Mineral and bone disorder and management in the China Dialysis Outcomes and Practice Patterns Study

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Abstract

Background: Despite a growing population of patients starting hemodialysis in China, little is known about markers of mineral bone disease (MBD) and their management. We present data on prevalence and correlates of hypocalcemia, hyperphosphatemia, and secondary hyperparathyroidism from the China Dialysis Outcomes and Practice Patterns Study (DOPPS), with evaluation of whether these laboratory markers triggered changes in management.

Methods: We compared the frequency of measurement and prevalence of poor control of MBD markers in China DOPPS with other DOPPS regions. We also used generalized estimating equations to assess correlates of MBD markers, and separate models to assess predictors of vitamin D and phosphate binder prescriptions in the China DOPPS.

Results: Severe hyperphosphatemia (>7 mg/dL) and secondary hyperparathyroidism (>600 pg/mL) were common (27% and 21% prevalence, respectively); both were measured infrequently (14.9% and 3.2% of patients received monthly measurements in China). Frequency of dialysis sessions was positively associated with hyperphosphatemia; presence of residual kidney function was negatively associated with both hyperphosphatemia and secondary hyperparathyroidism. Laboratory measures indicating poor control of MBD were not associated with subsequent prescription of active vitamin D or phosphate binder.

Conclusions: There are substantial opportunities for improvement and standardization of MBD management in China. Development of country-specific guidelines may yield realistic targets and standardization of medication use accounting for availability and cost.

Keywords: Mineral bone disease; Hyperphosphatemia; Hyperparathyroidism; China; Hemodialysis; Dialysis Outcomes and Practice Patterns Study

Introduction

In countries with established hemodialysis (HD) practices, laboratory markers of mineral-bone disorder (MBD) are monitored frequently and commonly treated. The majority of patients receiving HD are prescribed a phosphate binder and either activated vitamin D or cinacalcet.[1] However, data on monitoring of laboratory markers and treatment for MBD are lacking from China. China has a large and growing population of patients treated for end-stage kidney disease with HD, and as policymakers work to expand access to dialysis to a larger portion of this population, ancillary treatments for comorbid MBD will also require consideration.

There are several reasons to expect differences in MBD markers in patients receiving dialysis in China. Dietary surveys report lower intake of phosphorous in Chinese diets than that in Japanese, American, and Italian diets.[2,3] One study showed lower mean parathyroid hormone (PTH) levels among Asians compared with Caucasians even after adjusting for glomerular filtration rate.[4] On the other hand, medication sparsity and differences in dialysis prescription may result in poorer control of hyperphosphatemia and secondary hyperparathyroidism.

We used representative patient and facility data from the Dialysis Outcomes and Practice Patterns Study (DOPPS) for China to describe the current prevalence of severe hyperphosphatemia, hypocalcemia, and secondary hyperparathyroidism in three major metropolitan areas of China. We also present practices related to laboratory monitoring, facility targets, and medication prescription for MBD markers in China and, for reference, corresponding data from other countries and regions. Finally, within

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the China DOPPS population, we described correlates of poor control of MBD markers, and assessed whether patients with poorer MBD control were more likely to receive phosphate binders or vitamin D treatment.

Methods

Ethical approval

National and local ethics committees approved the study. We obtained informed consent for patient participation according to these regulations.

Patients and data collection

The present research utilizes data from phase 5 (2012–2015) of the DOPPS, an international prospective cohort study of patients receiving HD ≥18 years of age in 21 countries (Australia, Belgium, Canada, China, France, Germany, six Gulf Cooperation Council countries, Italy, Japan, New Zealand, Russia, Spain, Sweden, Turkey, the United Kingdom, and the United States). Patients were selected randomly from nationally representative samples of HD facilities in each country.[5,6] At the time of patient enrollment in the study, the study coordinator at each participating site abstracted demographic data, comorbid conditions, dialysis prescription, laboratory values, and medications from patient records. Medical directors at each facility also completed a survey of facility practice indicators.

Due to feasibility considerations, the China DOPPS was limited to representative data from the metropolitan areas in the three largest cities in China (Beijing, Guangzhou, and Shanghai). We identified these cities based on feasibility of data collection and availability of facility information. In each metropolitan area, we randomly selected 15 HD facilities (total number in three cities = 45) from a comprehensive roster of 152 HD units.

Definitions

Our primary outcomes of interest were prevalence of hypocalcemia (albumin adjusted calcium <8.4 mg/dL), severe hyperphosphatemia (phosphorus >7 mg/dL), and secondary hyperparathyroidism (PTH >600 pg/mL), in comparison with other DOPPS countries. We chose these thresholds based on the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, allowing a higher threshold of phosphorous due to the distribution of our data.

We also investigated whether MBD monitoring influenced prescription of a phosphate binder and/or vitamin D. Cinacalcet prescription rates were too low to include this drug in the analysis. In assessing subsequent prescription of medications, we used most recent laboratory values recorded in the three months preceding study enrollment, and ascertained prescriptions for vitamin D or phosphate binders as of the study enrollment date.

Statistical analysis

We used standard descriptive statistics to describe the patient characteristics, laboratory values, MBD treatment, and facility practices across regions. We constructed separate models to explore predictors of hypocalcemia (<8.4 mg/dL), hyperphosphatemia (>7 mg/dL), and hyperparathyroidism (PTH >600 pg/mL). We used generalized estimating equation (GEE) models to measure the association of correlates of interest with laboratory MBD markers, accounting for patient demographics including insurance status, comorbidities, vascular access, and dialysis treatment characteristics at the patient level, and frequency of actual laboratory measurements at the facility level. To account for the substantial proportion of patients on two-times weekly HD, we calculated standardized dialysis *Kt/V* from the equation reported by Leypoldt *et al*.[7]

We finally constructed separate models to explore predictors of vitamin D and phosphate binder prescriptions in the China DOPPS population. We again used GEE models to measure the association between laboratory values with medication prescription of vitamin D or phosphate binder, after accounting for the same potential confounders at the patient and facility level.

Overall, missingness for model covariates was low (<10% for the majority of covariates with the exception of standardized *Kt/V*, PTH, and the pre-enrollment laboratories which were missing for 11% to 40% of patients). For missing model covariates, we used the Sequential Regression Multiple Imputation Method implemented by IVEware[8] and analyzed using the MIAnalyze procedure in SAS/STAT® 9.4. All analyses were conducted by using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

Study sample and patient characteristics

The analytic cohort included 1186 patients from China compared with 1622 patients from Japan, 3737 from North America, and 3608 from European DOPPS countries. Compared with patients from the other regions, patients receiving HD from China were younger, and less likely to have diabetes as the cause of end-stage renal disease [Table 1]. Time on dialysis (vintage) in China was comparable with North America and Europe, but shorter than Japan. Dialysis session length was similar in China, Japan, and Europe, but shorter in North America. The mean blood flow rate in China was higher than Japan, but lower than North America and Europe. Chinese patients had lower standardized dialysis *Kt/V* than other DOPPS regions.

Prevalence of hypocalcemia, hyperphosphatemia, and secondary hyperparathyroidism

The prescribed dialysate calcium was higher in China (73% ≥1.500 mmol/L) than other regions. The average serum calcium concentration (albumin adjusted) in China (9.12 mg/dL) was lower than in North America and Europe [Table 1]. Patients from China had higher average serum phosphorus concentrations compared to patients from other regions [Table 1], and the median Chinese facility reported 27% of patients had serum phosphorus

Table 1: Patient characteristics, MBD markers, and MBD treatments, by DOPPS region (2012–2015).

Measures	China ($n=1186$)	Japan ($n=1721$)	North America ($n=13,080$)	Europe ($n=3651$)
Demographics				
Age (years)	58.6 ± 14.8	65.5 ± 12.3	63.0 ± 14.9	67.0 ± 14.8
Female (%)	46	36	45	39
Time on dialysis (years)	3.5 (1.6, 6.4)	6.4 (2.9, 13.3)	2.8 (1.2, 5.5)	3.5 (1.7, 6.9)
Primary cause of ESRD (%)				
Glomerulonephritis, vasculitis	44	41	12	20
Diabetes	18	35	45	25
Polycystic kidney disease	6	5	3	7
Hypertension	16	6	27	19
Other cause of ESRD	16	13	14	30
Nutrition and dialysis prescription				
Body mass index (kg/m^2)	21.8 ± 3.7	21.5 ± 3.5	28.4 ± 7.0	26.2 ± 5.5
Albumin (g/dL)	3.94 ± 0.47	3.67 ± 0.40	3.73 ± 0.45	3.72 ± 0.49
Sessions per week (n)	2.82 ± 0.43	2.98 ± 0.17	3.00 ± 0.28	3.03 ± 0.37
Treatment time (minutes)	242 ± 18	239 ± 28	220 ± 35	244 ± 39
Blood flow rate (mL/min)	236 ± 30	208 ± 44	413 ± 60	333 ± 59
Single pool Kt/V*	1.38 ± 0.30	1.41 ± 0.30	1.56 ± 0.29	1.57 ± 0.32
Standardized Kt/V†	2.05 ± 0.35	2.14 ± 0.28	2.24 ± 0.27	2.28 ± 0.35
nPCR (g urea nitrogen/kg per day)	0.82 ± 0.27	0.98 ± 0.22	0.98 ± 0.26	1.02 ± 0.25
Catheter use (%)	10	1	25	23
Dialysate calcium, mmol/L (%)				
<1.250	1	1	14	2
1.250	26	21	79	35
1.375	0	11	0	2
1.500	67	67	5	58
1.750	6	0	2	4
Comorbidities (%)				
Coronary artery disease	24	27	39	34
Congestive heart failure	20	16	27	18
Diabetes	26	39	56	38
MBD markers				
Serum calcium (mg/dL)‡	9.12 ± 0.98	9.09 ± 0.70	9.24 ± 0.70	9.25 ± 0.79
Serum calcium categories (%)‡				
<8.4 mg/dL	25	26	18	20
8.4–9.5 mg/dL	48	61	62	57
9.6–10.0 mg/dL	14	10	15	15
>10.0 mg/dL	13	4	6	9
Serum phosphorus (mg/dL)	6.00 ± 2.04	5.42 ± 1.34	5.11 ± 1.55	4.87 ± 1.53
Serum phosphorus categories (%)				
<3.5 mg/dL	7	5	12	17
3.5–5.5 mg/dL	39	52	56	54
5.6–7.0 mg/dL	28	34	22	21
>7.0 mg/dL	27	10	11	8
PTH (pg/mL)	430 ± 460	149 ± 130	404 ± 362	333 ± 320
PTH categories (%)				
<150 pg/mL	27	62	18	30
150–300 pg/mL	26	29	31	30
301–600 pg/mL	26	9	33	27
>600 pg/mL	21	1	18	14
MBD medication and treatment (%)				
Active vitamin D (any)	57	75	79	76
Active intravenous vitamin D	2	37	58	21
Active oral vitamin D	57	41	29	60
Cinacalcet	2	24	16	21
Phosphate binder	59	84	66	79
Calcium-based only	53	36	26	23
Calcium-based + sevelamer	0	11	8	12
Sevelamer only	1	5	22	21
Other binder or combination	6	32	9	24
History of parathyroidectomy (%)	3	8	5	5

Values are shown as mean ± standard deviation, median (interquartile range), or %; restricted to patients in initial enrollment cross-section; weighted by facility sampling fraction. * Restricted to patients having ESRD ≥1 year, and received three HD sessions per week; single-pool Kt/V was calculated using the Daugirdas formula. † Standardized Kt/V was calculated from the equation reported by Leypoldt *et al*[7] accounting for frequency of dialysis per week. ‡ Albumin-adjusted calcium. MBD: Mineral bone disease; DOPPS: Dialysis Outcomes and Practice Patterns Study; ESRD: End-stage renal disease; nPCR: Normalized protein catabolic rate; PTH: Parathyroid hormone.

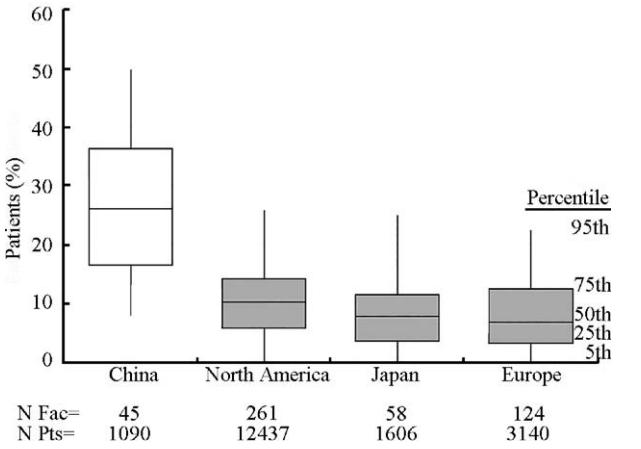

Figure 1: Distribution of patients with phosphorus >7 mg/dL, by DOPPS region (2012–2015). Restricted to initial cross-section of patients in facilities with at least seven patients with non-missing phosphorus data. DOPPS: Dialysis Outcomes and Practice Patterns Study.

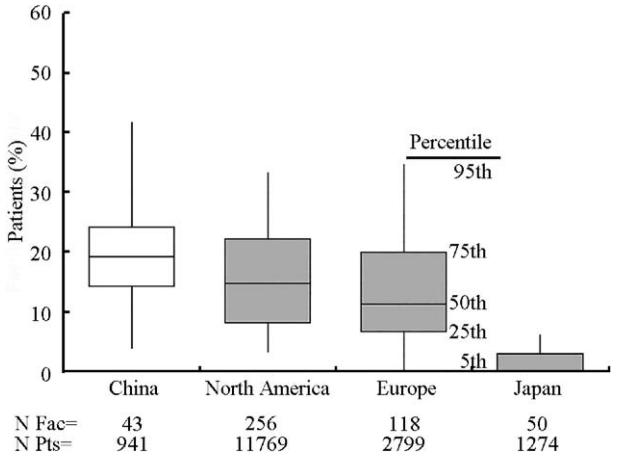

Figure 2: Distribution of patients with PTH >600 pg/mL, by DOPPS region (2012–2015). Restricted to initial cross-section of patients in facilities with at least seven patients with non-missing PTH data. DOPPS: Dialysis Outcomes and Practice Patterns Study; PTH: Parathyroid hormone.

concentrations >7.0 mg/dL compared with 7% to 10% in other DOPPS regions [Figure 1].

The mean PTH level (430 pg/mL) in China was higher than that seen in other DOPPS regions (means ranged from 149 to 404 pg/mL) [Table 1], and the median Chinese facility reported 19% of patients had serum PTH >600 pg/mL compared with 0% to 15% in other DOPPS regions [Figure 2].

Frequency of MBD marker measurement, use of medications, and facility targets

MBD markers were measured less frequently in China than in other DOPPS regions. Phosphorous concentrations were measured monthly in >70% of patients in the comparator DOPPS countries, but only in 14.9% of Chinese patients. Measurement frequencies for calcium and PTH were similarly lower in China [Table 2]. While phosphate binders were prescribed to 59% of Chinese patients, their use, especially the use of non-calcium based phosphate binders, was lower than other DOPPS countries. Active vitamin D was prescribed to 57% of patients, a frequency similar to Europe but lower than Japan and North America. Cinacalcet was rarely prescribed in China (2%) compared to other regions (16%–24%). Few patients had undergone parathyroidectomy before DOPPS enrollment [Table 2].

Facility directors from 47% of Chinese facilities described the upper limit of PTH to be 300 to 399 pg/mL, reflecting somewhat stricter targets than those set by a majority of facility directors in North America and Europe but more permissive than facility directors in Japan [Figure 3A]. A substantial proportion of Chinese facility directors (79%) reported upper phosphorous targets at 5.5 mg/dL or below [Figure 3B], reflecting targets similar to Europe but lower than those in Japan (Japanese Society for Dialysis Therapy recommends targets 3.5–6.0 mg/dL).[9]

Table 2: Frequency of calcium, phosphorus, and PTH measurement during the 4 months before study enrollment among patients on dialysis for at least 4 months, by DOPPS region (2012–2015).

Measures	China ($n=1039$)	Japan ($n=1497$)	North America ($n=10,992$)	Europe ($n=2934$)
Calcium measurement (%)				
No measurements	2.5	0.0	0.8	0.1
Once (every 4 months)	45.1	0.7	5.8	4.2
Twice	26.6	1.2	5.0	5.8
Three times	10.7	4.8	11.4	17.7
Four times (monthly)	15.1	93.3	77.0	72.2
Phosphorus measurement (%)				
No measurements	3.8	0.1	0.2	0.5
Once (every 4 months)	44.8	0.7	5.8	4.3
Twice	26.0	1.1	4.9	6.0
Three times	10.6	5.1	11.3	17.9
Four times (monthly)	14.9	93.0	77.8	71.3
PTH measurement (%)				
No measurements	14.6	19.2	4.9	10.0
Once (every 4 months)	56.9	30.7	32.2	41.4
Twice	20.5	19.7	26.5	24.7
Three times	4.8	7.4	13.2	8.9
Four times (monthly)	3.2	23.0	23.2	15.1

Includes patients initial enrollment cross-section of DOPPS phase 5 as well as replacement patients who were on dialysis for at least 4 months at enrollment. PTH: Parathyroid hormone; DOPPS: Dialysis Outcomes and Practice Patterns Study.

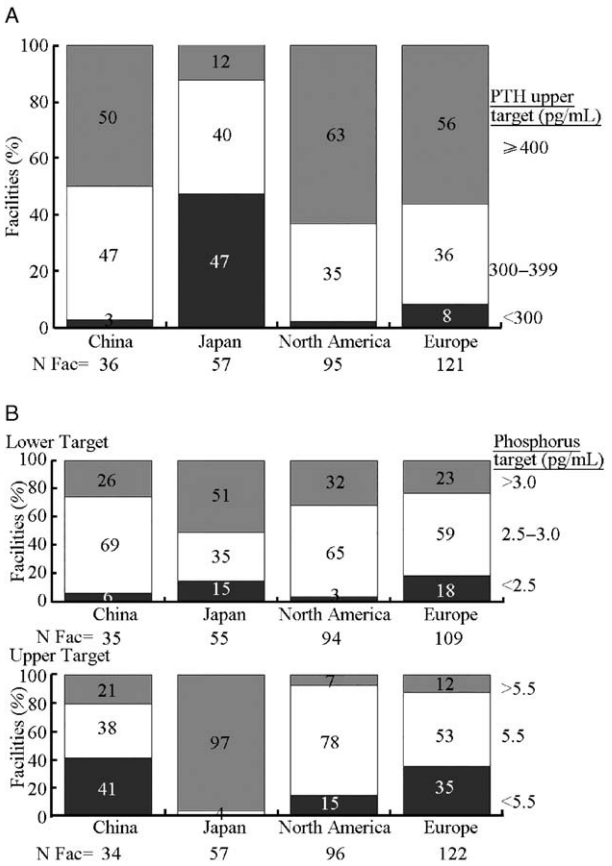

Figure 3: Facility upper PTH target (A) and lower and upper phosphorus targets (B), by DOPPS region (2012–2015, as reported by medical director). DOPPS: Dialysis Outcomes and Practice Patterns Study; PTH: Parathyroid hormone; N Fac: Number of facilities.

Patient characteristics and treatments associated with hypocalcemia, hyperphosphatemia, and secondary hyperparathyroidism in the China DOPPS

Higher phosphorus was positively associated with calcium <8.4 mg/dL [Table 3]. Older age, urine output >1 cup/day, and longer dialysis session length were negatively associated with phosphorous >7 mg/dL. In contrast higher body mass index, <3 dialysis sessions per week, and higher PTH were positively associated with hyperphosphatemia. Longer time on dialysis, higher body mass index, higher phosphorus, and higher calcium were positively associated with PTH >600 pg/mL while urine output >1 cup/day and diabetes were strongly and inversely associated with PTH >600 pg/mL.

Association of MBD markers with vitamin D or phosphate binder treatment in China DOPPS

Congestive heart failure and co-prescription of a phosphate binder were positively associated with vitamin D prescription [Table 4]. Longer dialysis session length was negatively associated with phosphate binder prescription while higher albumin levels and co-prescription with active vitamin D were positively associated with phosphate binder prescription. The most recent laboratory values for phosphorus, PTH, and calcium preceding the vitamin D and phosphate binder prescriptions were not clearly associated with prescription.

Discussion

Our study of patients from a representative sample of 45 randomly selected HD units in three major Chinese metropolitan areas shows that the current state of MBD management in patients receiving HD is sub-optimal in China. Thus, this study indicates large opportunities for improvements in MBD management.

Our findings of common and pronounced hyperphosphatemia in China corroborate earlier studies in Chinese patients receiving HD. The Practice Patterns and Improvement Study (PPIS), of 1711 patients receiving HD from nine provinces in China, reported an average serum phosphate level was 6.3 mg/dL; 27.4% of patients had a serum phosphate level over 7 mg/dL and 21% had PTH above 600 pg/mL.[10] In the China Collaborative Study on dialysis study, the majority of patients receiving HD (64.4%) had a serum phosphate level above 7 mg/dL, and half (48.8%) had PTH over 600 pg/mL.[11] A report on the status of maintenance HD in Beijing showed 47.4% of patients had severe hyperphosphatemia (over 7 mg/dL) and 29.7% had a PTH level over 600 pg/mL.[11,12] The prevalence of hyperphospatemia (over 5.5 mg/dL) in patients receiving HD in Shanghai increased from 44% in 2006 to 58.7% in 2012.[13] All these results indicate the sub-optimal MBD management in China. Meeting MBD targets, particularly those related to phosphorous, requires attention to dialysis clearance, dietary phosphate restriction, and pharmacological therapy.

We have previously noted that a quarter of patients underwent HD two times weekly in China DOPPS, compared with fewer than 5% in other DOPPS regions.[14] The frequency of dialysis is related to phosphorus clearance. Low-flux dialysis filters were the majority of filters used in dialysis centers in China from the PPIS study.[10] Even in patients receiving HD three times per week, 29% achieved a Kt/V <1.2 compared with below 10% in most other DOPPS regions.[14] Thus inadequate dialysis may be responsible for inadequate removal of phosphate.

In this DOPPS study, normalized protein catabolic rate (nPCR), a surrogate of dietary protein intake, was used to evaluate dietary protein intake. The nPCR values were lower in patients receiving HD in China compared with other DOPPS regions. However, the mean serum albumin level was 3.9 g/dL in Chinese patients receiving HD, higher than other DOPPS regions. Hyperphosphatemia is more common in patients receiving HD with near-normal albumin levels 3.9 g/dL.[15] It is possible that the nPCR calculation may underestimate protein intake, or non-protein sources (processed foods as opposed to dairy products) could supplant the lower protein intake.[16]

Phosphate binder prescription based on serum calcium and phosphate level is important for the treatment of hyperphosphatemia. We found that only 5% of patients

Table 3: Adjusted odds ratio (95% CI) of being within MBD category, by patient characteristics and treatment indicators in China DOPPS (2012–2015).

Patient characteristic/treatment	Calcium* <8.4 mg/dL (*n* = 204/1031)	Phosphorus > 7 mg/dL (*n* = 300/1090)	PTH > 600 pg/mL (*n* = 191/947)
Demographics and HD prescription			
Age, per 10 years	0.98 (0.87, 1.11)	**0.79 (0.71, 0.87)**	0.87 (0.76, 1.00)
Female	0.77 (0.50, 1.18)	0.64 (0.41, 1.01)	1.46 (0.95, 2.24)
Vintage, per year	1.00 (0.95, 1.06)	0.98 (0.94, 1.02)	**1.08 (1.04, 1.13)**
Body mass index, per kg/m^2	1.01 (0.96, 1.06)	**1.07 (1.03, 1.12)**	**1.06 (1.00, 1.11)**
Urine output >1 cup/day	1.37 (0.87, 2.16)	**0.58 (0.37, 0.90)**	**0.43 (0.26, 0.72)**
Insurance <90%	1.03 (0.69, 1.52)	1.24 (0.82, 1.86)	1.10 (0.69, 1.77)
Sessions per week, <3 *vs.* 3+	1.13 (0.83, 1.54)	**1.96 (1.42, 2.70)**	0.90 (0.59, 1.38)
Dialysis session length, per 30 min	1.11 (0.78, 1.57)	**0.80 (0.64, 1.00)**	1.12 (0.79, 1.57)
Blood flow rate, per 50 mL/min	1.03 (0.73, 1.46)	0.89 (0.65, 1.22)	0.96 (0.65, 1.43)
Standardized *Kt/V*	0.92 (0.40, 2.15)	1.02 (0.49, 2.14)	1.20 (0.44, 3.32)
Dialysate calcium			
<1.500 mmol/L	1.03 (0.67, 1.58)	1.16 (0.72, 1.86)	1.14 (0.74, 1.77)
1.500 mmol/L	1.00 (ref)	1.00 (ref)	1.00 (ref)
1.750 mmol/L	0.91 (0.26, 3.14)	1.04 (0.63, 1.72)	0.76 (0.39, 1.45)
Catheter use, *vs.* fistula or graft	1.16 (0.70, 1.92)	0.85 (0.50, 1.46)	1.38 (0.75, 2.53)
Comorbidities			
Coronary heart disease	1.14 (0.75, 1.75)	0.98 (0.68, 1.43)	0.83 (0.51, 1.34)
Congestive heart failure	1.31 (0.94, 1.82)	1.16 (0.77, 1.75)	0.76 (0.49, 1.16)
Diabetes	1.27 (0.89, 1.79)	0.85 (0.60, 1.22)	**0.29 (0.20, 0.43)**
Laboratory values			
Phosphorus, per 1 mg/dL	**1.10 (1.02, 1.18)**	N/A	**1.33 (1.23, 1.45)**
PTH, per 100 pg/mL	0.96 (0.93, 1.00)	**1.09 (1.06, 1.13)**	N/A
Calcium alb*, per 1 mg/dL	N/A	0.91 (0.79, 1.05)	**1.27 (1.08, 1.50)**
Albumin, per 1 g/dL	1.35 (0.90, 2.04)	1.40 (0.98, 2.00)	1.34 (0.79, 2.27)
Medications prescribed, yes *vs.* no			
Active vitamin D	0.93 (0.61, 1.40)	0.80 (0.56, 1.14)	1.30 (0.85, 1.99)
Phosphate binder	0.85 (0.61, 1.18)	0.97 (0.67, 1.40)	1.10 (0.76, 1.60)

Each column is from a separate model adjusted for all listed variables plus city (bold indicates $P < 0.05$). *Albumin-adjusted calcium; results similar if model adjustment for albumin (not shown). CI: Confidence interval; MDB: Mineral bone disease; DOPPS: Dialysis Outcomes and Practice Patterns Study; PTH: Parathyroid hormone.

receiving HD in China took non-calcium based phosphate binders and 75% had serum calcium over 8.4 mg/dL. Appropriate prescription of active vitamin D and calcimimetics is important for the treatment of hyperparathyroidism.[17] The DOPPS study showed that the percentage of active vitamin D prescribed was only 50.9% and calcimimetics was less than 1%. Calcium-free phosphate binders like lanthanum and sevelamer were not available and calcimimetics was still not approved for sale in China during the DOPPS5 study. Currently, calcium-free phosphate binders and calcimimetics are available in China; however, the high cost limits their use.[18]

Both the mean PTH and the proportion of patients with hyperparathyroidism in China are higher than other DOPPS regions. Previous studies have shown race- and ethnicity-based differences in PTH levels, with African Americans noted to have levels nearly 60% higher, and Asian Americans to have levels nearly 40% lower in comparison with Caucasians.[4,19] The Japanese Society for Dialysis Therapy continues to advocate for lower PTH targets than KDIGO targets.[9] Further studies to investigate whether PTH levels differ by race/ethnicity could further inform tailored PTH targets. Routine or universal use of calcimimetics may be prohibitive due to high cost in an ever-growing HD population in China. Parathyroidectomies, which have been shown to be equally or more effective at lowering PTH,[19] might be the best choice for patients in China.

Among patients receiving HD in China, older age was associated with lower serum phosphate and lower PTH. This finding is in accordance with a French cohort study including 2008 patients receiving HD, that found elderly patients to have lower phosphate levels compared with younger patients.[20] This finding was explained by the older patients tendency to having reduced bone turnover and lower protein intake. Another interesting point is that patients with diabetes and receiving HD were less likely to develop hyperparathyroidism. In a cohort study about Japanese patients with diabetes and receiving HD, poor glycaemic control was correlated with reduced serum PTH level. This was hypothesized that an impairment in serum PTH secretion exists in patients with diabetes.[21] The third interesting point was that patients with congestive heart failure were more likely to receive active vitamin D treatment. Vitamin D insufficiency is highly prevalent in chronic heart failure patients.[22] In a cross-section study

Table 4: Adjusted odds ratio (95% CI) of vitamin D or phosphate binder prescription, by patient characteristics and prior laboratory values/ treatments in China DOPPS (2012–2015).

	Medication prescription*	
Patient characteristic/treatment	**Active† vitamin D (any) (n = 610/1167)**	**Phosphate binder (n = 682/1160)**
Demographics and HD prescription		
Age, per 10 years	0.96 (0.88, 1.05)	0.96 (0.87, 1.05)
Female	1.16 (0.84, 1.60)	1.16 (0.88, 1.53)
Vintage, per year	**1.06 (1.02, 1.10)**	1.02 (0.99, 1.06)
Body mass index, per kg/m^2	1.01 (0.97, 1.05)	1.02 (0.98, 1.06)
Urine output >1 cup/day	0.89 (0.67, 1.17)	1.06 (0.83, 1.34)
Insurance <90%	0.78 (0.55, 1.11)	0.99 (0.73, 1.33)
Sessions per week, < 3 *vs.* 3+	1.14 (0.79, 1.63)	0.78 (0.57, 1.05)
Dialysis session length, per 30 min	1.25 (1.00, 1.57)	**0.81 (0.66, 1.00)**
Blood flow rate, per 50 mL/min	1.08 (0.85, 1.36)	1.11 (0.85, 1.45)
Standardized *Kt/V*	1.27 (0.57, 2.80)	0.85 (0.40, 1.77)
Dialysate calcium		
<1.500 mmol/L	1.19 (0.78, 1.82)	1.02 (0.67, 1.56)
1.500 mmol/L	1.00 (ref)	1.00 (ref)
1.750 mmol/L	1.88 (0.72, 4.95)	1.61 (0.72, 3.64)
Catheter use, *vs.* fistula or graft	1.00 (0.67, 1.51)	0.83 (0.57, 1.21)
Comorbidities		
Coronary heart disease	0.87 (0.63, 1.19)	1.15 (0.83, 1.59)
Congestive heart failure	**1.26 (0.97, 1.63)**	0.99 (0.74, 1.32)
Diabetes	1.04 (0.80, 1.34)	0.96 (0.74, 1.25)
Laboratory values†		
Phosphorus >7 mg/dL	0.81 (0.60, 1.08)	0.93 (0.65, 1.31)
PTH >600 pg/mL	1.28 (0.88, 1.87)	1.01 (0.71, 1.44)
Calcium, mg/dL		
<8.4	0.79 (0.56, 1.12)	0.85 (0.61, 1.19)
8.4–9.5	1.00 (ref)	1.00 (ref)
> 9.5	0.99 (0.73, 1.36)	0.99 (0.74, 1.33)
Albumin, per 1 g/dL	0.74 (0.54, 1.03)	**1.77 (1.25, 2.51)**
Medications prescribed*, yes *vs.* no		
Active vitamin D†	N/A	**2.05 (1.52, 2.76)**
Phosphate binder	**2.22 (1.61, 3.07)**	N/A

Each column is from a separate model adjusted for all listed variables plus city (bold indicates $P < 0.05$). * Prescription recorded during the month of study enrollment, subsequent to the most recent laboratory values recorded in the previous 3 months; laboratory values in Tables 1 and 3 are contemporary with the study enrollment prescriptions. † Calcitriol or one of its synthetic analogs. CI: Confidence interval; DOPPS: Dialysis Outcomes and Practice Patterns Study; HD: Hemodialysis; PTH: Parathyroid hormone.

on chronic heart failure patients with preserved ejection fraction, over 90% of patients had vitamin D deficiency.[23] Lack of vitamin D may cause hypocalcemia and increase the requirement of active vitamin D.

Our study has several limitations. Since this study represents three major metropolitan areas of China and does not include patients receiving HD in smaller cities or rural areas, our study cannot be viewed as representative of the whole Chinese HD population. Due to the cross-sectional observational nature of these analyses, we cannot establish cause-and-effect relationships for the observed associations.

In summary, our study highlights important aspects of MBD and practice patterns for patients receiving maintenance HD in China. We found that hyperphosphatemia and secondary hyperparathyroidism were common, with significant heterogeneity in practice of laboratory measurements. Current Chinese Society of Nephrology guidelines on MBD management support realistic targets for serum phosphorus and parathyroid levels, and according to recent survey data, providers and units demonstrate high level awareness of the new MBD guidelines. We also note that some progress on MBD management has been made in China since the DOPPS5 study was finished. These include the availability of non-calcium phosphate binders and calcimimetics, and the increased coverage for HD by national health insurance. A new guideline on management of MBD by Chinese Society of Nephrology was released in 2019. The release of this new guideline should increase clarity regarding management within the Chinese context and has the potential to achieve better practices including standardization of laboratory measurements and treatments. We hope that DOPPS7, which is just started, will capture subsequent standardization in practice.

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Conflicts of interest

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