

## A Study of Serum Calcium in Maintenance Haemodialysis Patient

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### Abstract

**Background:** To define the minimum and maximum levels for calcium concentration of dialysis fluid a combination of acute and long-term observations was carried out. The external calcium balance during dialysis was dependent on the gradient between plasma ultra filterable calcium and dialysis fluid calcium concentration. Changes in plasma calcium during dialysis did not correlate with measured external balance. The maximum level for the calcium concentration of the dialysis fluid is therefore the highest which does not cause complications due to the transient hypercalcaemia.

**Methods:** This study was a cross sectional study. This study was taken place 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). Patients getting maintenance haemodialysis in NIKDU and also BIRDEM were enrolled in this study. Dialysate calcium concentration was 1.8 mmol/L.

**Results:** Laboratory findings of the study patients, it was observed that mean serum calcium was found  $8.77 \pm 0.98$  mg/dl. Achievement of the four recommendations of K/DOQI guidelines was only 9 (7.5%). Laboratory findings of the study patients showed that 9 patients had  $\geq 10.2$  mg/dl serum calcium, among them 3 (33.3%) received Vitamin D. Drug history related to calcium supplementation regarding serum calcium level, it was observed that 39 patients had  $< 8.4$  mg/dl serum calcium level. Among them 25 (64.1%) patients use calcium supplementation. The percentages of patients (no drug history related vitamin D) who received dialysis twice & thrice per week and within the target range of levels were as follows: serum calcium: 73.1% & 57.6% respectively.

**Conclusion:** Higher levels of calcium containing dialysate that is used in Bangladesh; irrational use of drug related to calcium based phosphate binder and Calcitriol- these may be because of over suppression of parathyroid hormone (PTH) which is reflected in this study patients getting MHD twice or thrice weekly.

### INTRODUCTION

Chronic kidney disease has become a major health concern with a high prevalence worldwide. It is estimated that in China, nearly one in 10 people has some degree of kidney dysfunction, affecting almost 150 million individuals.<sup>1</sup> Rapid rise of common

risk factors, such as diabetes, hypertension, and obesity, especially among the poor, will result in even greater and more profound burdens that developing nations are not equipped to handle.<sup>2</sup> Based largely on observational and preclinical data and expert opinion, KDOQI, an initiative of the National Kidney

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Foundation, issued its clinical practice guideline for bone metabolism and disease in CKD in 2003.<sup>3</sup> This was followed by the KDIGO (Kidney Disease: Improving Global Outcomes) CKD-MBD guideline, which was published in 2009, following a KIDGO Controversies Conference held in 2005.<sup>4</sup> With the emergence of additional evidence, which was reviewed at the 2013 KDIGO Controversies Conference, the KDIGO issued a clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of CKD-MBD in 2017.<sup>5</sup> The updated guideline continue to commend monitoring of mineral metabolism parameters, but a more individualised approach is now suggested for medical management of CKD-MBD given the lack of benefit on intermediate biochemical and cardiovascular end points, but evident risks, such as hypercalcaemia.<sup>6</sup>

### MATERIALS AND METHODS

This cross sectional study was taken place 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 from the Arterio-venous Fistula (AVF) for measurement of serum creatinine, serum albumin, calcium. Specimens were allowed to clot at room temperature. Serum was separated from the cells by centrifugation. Serum creatinine, serum calcium, serum albumin was measured by automated analyzer, Humalyzer 3000, Germany. Calcium was corrected by using Payne's formula. 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  $\pm$ SD.

### RESULTS

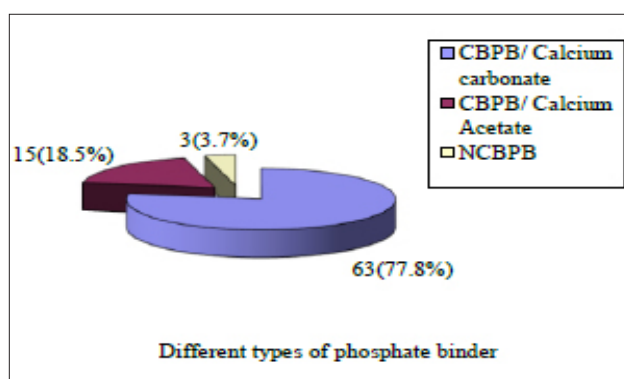
Majority 47 (39.2%) patients were age between 51-60 years and mean age was found 50.4 $\pm$ 13.13 years. Male were predominant and male female ratio was

1.3:1. BMI of the study patients showed that majority 49 (40.8%) patients had normal range (18.5-22.9 kg/m<sup>2</sup>) BMI. The mean BMI was found 23.5 $\pm$ 4.7 kg/m<sup>2</sup>. 114 (95.0%) patients had HTN and 56 (46.7%) patients had DM (Table I). Different types of phosphate binder were used including the calcium based phosphate binder which was 81 (67.5%). Calcium carbonate was 77.8% , Calcium Acetate was 18.5% and NCBPB is 3.7% (Figure 1). In our study patients, it was observed that 61 (50.8%) were using Vitamin-D (Calcitriol) (Figure 2). Duration of haemodialysis was 25.55 $\pm$ 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 calcium was found 8.77 $\pm$ 0.98 mg/dl (Table III). Achievement of the four recommendations of K/DOQI guidelines was only 9 (7.5%) (Figure 3). Laboratory findings of the study patients showed that 9 patients had  $\geq$ 10.2mg/dl serum calcium, among them 3(33.3%) was receiving Vit D (Table IV). Drug history related to calcium supplementation regarding serum calcium level, it was observed that 39 patients had <8.4 mg/dl serum calcium level, among them 25 (64.1%) patients use calcium supplementation. Nine patients had  $\geq$ 10.2 mg/dl serum calcium level, among them 5(55.6%) patients use calcium supplementation (Table V). 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 calcium: 51.0% & 56.5% respectively (Table VI). 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 calcium: 66.7% & 61.5% respectively (Table VII). 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 calcium: 53.3% & 62.5% respectively (Table VIII). 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 calcium: 73.1% & 57.6% respectively (Table IX).

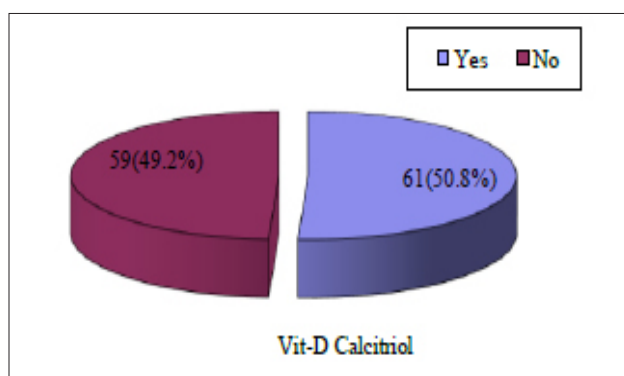
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**Table I.** Distribution of the patients by demographic profiles(n=120)

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



**Fig 1.** Different types of phosphate binder used by the study patients



**Fig 2.** Drug history related to Vitamin-D (Calcitriol) of the study patients

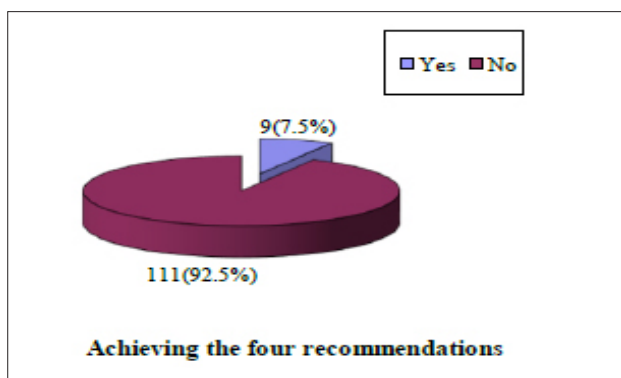
**Table II.** Distribution of the study patients related to haemodialysis (n=120)

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)	
<b>Haemodialysisession/Wk</b>		
Twice(<8 hours)	71	59.2
Thrice(>8 hours)	49	40.8

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

Laboratory findings	Number of patients	Percentage
<b>S. Ca (mg/dl)</b>		
< 8.4	39	32.5
8.4-9.5	56	46.7
9.6-10.2	16	13.3
≥10.2	9	7.5
Mean±SD	8.77±0.98	
Range(min-max)	(6.2-11.2)	



**Fig 3.** Showing achievement of the four recommendations of the study patients.

**Table IV.** Distribution of the study patients related to the drug Vit -D according to S. Ca level

Laboratory findings	Number	Vit D Received	Percentages
<b>S. Ca (mg/dl)</b>			
≥10.2	9		33.3%

**Table V.** Distribution of the study patients by drug history related to calcium supplementation regarding serum calcium level.

Laboratory findings	Number	Calcium supplementation	n (%)
<b>S. Ca(mg/dl)</b>			
< 8.4	39	25	64.1%
≥10.2	9	5	55.6%

**Table VI.** Distribution by drug history related to phosphate binder in patients with MHD twice and thrice per week (n=79)

Received phosphate binder (n=79)				
	Twice weekly (n=56)		Thrice weekly (n=23)	
	n	%	n	%
<b>S.Ca (mg/dl)</b>				
Within target range (8.4-10.2)	29	51.8	13	56.5
Out of target range	27	48.2	9	39.1

**Table VII.** Distribution by drug history not related to phosphate binder in patients with MHD twice and thrice per week(n=41)

Nor received phosphate binder (n=41)				
	Twice weekly (n=15)		Thrice weekly (n=26)	
	n	%	n	%
<b>S.Ca (mg/dl)</b>				
Within target range(8.4-10.2)	10	66.7	16	61.5
Out of target range	5	33.3	10	38.5

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**Table VIII.** 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	%
<b>S.Ca (mg/dl)</b>				
Within target range(8.4-10.2)	24	53.3	10	62.5
Out of target range	21	46.7	6	37.5

**Table IX.** 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	%
<b>S.Ca (mg/dl)</b>				
Within target range(8.4-10.2)	19	73.1	19	57.6
Out of target range	7	26.9	14	42.4

## 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.<sup>7</sup> study reported that the mean age was found 56.0±15.4 years. Similarly, Mahdavi-Mazdeh et al.<sup>5</sup> 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.<sup>6</sup> and Danese et al.<sup>7</sup> has observed higher mean age of the haemodialysis patients, which were was 60± 17 years and 61±15 years respectively. Kim et al.<sup>8</sup> study showed that the mean age was found 54.0±13.34 years.

In this study it was observed that male were predominant (55.8%). Male female ratio was 1.3:1. Soleymanian et al.<sup>2</sup> study observed that males were found 57.0%. Kim et al.<sup>8</sup> showed females were found 507 (49.8%).

In this study it was observed that BMI of the study patients, it was observed that majority 49 (40.8%) patients had normal range (18.5-22.9kg/m<sup>2</sup>) BMI. The mean BMI was found 23.5±4.7 kg/m<sup>2</sup> with range from 15.6 to 45.5 kg/m<sup>2</sup>. Kim et al.<sup>8</sup> study observed that the mean body mass index was found 21.9±3.2 kg/m<sup>2</sup>. Similar observations regarding the mean body mass index were also made by Kimata et al.<sup>9</sup> body mass index, which were 24.5±5.4 kg/m<sup>2</sup>. In another study, Danese et al.<sup>7</sup> found BMI ≥30 kg/m<sup>2</sup> in 33.0% of their study patients, which is a little higher with the current study. Soleymanian et al.<sup>2</sup> study reported that the mean body mass index was found 24.4±4.6kg/m<sup>2</sup>

In this study drug history related to phosphate management, it was observed that among the different type of phosphate binder 81 (67.5%) is used by the study patients were Calcium carbonate is 77.8%, Calcium Acetate is 18.5% and NCBPB is 3.7%. Lorenzo et al.<sup>10</sup> showed 71% of the patients received phosphate binders, which are comparable 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. Kim et al. observed that Vitamin D receptor agonists was found 429 (42.1%). Oral calcitriol was the only vitamin D derivative used and was prescribed in 33% of the patients observed by Lorenzo et al.<sup>10</sup>. In another study, Vitamin D treatment was administered in 48% of patients obtained by Maduell et al.<sup>11</sup>, 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.<sup>5</sup> 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 Laboratory findings of the study patients, it was observed that mean serum calcium was found 8.77±0.98 mg/dl. Kim et al. study showed 122 patients (45.2%) had serum Calcium levels 49.5 mg/dL, where as only 35 patients (13.0%) had serum Calcium levels 08.4 mg/dL. Soleymanian et al.<sup>2</sup> study observed that the mean serum calcium was found 8.9±0.8 mg/dl. Similarly, Mahdavi-Mazdeh et al.<sup>5</sup> showed the mean

serum calcium was found  $8.98 \pm 1.23$  mg/dl varied from 3.1 - 14.4 mg/dl. On the other hand, Kimata et al.<sup>9</sup> and Maduell et al.<sup>11</sup> observed the higher mean serum calcium level of the haemodialysis patients, which were  $9.6 \pm 0.9$  mg/dl and  $9.57 \pm 0.7$  mg/dL respectively. Lorenzo et al.<sup>10</sup> and Danese et al.<sup>7</sup> also observed higher mean serum calcium level.

In present study observed that achievement of the four recommendations of K/DOQI guidelines was only 9(7.5%) Mahdavi-Mazdeh et al.<sup>5</sup> 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. Other studies Maduell et al.<sup>11</sup> and Young et al.<sup>12</sup> pointing out that the subject have proved the failure to comply with the guideline, too. Young et al.<sup>12</sup> showed that only 4.6% and 5.5% of patients, respectively, achieved all the 4 goals of the K/DOQI for mineral metabolism. In their well designed study, Maduell et al.<sup>11</sup> highlighted that 7.3% (out of 2392 dialysis patients) achieved all the targets.

In present study laboratory findings of the study patients showed that 9 patients had  $\geq 10.2$  mg/dl serum calcium, among them 3(33.3%) received Vit D. Kim et al.<sup>8</sup> study performed Serum mineral levels among patients taking the different vitamin D receptor agonists.

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 calcium: 51.1% & 56.5% respectively. Kim et al.<sup>8</sup> study showed as expected, there was a tendency to use calcium-based binders and calcium-free agents in patients with rather low and high serum calcium, 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 calcium: 66.7 & 61.5% 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 calcium: 53.3% & 62.5% respectively. 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 calcium: 73.1% & 57.6% 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 6<sup>th</sup> decade and with male predominance. Most of the haemodialysis patients came from urban area. Higher levels of calcium containing dialysate that is used in Bangladesh; irrational use of drug related to calcium based phosphate binder and Calcitriol- these may be causes of over suppression of parathyroid hormone (PTH) which is reflected in this study patients getting MHD twice or thrice weekly. The highly unsatisfactory results found in this study may be due to not implementation of K/DOQI guidelines at HD units and poor patient's compliance.

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