

Original Research Article

Calcium levels and metabolic disturbance in renal disease patients receiving hemodialysis: a cross sectional study highlighting its association in dialysis patients

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ABSTRACT

Background: The aim of this study was to determine the disturbances in Calcium and other mineral levels in patients on hemodialysis at Tabba Kidney Institute, Karachi, Sindh, Pakistan.

Methods: A cross sectional observational study through convenient sampling technique was conducted from January 2017 to August 2017 at Tabba Kidney Institute, Karachi after obtaining ethical approval. 255 patients, all above 18 years of age and on hemodialysis were included in the study. Multi-organ failure patients on dialysis, other systemic diseased patients on hemodialysis were excluded. Demographic variables, mineral levels, symptoms and supplementations were recorded. SPSS version 20.0 was used for data analysis.

Results: A total of 255 patients on hemodialysis were selected and divided into groups depending upon median years of hemodialysis below and above 5 years of hemodialysis. Median and IQR of calcium were 8.8 and 8.2-9.1 mg/dl for below 5 years, 8.6 and 8.1-9.1 mg/dl for above 5 years (P value=0.44). Median and IQR of phosphate were 4.9 and 3.9-5.7 mg/dl for below 5 years and 4.6 and 3.7-5.5 mg/dl for above 5 years (P value=0.21). Median and IQR of parathyroid hormone were 393 and 212-699 pg/ml for below 5 years and 329 and 128-657 pg/ml for above 5 years. (P value=0.13) Median and IQR of albumin were 4.0 and 3.6-4.2 mg/dl for below 5 years and 4.0 and 3.8-4.3 for above 5 years (P value=0.30). Total of 18 (10.9%) had para thyroidectomy.

Conclusions: Present study showed that significant difference in mineral levels did not exist in patients on hemodialysis as regards to the duration of dialysis. However clinical features had a tendency to decrease as duration of dialysis increased to above 5 years. Para thyroidectomy and itching were two main significant findings in this study.

Keywords: Calcium, Cross sectional study, Developing country, Hemodialysis, Metabolic disturbance, Renal disease

INTRODUCTION

Both morbidity as well as mortality in patients on hemodialysis remains exceptionally high.¹ Since

hemodialysis accompanies profound change in mineral metabolism, abnormal metabolism of minerals leads towards metabolic diseases of bone.² Minerals and bone disorder (MBD) is a predictable complication of dialysis

which is linked with greater risk for cardiovascular calcification as well as arterial dysfunction.³ In dialysis patients the decline of kidney functions are often supplemented by secondary hyperparathyroidism (SHPT) which involves disturbance in mineral metabolism that includes increased levels of serum phosphorus, lower calcium, and elevated parathyroid hormone (PTH).^{4,5} Observational studies have suggested that the biochemical markers in altered mineral metabolism have been linked to poorer clinical consequences among patients having End Stage Renal Disease (ESRD) requiring dialysis.⁶ At the time of starting dialysis, majority of patients have hyperplastic parathyroid glands and so significantly elevated PTH level, that predisposes to its increase along with longer duration of Renal Replacement Therapy (RRT).⁷⁻¹⁰ Numerous other studies report that higher PTH levels might be linked with higher mortality in these populations of patients.^{11,12} PTH's association has not been seen in recent meta-analysis.¹³ Fresh clinical practice guidelines emphasize a PTH targeted level depending upon the stage of CKD and GFR, lesser the GFR, more the PTH level.¹⁴ Biochemical changes in Chronic Kidney Disease and Metabolic Bone Disease (CKD-MBD) includes increased fibroblast growth factor-23 (FGF23) as well as parathyroid hormone (PTH), decreased 1,25-dihydroxyvitamin D (1,25D), elevated serum phosphate, and decreased serum calcium. In addition, reduced calcium absorption and diminished urinary calcium excretion are witnessed, with various other bone disease and extreme vascular and soft tissue calcification. CKD-MBD is linked with an increased risk of fracture and increased rate of cardiovascular events leading to cardiovascular-related deaths.¹⁵ Nonetheless, the underlying disease progression is not fully understood, the originators of the detected abnormalities are uncertain, and conclusive therapies are inadequate. Both negative as well as positive calcium balance pose possible health threats in CKD-MBD: negative balance might raise risk of osteoporosis as well as fracture, and positive balance might raise risk for extra-skeletal calcification and cardiovascular events.¹⁶ There is substantial relationship between factors which influence calcium and phosphate regulation. These influences are more complicated in patients having impaired renal function. Factors which influence phosphate regulation principally modify phosphate absorption from intestines, reabsorption from the kidney and mobilization from and/or uptake by bone. In order to understand potential causes, it is critical to evaluate this association specifically with regards to Parathyroid Hormone (PTH) and Fibroblast Growth Factor-23 (FGF23).¹⁷ PTH plays a vital role in the regulation of both calcium and phosphate homeostasis. Parathyroid glands contain calcium-sensing receptors that sense the extracellular ionized calcium concentration and regulate PTH secretion.¹³ If ionized calcium is reduced (with increased serum phosphate concentration, PTH will be released and exert its phosphaturic effect directly on the kidney.⁶ In addition, PTH stimulates osteoclast activity in the bone to release calcium and phosphate into the

extracellular pool, and also stimulate the activation of vitamin D into its active form.⁸ PTH also reduces the number of Sodium Phosphate (Na-Pi) co-transporters in the proximal tubules, leading to reduced phosphate reabsorption and therefore greater excretion of phosphate by the kidney. This results in decreased serum phosphate, a reduction in calcium excretion and an increase of serum calcium concentration.¹⁸

The aim of this study was to determine the disturbances in the levels of mineral in the body due to hemodialysis and to assess its association with the duration of dialysis.

METHODS

This was a cross sectional observational study through convenient sampling technique conducted for duration of 6 months from January to August 2017 at Tabba Kidney Institute Karachi. Ethical approval was taken from the Institutional review board of Tabba Kidney Institute, Karachi. A total of 255 patients were enrolled in the study after attaining their informed consent. The patients who were on hemodialysis for more than 6 months and were above the age of 18 years were included in the study. Multi-organ failure patients, patients with illnesses other than kidney disease, incomplete data and those who refused to give consent were excluded from this study. The demographic variables such as age, gender dialysis related information such as duration of hemodialysis, levels of calcium, phosphorus, albumin, PTH, ALP were observed and recorded. The recordings of the variables were reported as the median years of hemodialysis, i.e. below (n=143) and above 5 years (n=112) of hemodialysis. Mean rank, sum of ranks along with median and inter quartile range were reported. 91 patients were diabetic, 238 were hypertensive and 65 had ischemic heart disease. Clinical features like fits, fractures, body ache, joint mobility, itching were recorded. Usage of mineral supplements was also reported.

After coding, the data was entered and analyzed using SPSS version 20.0. Descriptive analysis was performed by reporting median and IQR for laboratory investigations. Shapiro-Wilk test was applied to assess the normality of data. Mann Whitney test was applied for quantitative variables. Chi-square test was applied to signify symptoms relating to hemodialysis. The significant P value was set at ≤ 0.05 .

RESULTS

This study comprised of a total of 255 patients having a mean age of 49.43 ± 14.62 years. The mean rank of Calcium in patients of below 5 years of hemodialysis, was 131. Median and IQR of Calcium were 8.8 and 8.2-9.1. For Calcium in patients of above 5 years of hemodialysis, mean rank was 124. Median and IQR of Calcium were 8.6 and 8.1-9.1 (P value 0.44). For phosphate in patients of below 5 years of hemodialysis,

mean rank was 133. Median and IQR of phosphate were 4.9 and 3.9-5.7. For Phosphate in patients of above 5 years of hemodialysis, mean rank was 121. Median and IQR of Phosphate were 4.6 and 3.7-5.5 (P value 0.21). For PTH in patients of below 5 years of hemodialysis, mean rank was 134.14. Median and IQR of PTH were 393 and 212-699. For PTH in patients of above 5 years of hemodialysis, mean rank was 120. Median and IQR of PTH were 329 and 128-657 (P value 0.13). For ALP in patients of below 5 years of hemodialysis, mean rank was

133. Median and IQR of ALP were 153 and 118-254. For ALP in patients of above 5 years of hemodialysis, mean rank was 120. Median and IQR of ALP were 137 and 101-219 (P value 0.16). For albumin in patients of below 5 years of hemodialysis, mean rank was 123. Median and IQR of albumin were 4.0 and 3.6-4.2. For albumin in patients of above 5 years of hemodialysis, mean rank was 133. Median and IQR of albumin were 4.0 and 3.8-4.3 (P value 0.30) (Table 1).

Table 1: Mineral levels with median and IQR in relation to hemodialysis groups.

Variables, n=255	Below 5 years of HD (n=143)		Above 5 years of HD (n=112)		P value
	Mean Rank (Sum of ranks)	Median (IQR)	Mean Rank (Sum of ranks)	Median (IQR)	
Calcium mg/dl	131 (18753)	8.8 (8.2-9.2)	124 (13887)	8.6 (8.1-9.1)	0.44
Phosphate mg/dl	133 (19044)	4.9 (3.9-5.7)	121 (13595)	4.6 (3.7-5.5)	0.21
PTH pg/ml	134.14 (19182)	393 (212-699)	120 (13457)	329 (128-657)	0.13
ALP I/U	133 (19127)	153 (118-254)	120 (13513)	137 (101-219)	0.16
Albumin mg/L	123 (17698)	4.0 (3.6-4.2)	133 (14942)	4.0 (3.8-4.3)	0.30

Table 2: Chi-square test applied for association of symptoms with hemodialysis groups.

Variables n=255	Below 5 years of HD (n=143)		Above 5 years of HD (n=112)		P value
	Yes (%)	No (%)	Yes (%)	No (%)	
Fits	05 (3.5)	138 (96.5)	02 (1.8)	110 (98.2)	0.41
Para thyroidectomy	11 (7.7)	132 (92.3)	17 (15.2)	95 (84.8)	0.05
Fractures	12 (8.4)	131 (91.6)	06 (5.4)	106 (94.6)	0.35
Body ache	88 (61.5)	55 (38.5)	67 (60)	45 (40.2)	0.78
Tetany	20 (14)	141 (98.6)	02 (1.8)	110 (98.2)	0.81
Mobility	56 (39.2)	87 (60.8)	45 (40.2)	67 (59.8)	0.87
Itching	12 (8.4)	131 (91.6)	20 (17.9)	92 (82.1)	0.02

Frequency of symptoms in hemodialysis patients were recorded as below and above 5 years of hemodialysis. The presence of fits in patients below 5 years of hemodialysis was 05 (3.5%) while 138 (96.5%) had no reporting of fits. The presence of fits in patients above 5 years of hemodialysis was 02 (1.8%) while 110 (98.2%) had no reporting of fits (P-value 0.41). Para thyroidectomy in patients of hemodialysis below 5 years was present in 11 (7.7%) of patients while in 132 (92.3%) patients, no report of para thyroidectomy was seen. Para thyroidectomy in patients of hemodialysis above 5 years was present in 17 (15.2%) of patients while in 95 (84.8%) patients, no report of para thyroidectomy was seen (P value 0.05). Fractures in patients of hemodialysis below 5 years were present in 12 (8.4%) of patients while in 131 (91.6%) patients, fracture were not reported. Fractures in patients of hemodialysis above 5 years were present in 06 (5.4%) of patients while in 106 (94.6%) patients, fractures were not reported (P value 0.35). Body ache in patients of hemodialysis below 5 years were present in 88 (61.5%) of patients while in 55 (38.5%) patients, fracture was not reported. Fractures in patients of hemodialysis

above 5 years were present in 67 (60%) of patients while in 45 (40.2%) patients, fractures were not reported (P value 0.78) Tetany in patients of hemodialysis below 5 years was present in 20 (14%) of patients while in 141 (98.6%) patients, fracture were not reported. Fractures in patients of hemodialysis above 5 years were present in 02 (1.8%) of patients while in 110 (98.2%) patients, fractures were not reported (P value 0.81). Joint mobility in patients of hemodialysis below 5 years was affected in 56 (39.2%) of patients while in 87 (60.8%) patients, joint mobility was not affected.

Joint mobility in patients of hemodialysis above 5 years were present in 45 (40.2%) of patients while in 67 (59.8%) patients, joint mobility was not affected (P value 0.87). Itching among patients of hemodialysis below 5 years was present in 12 (8.4%) of patients while in 131 (91.6%) patients, fracture was not reported. Itching among patients of hemodialysis above 5 years were present in 20 (17.9%) of patients while in 92 (82.1%) patients, itching was not reported (P value 0.02) (Table 2).

Frequency of medication in patients of hemodialysis in below and above 5 years was also reported. Phosphate binders were taken by 52 (36.4%) patients with less than 5 years of hemodialysis. In patients of above 5 years of hemodialysis, 39 (34.8%) patients were reported. Vitamin D supplements were used by 75 (52.4%) patients with less than 5 years of hemodialysis. In patients of above 5 years of a hemodialysis, 57 (50.9%) patients were reported using Vitamin D supplements. Calcium supplements were used by 37 (25.9%) patients with less than 5 years of hemodialysis. In patients of above 5 years of a hemodialysis, 38 (33.9%) patients were reported using calcium supplements (Figure 1).

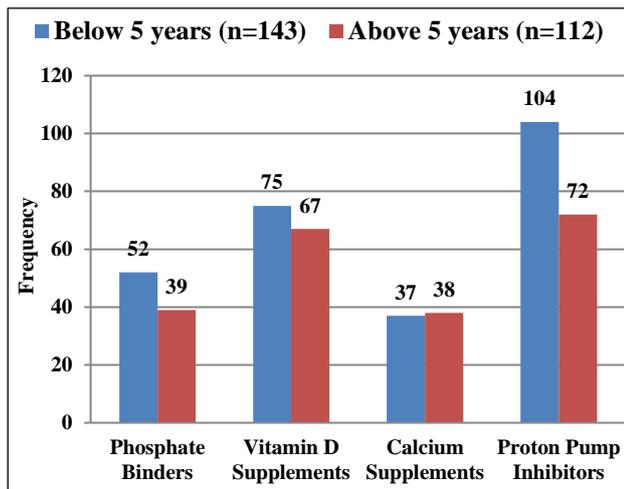


Figure 1: Frequency of medication in different dialysis groups (n=255).

DISCUSSION

Present study reported the metabolic changes or derangements along with different clinical features experienced by these patients. A study by Kong X et al, showed that in 1711 patients of hemodialysis the mean age was 57.1 ± 14.2 years in which calcium level was 9.3 ± 1.1 mg/dl as compared to 9.2 ± 1.1 mg/dl for peritoneal dialysis group (P value 0.03), phosphorous levels of 6.3 ± 2.1 mg/dl as compared 5.7 ± 2.0 mg/dl for peritoneal dialysis group (P value 0.001) and a median and IQR of PTH recorded were 265 (127.2-456.3) pg/ml as compared to 304.5 (162.0-486.7) pg/ml for peritoneal dialysis group (P value 0.030) Phosphate binders were used by 70.8% patients and vitamin D supplements by 77.5% of patients. 11.6% patients were hypertensive and 8.9% patients were diabetic.¹⁹ Another study by Kim GH et al., stated that in the study of 1,018 patients the mean age reported was 54 years with a mean value of calcium as 9.1 ± 0.7 mg/dl, phosphorus was 5.3 ± 1.4 mg/dl and PTH level of 262.1 ± 298.8 pg/ml. Phosphate binders were used by 87.2% of patients and 45.9% of patients were on vitamin D supplements.²⁰ In another study by Kimata N et al, mean values of serum calcium were 9.4 ± 1.0 mg/dl, phosphorus was 5.7 ± 1.6 mg/dl and iPTH was 194 ± 263 pg/ml.²¹ An additional study by Young EW et al, which

was performed in a total number of 17,236 patients from United States, Europe and Japan, it was reported that the median levels of phosphorus in the three respective countries were 5.7, 5.5 and 5.6 mg/dl, albumin was 9.4, 9.6 and 9.5 mg/dl and PTH level was 111, 149 and 158 pg/ml respectively.²² With regards to the above findings, our study has reported a mean age of 49.43 ± 14.62 years in which the overall median level of calcium reported was 8.7 mg/dl, for phosphorus it was 4.75 mg/dl, PTH median was 361 pg/ml and for albumin was 4.0 mg/L. The probable reason for decreased median calcium as well as phosphorus in our study owes to the fact of dietary habits in the daily routine of people in our part of the world. However, increased median PTH levels could be due to decreased mineral level which by positive feedback may increase the levels of PTH in the body. In addition, majority of the patients in our study, 238 (93%) were hypertensive, indicating a mild to moderate systemic illness which also could lead to derange levels of minerals. We also reported supplementations in our study in which, 91 (35.6%) patients were recorded using phosphate medication, 132 (51.7%) were on vitamin D supplementation, 75 (29.4%) were on calcium supplements. Slightly raised median calcium levels might be a reason for decreased calcium supplementation in our study as compared to the study mentioned above. Our study also mentioned the symptoms occurring in patients of hemodialysis, a feature not usually reported in majority of studies. Majority of the patients 155 (60.7%) reported body ache, after which joint mobility was affected in 101 (39.6%). Only 7 patients (2.7%) reported fits, 18 (7.1%) reported fractures and 22 (8.6%) reported tetany. Decreased average age as well as increased median mineral levels in our study could be one reason for reduction in the frequency of fits, fractures and tetany.

The qualitative and quantitative approach of our study as assured that we have assessed the extensive range of metabolic disturbances in patients undergoing dialysis. However, the study might not be immune from selection and observer bias. Considering the views of our observations and to what extend they are consistent with the demographic variables would be revealing to discover more facts about the metabolic disturbance in dialysis patients.

CONCLUSION

This study showed that significant difference in mineral levels did not exist in patients on hemodialysis as regards to the duration of dialysis. However clinical features had a tendency to decrease as duration of dialysis increased to above 5 years. Para thyroidectomy and itching were two main significant findings in our study.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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