Original Article

A study of serum phosphate in maintenance Haemodialysis patients

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Abstract: *Hyperphosphataemia is associated with various adverse effects. Its management is a challenge to maintain a good quality of life in a patient chronic kidney disease (CKD) with maintenance haemodialysis (MHD). Currently it is managed by maintaining adequate haemodialysis (HD), reducing circulating level of phosphate with oral binders and parathyroid hormone (PTH) with vitamin D analogs and/or the calcimimetics. There is no baseline study in Bangladeshi patients who are getting the management of chronic kidney disease- bone mineral derangement CKD-MBD) according to guideline given by Kidney Disease Outcome Quality Initiative (K/DOQI). So this study aims to determine the serum phosphate level in haemodialysis patients in Bangladesh according the target range of K/DOQI. This study was a cross sectional observational study conducted in the haemodialysis unit of National Institute of Kidney Disease and Urology (NIKDU) and Bangladesh Institute of Research & Rehabilitation on Diabetes, Endocrine and Metabolism (BIRDEM). The patients getting maintenance haemodialysis in National Institute of Kidney Disease and Urology (NIKDU) and also Bangladesh Institute of Research & Rehabilitation on Diabetes, Endocrine and Metabolism (BIRDEM) were enrolled in this study. Laboratory findings of the study patients, it was observed that the percentages of patients (drug history related to phosphate binder) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 41.1% & 39.1% respectively and patients (no drug history related to phosphate binder) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 33.3% & 46.2% respectively. The patients (no drug history related vitamin D) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 42.3% & 42.4% respectively. More than a half of the patients presented with hyperphosphataemia and half of the patients presented with below the target range of parathormone in respect to the degree of achievement of the status of serum phosphate and parathyroid hormone level according to K/DOQI guidelines in maintenance haemodialysis patients.*

Keywords: *Chronic kidney disease, Haemodialysis, Kidney Disease Outcome Quality Initiative, Chronic kidney disease- bone mineral derangement, Calcimimetics, Parathyroidectomy*

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Introduction

Chronic kidney disease has become a major health concern with a high prevalence worldwide. It is estimated that in Asia, nearly one in 10 people has some degree of kidney dysfunction, affecting almost 150 million individuals. A common consequence of chronic kidney disease is secondary hyperpara-thyroidism, which is largely attributed to the retention of phosphate.[1] Streja et al. reported that in patients on maintenance hemodialysis, hyperphosphatemia is associated with both high serum PTH levels and excessive dietary protein intake.[2] Secondary hyperparathyroidism (SHPT) is managed by reducing circulating levels of phosphate with oral binders and parathyroid hormone (PTH) with vitamin D analogs and/or the calcimimetic cinacalcet.[3] Prior to the availability of commercial

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intact parathyroid hormone (PTH) assays, serum total alkaline phosphatase (TAP) measurements were used as one of the surrogate markers of high bone turnover that was utilized in the management of chronic kidney disease mineral and bone disorder (CKD-MBD).[4] A study showed that elevated levels of alkaline phosphatase, independent of PTH, calcium, or phosphorus as predictor of coronary artery calcification in haemodialysis patients.[5] Interestingly, in a recent secondary analysis of HERO trial, there were association between high levels of alkaline phosphatase and hypo responsiveness of erythropoietin stimulating agent.[6] These findings may likely explain the unclear pathophysiologic link between high serum alkaline phosphatase and mortality in haemodialysis patients.[5]

Materials and Methods: This study was a cross sectional study. This study was done in the haemodialysis unit of National Institute of Kidney Disease and Urology (NIKDU) and Bangladesh Institute of Research & Rehabilitation on Diabetes, Endocrine and Metabolism (BIRDEM). The patients getting maintenance haemodialysis in National Institute of Kidney Disease and Urology (NIKDU) and also Bangladesh Institute of Research & Rehabilitation on Diabetes, Endocrine and Metabolism (BIRDEM) were enrolled in this study. Blood specimens were collected for measurement of serum iPTH, serum creatinine, serum albumin, phosphate and alkaline phosphatase. Fasting blood samples were collected from the AVF. Specimens were allowed to clot at room temperature. Serum was separated from the cells by centrifugation. Serum iPTH was quantitatively measured by IMMULITE 2000, is a solid phase, two site chemiluminescent enzyme-leveled immunometric assay in Department of Microbiology of Bangabandhu Shiekh Mujib Medical University (BSSMU). Serum creatinine, serum calcium, serum inorganic phosphorus, serum alkaline phosphatase, serum albumin was measured by automated analyzer, Humalyzer 3000, Germany. Collected data were compiled and appropriate analyses were done by using computer based software, Statistical Package for Social Sciences (SPSS) version 23. Results were expressed as frequency, percentage and mean ±SD.

Results:

Majority 47(39.2%) patients were age belonged to 51-60 years and mean age was found 50.4±13.13 years. Male were predominant in this study patients. Male female ratio was 1.3:1. BMI of the study patients, it was observed that majority 49(40.8%) patients had normal range (18.5-22.9 kg/m^2) BMI. The mean BMI was found 23.5±4.7 kg/m^2 with range from 15.6 to 45.5 kg/m^2. 114(95.0%) patients had HTN and 56(46.7%) patients had DM (Table I). In this study patients, drug history related to Vit-D (Calcitriol), it was observed that 61(50.8%) were using that drug (Figure 1). Duration of haemodialysis was 25.55±25.0 months and 71(59.2%) patients had twice haemodialysis session/weeks (Table II). Laboratory findings of the study patients, it was observed that mean serum PO_4 was 5.74±1.49 mg/dl (Table III). Achievement of the four recommendations of K/DOQI guidelines was only 9(7.5%) (Figure 3). The percentages of patients (drug history related to phosphate binder) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 41.1% & 39.1% respectively (Table IV). The percentages of patients (no drug history related to phosphate binder) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 33.3% & 46.2% respectively (Table V). The percentages of patients (drug history related vitamin D) who received dialysis twice & thrice per week and within the target range of serum levels were as follows : serum phosphate: 37.8% & 43.8% respectively (Table VI). The percentages of patients (no drug history related vitamin D) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 42.3% & 42.4% respectively (Table VII).

Table I: Distribution of the patients by demographic profiles (n=120)

Patients profile	Number of patients	Percentage
Age (years)		
Mean±SD	50.4±13.31	
Range (min-max)	(19-76)	
Sex		
Male	67	55.8
Female	53	44.2
BMI (kg/m$^{2)}$	23.5±4.7	
Range (min-max)	(15.6-45.5)	
HTN	114	95.0
DM	56	46.7

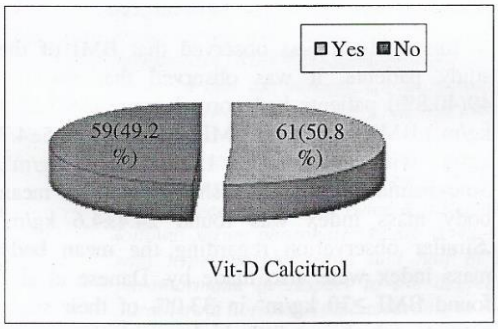

Figure 1: Drug history related to Vitamin-D (Calcitriol) of the study patients

Table II: Distribution of the study patients related to haemodialysis (n=120)

Haemodialysis (months)	Number of patients	Percentage
<6	8	6.7
6-18	52	43.3
>18	60	50.0
Mean±SD	25.55 ±25	
Range (min-max)	(1.5 -228)	
Haemodialsysis session/Wk		
Twice(<8 hours)	71	59.2
Thrice(>8 hours)	49	40.8

Table III: Distribution of the study patients by laboratory findings (n=120)

Laboratory findings	Number of patients	Percentage
S. PO_4 (mg/dl)		
<3.5	5	4.2
3.5-5.5	49	40.8
>5.5	66	55.0
Mean±SD	5.74 ±1.49	
Range (min-max)	(2.8 -9.1)	

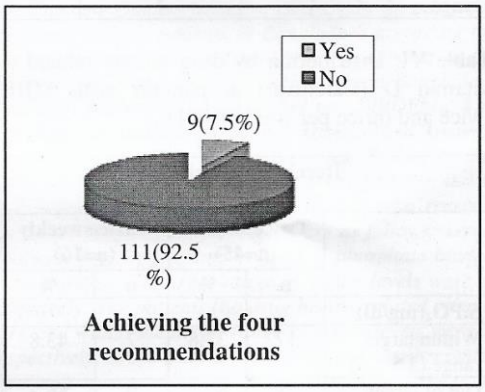

Figure 3: Showing achievement of the four recommendations of the study patients.

Table IV: Distribution by drug history related to phosphate binder in patients with MHD twice and trice per week (n=79)

Received phosphate binder (n=79)				
	Twice weekly (n=56)		Thrice weekly (n=23)	
	n	%	n	%
S.PO_4(mg/dl)				
Within target range (3.5-5.5)	23	41.1	9	39.1
Out of target range	33	58.9	14	60 .9

Table V: Distribution by drug history not related to phosphate binder in patients with MHD twice and trice per week (n=41)

	Nor received phosphate binder (n=41)			
	Twice weekly (n=15)		Thrice weekly (n=26)	
	n	%	n	%
S.PO_4(mg/dl)				
Within target range (3.5-5.5)	5	33.3	12	46.2
Out of target range	10	66.7	14	53.8

Table VI: Distribution by drug history related to vitamin D (Calcitriol) in patients with MHD twice and thrice per week (n=61)

	Received vitamin-D (n=61)			
	Twice weekly (n=45)		Thrice weekly (n=16)	
	n	%	n	%
S.PO_4(mg/dl)				
Within target range (3.5-5.5)	17	37.8	7	43.8
Out of target range	28	62.2	9	56.3

Table VII: Distribution by drug history not related to vitamin D (Calcitriol) in patients with MHD twice and thrice per week (n=59)

	Not received vitamin-D (n=59)			
	Twice weekly (n=26)		Thrice weekly (n=33)	
	n	%	n	%
S.PO_4(mg/dl)				
Within target range (3.5-5.5)	11	42.3	14	42.4
Out of target range	15	57.7	19	57.6

Discussion:

In this study majority 47(39.2%) patients were age belonged to 51-60 years and mean age was found 50.4±13.13 years. Soleymanian et al.[7] study observed that the mean age was found 56±415.4 years. Similarly, Mahdavi-Mazdeh et al.[8] have observed the mean age of the patient's was 53.4 ± 17.1, which support the present study. On the other hand, Stevens et al.[9] and Danese et al.[10] has observed higher mean age of the haemodialysis patients, which were was 60± 17 years and 61±15 years respectively. The higher mean age maybe due to increased life expectancy, geographical and racial influences have significant impacts on CKD patients.

In this series it was observed that male were predominant in this study patients. Male female ratio was 1.3:1. Soleymanian et al.[7] study observed that males were found 57.0%, which is consistent with Mahdavi-Mazdeh et al.[8]; Danese et al.[10], where all the above authors found renal disease is predominant in male subjects.

In this study it was observed that BMI of the study patients, it was observed that majority 49(40.8%) patients had normal range (18.5-22.9 kg/m^2) BMI. The mean BMI was found 23.5±4.7 kg/m^2 with range from 15.6 to 45.5 kg/m^2. Soleymanian et al.[7] study showed that the mean body mass index was found 24.4±4.6 kg/m^2 .Similar observation regarding the mean body mass index were also made by, Danese et al.[10] found BMI ≥30 kg/m^2 in 33.0% of their study patients, which is a little higher with the current study.

In this study patients, drug history related to Vit-D (Calcitriol), it was observed that 61(50.8%) were using that drug. Oral calcitriol was the only vitamin D derivative used and was prescribed in 33% of the patients observed by Lorenzo et al.[11]. In another study, Vitamin D treatment was administered in 48% of patients obtained by Maduell et al.[13], which support with the present study.

Duration of haemodialysis was 25.55±25.0 months and 71(59.2%) patients had twice haemodialysis session/weeks. In study of Mahdavi-Mazdeh et al.[8] found more than ninety percent (90.3%) received thrice haemodialysis session per week, 9.0% received twice

haemodialysis session per week and 0.7% received once haemodialysis session per week.

In present study observed that Laboratory findings of the study patients, it was observed that mean serum PO_4 was 5.74±1.49 mg/dl. Soleymanian et al.[7] study reported that the mean serum phosphorus was 5.5±1.3 mg/dl. Fernandez-Martin et al.[14] study observed mean serum phosphorus was 5.4 ± 1.4 mg/dl. Kimata et al.[13] and Danese et al.[10] found the mean serum phosphorus were 5.6±1.8 mg/dl and 5.4±1.5 mg/dl respectively, which are also consistent with the current study. Kimata et al.[13]; Danese et al.[10]; Maduell et al.[13] and Lorenzo et al.[11] made higher observations. The findings of the all above authors are comparable with the current study.

In current study observed that achievement of the four recommendations of K/DOQI guidelines was only 9(7.5%). Mahdavi-Mazdeh et al.[8] study illustrated the difficulty in the management of calcium and phosphorus metabolism, and showed that less than 2% and 35% of the population achieved all the 4 or 3 K/DOQI guideline targets for the laboratory tests, respectively. Young et al.[16] showed that only 4.6% and 5.5% of patients, respectively, achieved all the 4 goals of the K/DOQI for mineral metabolism. Maduell et al.[13] highlighted that 7.3% (out of 2392 dialysis patients) achieved all the targets.

The percentages of patients (drug history related to phosphate binder) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 41.1% & 39.1% respectively. The percentages of patients (no drug history related to phosphate binder) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 33.3% & 46.2% respectively. The percentages of patients (drug history related vitamin D) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 37.8% & 43.8% respectively. Kim et al.[17] study observed that phosphorus binders were used by 72.3% of the study participants and vitamin D receptor agonists were used by 45.9% of the participants. The percentages of patients (no drug history related vitamin D) who received dialysis twice & thrice per week and within the target range of serum levels were as follows: serum phosphate: 42.3% & 42.4% respectively.

Conclusion: This study was undertaken to evaluate the degree of achievement of the status of serum calcium, phosphate and parathyroid hormone level according to K/DOQI guidelines in maintenance haemodialysis patients. Majority of the haemodialysis patients were in 6th decade and with male predominance. Most of the haemodialysis patients came from urban area. More than two thirds of the haemodialysis patients got phosphate binder and hypocalcaemia was more than hypercalcaemia. More than a half of the patients presented with hyperphosphotaemia. The individual parameters (Ca, PO4, iPTH and Ca X P), according to K/DOQI guidelines for mineral metabolism in haemodialysis patients, were achieved in various proportion but only a little proportion was achieved by all the four recommendations. Almost a half of the patients presented with below the target range of parathormone.

Authors Contributions: Research idea and study design: MEJ, MMR; data acquisition: MEJ, MMR, MSI, MAR, ANMAH; data interpretation: MEJ, MMR, MSI, MAR, ANMAH; Supervisions or mentorship: MMR; Muhammad Ehsan Jalil is the primary author and other authors contributed important intelectual content during manuscript drafting or revision accepts accountability of the overall work.

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