochemical SHPT are crucial to prevent or control the consequences of complications of CKD.[15]

In our study, it was found that in the stage IV ND CKD group, the mean ± SD of patients' serum calcium was 8.30±0.33. In the stage V ND CKD group, the mean ± SD of patients' serum calcium was 7.05±0.50. The mean serum calcium level was lower in stages IV and V, which was statistically significant (p<0.0001). The study by Jahan et al. reported that the mean values of serum calcium and phosphorus levels in the patient group were 2.53±0.50 mg/dl and 3.77±0.42 mg/dl and in the controls, group were 3.67±2.37 mg/dl and 13 .66±6.34 mg/dl. This is slightly lower than reported by Jahan et al.[16]

In-depth analysis of serum phosphate levels in our study revealed that 71 (71.0%) patients had high serum phosphate levels and 29 (29.0%) patients had normal serum phosphate levels. There is a strong association between serum phosphate levels between the CKD dialysis and ND-CKD groups and it was found to be statistically significant (p<0.0001). Our study results agree with the results of Li et al with serum higher phosphorus levels in end-stage renal disease and levels >5.5 mg/dl leads to increased mortality.[17] In our study, we found that in the stage IV group, the mean (SD) of serum phosphate was 4.50±0.27, while the mean (SD) in the stage V group was 5.70±0.23. The difference in mean serum phosphate was higher and statistically significant in stages IV and V (p<0.0001). Our study confirms the results of an Indonesian study by Masyeni et al and Bellasi et al.[17,19] Masyeni et al reported that higher than normal phosphate levels were found in up to 69% of samples.[18] In their study of stage V patients, the mean (SD) phosphate level was 4.98 (1.6). Your findings. Additionally, their study reported that older participants had high serum phosphate levels. As kidney failure progresses, chronic phosphate exposure occurs188. The authors reported that in their study in older people, the correlation of age with higher phosphate levels may be related to worsening kidney function.

Our study results indicate high serum phosphate levels, which is consistent with the results of Valson et al, which showed that 59% of patients with stage IV and V chronic kidney disease had high serum phosphate levels.[20] Our study found increased phosphorus content, which is consistent with the study of NafarMet al and Tonelli et al.[21,22] Nafar et al found hyperphosphatemia in 34.2% of patients on dialysis over 3 months in their study in Iran.[21] Furthermore, our study results are consistent with the study by Singh et al which found that virtually all patients develop hyperphosphatemia, and those with serum phosphorus (>6.5 mg/dL) are at higher risk of death.[23] The increase in PTH levels reduces the filtered phosphate load and maintains phosphate elimination at a normal

level, although the decrease in the filtered phosphorus load is due to the reduction in the glomerular filtration.[19]

For dialysis CKD serum phosphate with high phosphorus levels, 49 (69.0%) patients had statistically significant use of phosphate binders (p=0.0004). In the dialysis CKD group with high serum phosphorus level, 40 (56.3%) patients had a history of dietary restriction. We found that there was a strong association between history of dietary restrictions and serum phosphate level, which was statistically significant (p=0.0014). Phosphorus accumulation is associated with poor outcomes.[7] The main challenge is in what range serum phosphate levels should be maintained in the stages of CKD to improve clinical outcomes. Dietary restrictions and phosphate binders play an important role.

In this study, we found that the mean (SD) serum PTH in the dialysis CKD group was 622.64±59.91. In the ND-CKD group, the mean (SD) serum PTH was 478.04±123.02. The difference in mean serum PTH was higher in the dialysis CKD group and this was found to be statistically significant (p<0.0001). Our study is consistent with the studies of Valson et al who found hyperparathyroidism in 89.3% of patients with stage IV and V CKD.[20] Furthermore, in our study, it was found that the mean serum PTH level was higher in stage IV and V was statistically significant (p<0.0001). Our findings of increased PTH are consistent with the results of Pontoriero et al 208 who showed an increase in PTH levels in stage III-V CKD.

The mean PTH level increases as kidney failure progresses. Our study confirms the study by Martins et al in Brazil, which showed (iPTH>300 pg/ml).[24] A study by Nafar et al in Iran among HD patients reported that about 29.3% had iPTH > 300 pg/ml.[21] The difference in mean PTH may possibly be due to variability in bioassays and standards in a different laboratory. Hypercalcemia and hyperphosphatemia were observed in 20.6% and 34.2% of patients.

Phosphorus may be one of the key factors in the relationship between vascular calcification and low bone turnover. In contrast to the previous changes observed in FGF-23, Klotho, calcitriol and PTH, they only began to increase in CKD IIIb. Hyperphosphatemia is one of the most important uremic non-traditional risk factors associated with vascular calcification in CKD patients. Although studies of phosphate binders have shown that they are effective in reducing serum phosphate levels, their role and contribution to clinical outcomes are still controversial.[25] Well-designed, large-scale, placebo-controlled studies are needed to demonstrate the reduction of serum phosphate by phosphate binders improves clinical outcomes.

We found that in the dialysis CKD group, the mean (SD) blood urea nitrogen of the patients was 73.44±6.88. In the ND-CKD group, the mean (SD) blood urea nitrogen of the patients was 66.08±11.99. Mean blood urea nitrogen was higher in the ND-CKD group and this was statistically significant (p=0.0003). In the dialysis-CKD group, the mean ± SD of patients' serum creatinine was 7.14±0.25. In the ND-CKD group, the mean±SD of patients' serum creatinine was 5.77±1.28. The mean serum creatinine level was higher in the dialysis CKD group and this was statistically significant (p<0.0001). As the stage progresses, the serum creatine level also increases. The mean blood urea nitrogen level and serum creatinine level were higher in stages IV and V which were statistically significant (p<0.0001). The accumulation of urea in the blood serum of patients with kidney failure arises mainly from the breakdown of food and tissues such as muscles. This causes the body to become very sick if it is not eliminated through the kidneys. Our study results on the association between kidney failure and serum creatinine levels were reported by Noor et al supported.[26]

In our study, we found that the mean (SD) estimated GFR among patients in the dialysis CKD group was 12.22±1.69. In the ND CKD group, the mean (SD) estimated GFR of patients was 27.14±12.73. The mean estimated GFR was higher in the ND-CKD group and this was statistically significant (p<0.0001). Furthermore, the mean estimated GFR was lower in stages IV and V, which was found to be statistically significant (p<0.0001). In our study, GFR was found to be higher in dialysis CKD patients than in Europe and the USA.[27,28] The high GFR in our study might be due to the inclusion of dialysis patients with unstable diseases such as acute left heart failure, hyperkalemia, and others

Recent observational studies in patients with stage III-V CKD who were not on dialysis have shown that mild increases in PTH levels are also associated with increased cardiovascular risk, independent of serum levels of phosphorus, calcium and vitamin D. Treatment. Singh et al found that almost all patients with end-stage renal disease develop hyperphosphatemia and those with serum phosphate levels >6.5 mg/dl have a significantly higher risk of mortality, mainly due to calcification of the heart, lungs and Soft tissue.[23,29] In conclusion, treatment of hyperphosphatemia is critical factor in preventing death and disability in CKD patients and in CKD stage III and IV patients between >2.7 and <4.6 and in CKD or dialysis patients in stage V should be between 3.5 and 5.5.

Limitations

This study despite having various strengths still reports few limitations. The notable shortcoming of this study was that it has been done in a single centre. Besides, it was carried out in a tertiary care hospital, so Berkson's bias cannot be ruled out. To generalize the study findings to a wider population there is a need to increase the sample size and conduct a multi-centric study.

CONCLUSION

Compared with CKD patients in the ND group, we found that serum phosphate levels were significantly higher in dialysis patients. In CKD patients without dialysis, serum phosphate levels increased gradually from stage IIIA to V, and this was found to be statistically significant. Dialysis patients with CKD and those in the stage V ND group are associated with hyperphosphatemia. According to our findings, there may be an association between dialysis patients with chronic kidney disease and those in the stage V ND group with low serum calcium levels. A statistically significant correlation was found between the proportion of phosphate binder used in patients with stage V chronic kidney disease and that of stages III and IV. Compared to ND-CKD patients, dialysis CKD patients used phosphate binders more frequently. A statistically significant increase in history of dietary phosphate restriction was observed in ND-CKD patients. More CKD patients receiving dialysis used dietary phosphate restrictions and phosphate binders, and these correlations were found to be statistically significant.

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