Serum calcium, phosphate and parathormone levels status in patients with end stage renal disease on maintenance haemodialysis

R Hasan[1], MN Chowdhury[2], MM Rahman[3], ASMT Anwar[4], A Wazib[5], T Shams[6]

Abstract

Background: Chronic kidney disease (CKD) has a progressive course in most cases, and final results may be End Stage Renal Disease (ESRD). Hemodialysis (HD) is one of the mainstays in the treatment of these patients. Disturbance in calcium (Ca), phosphate (PO4) and parathormone (PTH) metabolism are observed in these patients. The aim of this study was to determine serum calcium, phosphate and parathormone levels in patients with CKD stage 5 on maintenance haemodialysis (MHD), as well as to compare these levels with reference of National Kidney Foundation Dialysis Outcomes Quality Initiative (KDOQI) targets in patients on MHD. ***Methodology:*** This descriptive, cross-sectional study was performed over 191 patients on MHD for > 3 months in department of Nephrology of Dhaka Medical College Hospital, National Institute of Kidney Diseases and Urology and Bangabandhu Sheikh Mujib Medical University, Dhaka, in 2014. ***Results:*** Among the 191 study patients, 60 percent subjects presented with the serum calcium level bellow, 33% had serum calcium level within and 7 percent had serum calcium level above the target level (8.4 - 9.5 mg/dl) according to KDOQI guideline. Eighty six (45 percent) subjects had serum phosphate within the target level (3.5 - 5.5 mg/dl). Sixty four (33 percent) were hypophosphataemic and 22 percent were hyperphosphataemic. Serum parathormone level was below normal (<150 pg/ml), normal (150-300 pg/ml) and above normal (>300 pg/ml) in 55 (28.8 percent), 95 (49.7 percent) and 41 (21.5 percent) study subjects, respectively. ***Conclusions:*** Most of patients with ESRD on MHD of study population did not achieve the recommended K/DOQI target ranges of serum calcium, phosphate and parathormone levels. It is necessary to carry out more extensive study for the improvement of mineral metabolism using multi-disciplinary management approaches.

Key words : End stage renal disease, haemodialysis, calcium, phosphate, parathormone, Bangladesh.

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Introduction

End Stage Renal Disease (ESRD) is one of the main health problems of the communities worldwide. Hemodialysis (HD) is one of the main options of treatment of ESRD[1]. The incidence of CKD is increasing rapidly. According to the data of Bangladesh Renal Registry report, almost twenty millions of Bangladeshi adults are suffering from various stages of CKD. In Bangladesh approximately 100-120 patients per million populations (PMP) reach End Stage Renal Disease (ESRD) every year[2]. Over 500000 patients live with ESRD in the United State, of whom 72% have undergone long-term dialysis and 28% have received kidney transplantation[3].

Calcium and phosphate are essential for normal cardiovascular and neuromuscular function, and for many enzyme-mediated and cellular signaling processes. Calcium, phosphate and parathormone provide structural integrity to the skeleton, which is the primary depot of mineral ions in the body. The management of abnormal calcium with phosphate metabolism as well as hyperparathyroidism in patients with CKD is a common problem. The bone mineral metabolism abnormalities that occur in renal disease are now encompassed in the term chronic kidney disease mineral bone disorder (CKD-MBD)[4]. When glomerular filtration rate

1. Dr. Rafiqul Hasan
Assistant Professor (Nephrology)
Cox's Bazar Medical College.

2. Prof. Md Nizamuddin Chowdhury
Professor and Head, Department of Nephrology,
Dhaka Medical College.

3. Prof. M Muhibur Rahman
Professor and Head, Department of Nephrology
Sir Salimullah Medical College.

4. Dr. ASM Tanim Anwar
Registrar, Department of Nephrology
Dhaka Medical College.

5. Dr. Amit Wazib
Junior Consultant, Department of Neurology
Dhaka Medical College.

6. Dr. Tarek Shams
Medical Officer, Chittagong Medical College Hospital.

Correspondence
Dr. Rafiqul Hasan
e-mail : rafiquek54@yahoo.com

(GFR) falls, the phosphorus clearance decreases significantly, leading to phosphorus retention. This hyperphosphatemia remains subclinical when estimated GFR is >30 mL/min, and suppresses calcitriol (dihydroxy vitamin D3) production. Accompanied by decreased calcitriol production by reduced kidney mass, decreased calcitriol causes reduced calcium absorption from the gastrointestinal tract resulting in hypocalcemia. Phosphorus induces PTH secretion by 3 mechanisms: direct stimulatory effect on the parathyroid glands, induction of mild hypocalcemia by precipitating with calcium as CaHPO4, and stimulation of fibroblast growth factor-23 (FGF-23), which leads to severe inhibition of 1-a hydroxylase and depressed level of 1,25 dihydroxy vitamin D[5]. PTH secretion is appropriate in this case and along with FGF-23 it can decrease the tubular reabsorption of phosphorus to <15%. This is a relatively steady state: the phosphorus and calcium levels are back to normal, though at the expense of high PTH and FGF-23. When GFR falls below 30 ml/min (CKD stage 5), the tubular reabsorption of phosphorus cannot be further lowered, causing more PTH and FGF-23 secretion. Even though tubular reabsorption of phosphorus is maximally suppressed, there are too few nephrons left to balance the continuing phosphorus intake. Although PTH is no more active on the kidney, its action on the bone is maintained and continues to promote calcium and phosphorus release. The end result is a vicious cycle in which high phosphorus causes PTH secretion and PTH causes more hyperphosphatemia. Elevated phosphorus and calcium- phosphorus product have also been linked to increased mortality among patients on dialysis[6-10]. Elevated phosphate levels may hasten the loss of kidney function, possibly via calcium-phosphorus precipitation. Abnormal serum calcium, phosphate and PTH level have been associated with mortality in dialysis patients and are important in the strategy of controlling all aspects of CKD-MBD. A large number of treatment options are now available: diet, calcium, calcium content of the dialysate, phosphate binders, vitamin D supplement and parathyroidectomy[7,10].Moreover excessive calcium supplements are associated with an increased risk of myocardial infarction[11,12]. So, such patients need treatment to correct abnormal calcium metabolism and periodic monitoring to avoid adverse events. In this study, we had tried to evaluate calcium, phosphate and parathormone levels in ESRD patients on MHD and compare it with reference to National Kidney Foundation Dialysis Outcomes Quality Initiative (KDOQI) targets in patients on haemodialysis[13].

Methods

This descriptive, cross-sectional study was carried out from 1st January 2014 to 31st December 2014 with the study population of patients of CKD-5(D) older than 18 years on maintenance haemodialysis (MHD) for more than 3 months in department of Nephrology of DMCH, NIKDU and BSMMU.

Purposive sampling method was followed and total 191 patients were selected.

The aims of this study were to describe serum calcium, phosphate and parathormone status of ESRD patient on MHD as well as to compare these levels with reference to KDOQI targets in patients on haemodialysis.

Prior to the commencement of this study, the research protocol was approved by the responding authority of Dhaka University. The objectives of this study along with risks and benefit were fully explained to the patients in easily understandable local language and then informed written consent was taken from each patient.

All the relevant collected data were compiled on a master chart first. Then organized by using scientific calculation and standard statistical formulas, percentage was calculated to find out the proportion of the findings. The results were presented in tables and figures.

Results

Total number of patients was 191, male were 113, female 78. Mean age was 54.6 ±10.4 (range 19-76) years. Majority of the patients aged between 35 and 55 years, from urban areas and married with monthly income of Taka 20,000 or more. The basic demographic variables of the patients in this study were shown in table I. Mean ± SD of duration of dialysis was 18.01±11.94 and all patients of the study population took haemodialysis 2 times per week.

Table I: Demographic variables

Variable	Data	Frequency	Percentage
Age	Below 35 yrs	41	21.5
	35-55 yrs	86	45.0
	Above 55 yrs	64	33.5
Sex	Male	113	59.2
	Female	78	40.8

Figure 1 shows the serum calcium level of the study subjects in three categories.60 percent subjects had serum calcium level below normal; 33 percent subjects had normal serum calcium and 7 percent subjects had serum calcium above normal level. In CKD patients (Stage 5) treated with hemodialysis the serum albumin corrected total calcium should be maintained within the normal range preferably toward the lower end (8.4 to 9.5 mg/dl)[13].

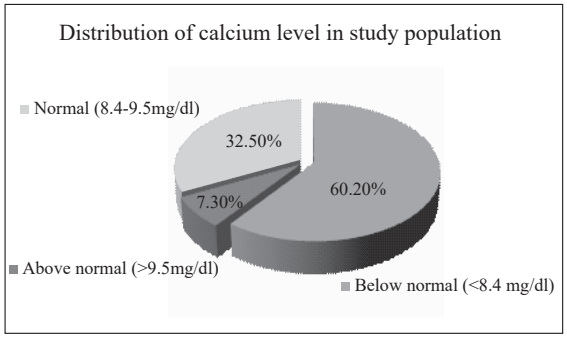

Figure 1: Serum Calcium level

Figure 2 shows the serum phosphate level of the study subjects in three categories. 45 percent subjects had normal serum phosphate, 33 percent subject had serum phosphate level bellow normal and 22 percent subjects had serum phosphate above normal. In CKD patients (Stage 5) treated with hemodialysis the target level of serum phosphate is 3.5 to 5.5 mg/dl[13].

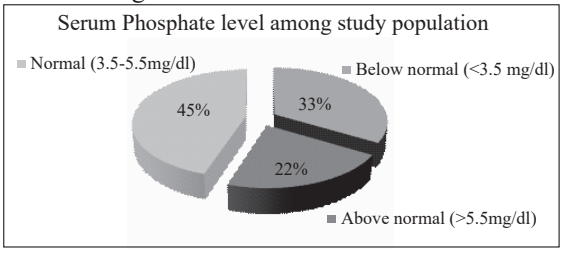

Figure 2: Serum phosphate level

Figure 3 shows the serum parathormone level of the study subjects in three categories. Serum parathormone level was bellow normal, normal, and above normal in 55 (28.8 percent), 95 (49.7 percent) and 41 (21.5 percent) study subjects, respectively. The target level of parathormone in (CKD) stage 5 patients on maintenance haemodialysis is 150-300 pg/ml[13].

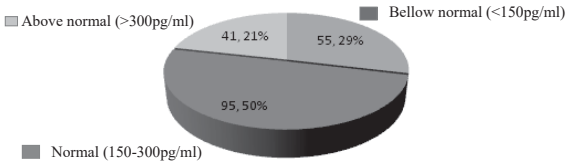

Figure 3: Serum parathormone level

Table-II shows the serum calcium, phosphate and parathormone levels of the study subjects in three categories- normal; bellow normal and above normal categories according to National Kidney Foundation Dialysis Outcomes Quality Initiative (KDOQI) targets in patients on haemodialysis[13].

Table- II: serum calcium, phosphate and parathormone level distribution in study subject

Subject	Category	Value	Frequency	Percentage	Mean
Serum calcium	Below normal	< 8.4 mg/dl	115	(60.2%)	8.07±1.22
	Normal	8.4 - 9.5)mg/dl	62	(32.5%)	8.92±1.03
	Above normal	>9.5 mg/dl	14	(7.3%)	10.97±1.41
Serum phosphate	Below normal	< 3.5mg/dl	64	(33.5%)	3.01±1.03
	Normal	3.5 – 5.5 mg/dl	86	(45.0%)	4.65±1.92
	Above normal	>5.5 mg/dl	41	(21.5%)	6.85±3.11
Serum PTH	Below normal	<150 pg/ml	55	(28.8%)	39.75±15.43
	Normal	150-300 pg/ml	95	(49.7%)	118.23±27.69
	Above normal	>300 pg/ml	41	(21.5%)	247.83±18.61

Discussion

One hundred and ninety one patients of chronic kidney disease (CKD) Stage 5 on maintenance haemodialysis (HD) were included in this study. Majority of cases aged between 35 and 55 years (45 %). The age distribution was similar to that of the previous study conducted in Bangladesh[14]. One hundred and thirteen (59.2 percent) were males and seventy eight (40.8 percent) were females. Similar sex distribution was found in the study on CKD patients in Bangladesh[14]. One hundred and fifteen (60.2 percent) were urban and 76 (39.8 percent) were rural. Similar distribution of residence is found in a study on patients on maintenance haemodialysis, in urban and rural areas of Bangladesh[15,16].

In our study, one hundred and fifteen (60.2 percent) subjects were hypocalcaemic (serum calcium < 8.4 mg/dl), sixty two (32.5 percent) subjects had normal serum calcium (8.4-9.5 mg/dl) and fourteen (7.3 percent) subjects were hypercalcaemic (> 9.5 mg/dl). Francisco M et al found hypocalcemia (<8.4 mg/dL) in 5% of patients and hypercalcemia (>10.2 mg/dL) in 17.8% of ESRD patients on maintenance haemodialysis in Spain[17]. Hosam A S et al. found hypocalcemia (<8.4 mg/dL) in 12.4% of patients and hypercalcemia (>10.2 mg/dL) in

46.3% of ESRD patients on maintenance haemodialysis in Palestine[18]. Dietary deffiency, poor treatment compliance and low sunlight exposure may be responsible for the discriminating findings.

Eighty six (45 percent) subjects had normal serum phosphate (3.5 - 5.5 mg/dl) level. Sixty four (33.5 percent) were hypophosphataemic (serum phosphate < 3.5 mg/dl). Forty one (21.5 percent) subjects were hyperphosphataemic (> 5.5 mg/dl). Francisco M et al found that 16% of patients had hypophosphataemia (<3.5 mg/dl) and 29% of patients presented with hyperphosphotemia (>5.5 mg/dL)[17]. Dietary phosphate restriction, protein energy malnutrition and nonjudicious phosphate binder utilization may play a role in this findings.

Serum parathormone level was below normal (<150 pg/ml), normal (150-300 pg/ml) and above normal (>300 pg/ml) in 55 (28.8 percent), 95 (49.7 percent) and 41 (21.5 percent) study subjects, respectively. In a study in Spain, thirty one percent of patients presented secondary hyperparathyroidism (iPTH >300 pg/mL) and 43% of patients presented iPTH <150 pg/ml[17]. Inappropriate vitamin D3 intake may be responsible for the high distribution of hypoparathyroidism.

Excess use of calcium salts and calcitriol analogs need to be avoided to prevent adynamic bone disease (ABD)[19]. Some study showed doctors should follow the recommendations given in clinical practice guidelines. Furthermore, they must consider the economic impact that their treatment decisions may have[20].

This study had some limitations. Limited number of patients was studied and sampling was done by non-probability technique. Treatment history and its effect on metabolic derangement were not evaluated.

Conclusion

From the findings of this present study, it can be recommended that physicians should evaluate serum PTH, calcium and phosphate levels before prescribing vitamin D and/or calcium supplementation and periodically monitor these levels for those who were already on treatment. However, further studies can be carried out by including large number of study subjects.

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