NEPHROLOGY - ORIGINAL PAPER

The association of normal-range serum phosphorus with immunoglobulin A nephropathy progression: a retrospective cohort study

Xin An[1] · Lin Ding[1] · Yanjiang Yang[1] · Zhanli Yang[2] · Yimeng Zhang[1] · Fang Bai[1] · Lei Liu[1] · Weiwei Shi[3] · Xiangdong Yang[1]

Abstract

Purpose The relationship between serum phosphorus and immunoglobulin A (IgA) nephropathy progression remains uncertain, especially normal-range serum phosphorus. Therefore, we herein examined the relationship between the normal-range serum phosphorus and the progression of IgA nephropathy.

Methods One hundred sixty-two patients with primary IgA nephropathy were divided into three groups according to tertiles of baseline serum phosphorus (first tertile: 0.73–1.04 mmol/L; second tertile: 1.04–1.21 mmol/L; third tertile: 1.21–1.60 mmol/L). Estimated glomerular filtration rate (eGFR) was calculated using the chronic kidney disease epidemiology collaboration. The composite outcome was defined as a decrease of at least 50% in eGFR from baseline or end-stage kidney disease (ESKD). The association of serum phosphorus with IgA nephropathy progression was estimated using Cox proportional hazards models, adjusting for potential confounders.

Results During a median 16 month follow-up period, 15 patients reached a composite outcome. In the crude Cox proportional hazard model, baseline serum phosphorus as a continuous variable was associated with increased risk for adverse renal outcomes [hazard ratio (HR) = 63.510, 95% confidence interval (CI) = 3.953–1020.284, $P = 0.003$], and the high tertile of serum phosphorus group had an increased risk of the composite outcome by using the low tertile group as the reference (HR = 11.895, 95% CI = 1.522–92.993, $P = 0.018$). After adjustment for traditional risk factors, the high tertile of serum phosphorus group was significantly related to IgA nephropathy progression compared with the low tertile group (HR = 9.424, 95% CI = 1.019–87.165, $P = 0.048$).

Conclusions Relatively higher serum phosphorus levels within the normal range were significantly associated with the progression of IgA nephropathy.

Keywords IgA nephropathy · Serum phosphorus · Risk factors · Renal prognosis · Chronic kidney disease

✉ Xiangdong Yang
yxd@email.sdu.edu.cn

1 Department of Nephrology, Qilu Hospital of Shandong University, No. 107, West Culture Road, Jinan 250000, Shandong, China

2 Department of Neurosurgery, People's Hospital of Zhangdian District, Zibo, Shandong, China

3 Department of Ultrasonography, Cental Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, China

Introduction

Chronic kidney disease (CKD) is a major public health problem, especially in developing countries [1]. A cross-sectional study in China showed that the prevalence of chronic kidney disease was 10.8% among adults aged 18 years and older [2]. Immunoglobulin A (IgA) nephropathy, one of the primary glomerulonephritis, is the most common cause of chronic renal failure [3]. IgA nephropathy is defined by the presence of IgA-dominant or co-dominant immune deposits within glomeruli [4]. The disease can present with a spectrum of clinical syndromes ranging from asymptomatic abnormalities noted on urinalysis to rapidly progressive glomerulonephritis,

and there is a substantial variation in clinical course and outcomes [5]. In recent researches, the mucosal immune system and complement system play an important role in IgA nephropathy pathogenesis. Up to now, there is no ideal therapy to treat IgA nephropathy. Several risk factors have been identified for IgA nephropathy progression and need to be intervened as early as possible, which include proteinuria, high blood pressure, and estimated glomerular filtration rate (eGFR) at the time of renal biopsy [6–8]. However, there are still some patients at high risk of evolving into end-stage kidney disease (ESKD) even after 20 years [9]. Therefore, there is an urgent and pressing need to explore new predictive factors to prevent the progression of IgA nephropathy.

Recently, a meta-analysis of 12 cohort studies with 25,546 patients found every 1 mg/dL (0.32 mmol/L) increase in serum phosphorus level was associated independently with an increased risk of kidney failure [hazard ratio (HR) = 1.36, 95% confidence interval (CI) = 1.20–1.55] [10], and a prospective study in China showed that serum phosphorus was an independent risk factor for adverse renal outcomes in patients with CKD [11]. However, studies on the effect of serum phosphorus on adverse renal outcomes in IgA nephropathy are scarce, and the relationship between serum phosphorus and IgA nephropathy progression remains uncertain, especially normal-range serum phosphorus. Therefore, our study aims to explicit the relationship between the normal-range serum phosphorus and the progression of IgA nephropathy.

Materials and methods

Study population

We assessed the patients with primary IgA nephropathy who were diagnosed by percutaneous renal biopsy at the Department of Nephrology, Qilu Hospital of Shandong University, between January 1, 2017, and August 30, 2021. The inclusion criteria were that patients were ≥ 18 years old, baseline serum phosphorus was within the normal reference range for the laboratory at Qilu Hospital of Shandong University, and eGFR (according the chronic kidney disease epidemiology collaboration) was above 15 mL/min per 1.73m^2 at baseline. The exclusion criteria included patients with secondary IgA nephropathy or other kidney diseases, such as IgA vasculitis, systemic lupus erythematosus, diabetes nephropathy, and hypertensive nephropathy. Patients who received phosphate binder or other drugs that affected serum phosphate levels therapy and with unavailable clinical data and follow-up time of fewer than three months were also excluded.

Data collection and definitions

All data were obtained from the database of Qilu Hospital of Shandong University. Clinical data at the time of renal biopsy were used as baseline data, including age, sex, height, weight, systolic and diastolic blood pressure, hemoglobin, urine albumin to creatinine ratio (UACR), plasma albumin, triglyceride, cholesterol, serum creatinine, serum uric acid, and serum phosphorus. Medications used during follow-up were also collected, including glucocorticoid or other immunosuppressants, angiotensin-converting enzyme inhibitors (ACEIs), and angiotensin II receptor blockers (ARBs).

The Chronic kidney disease epidemiology collaboration equation was used for reporting eGFR [12]. Baseline serum phosphorus levels at the time of renal biopsy were measured using an automatic biochemical analyzer (Hitachi AutoAnalyzer 7100, Hitachi, Japan) with a reference range of 0.60–1.60 mmol/L, and serum phosphorus levels above 1.6 mmol/L were considered hyperphosphatemia [13]. Patients were categorized into three groups according to tertiles of baseline serum phosphorus (first tertile: 0.73–1.04 mmol/L; second tertile: 1.04–1.21 mmol/L; third tertile: 1.21–1.60 mmol/L). The composite outcome was a decrease of at least 50% in the eGFR from baseline or ESKD (defined as eGFR < 15 mL/min/1.73 m^2 or need for kidney replacement therapy).

Histopathologic parameters

All kidney tissue specimens were obtained by percutaneous renal biopsy in Qilu Hospital of Shandong University and were scored according to the Oxford Classification of IgA nephropathy [14], including mesangial hypercellularity (M), endocapillary hypercellularity (E), segmental glomerulosclerosis (S), tubular atrophy/interstitial fibrosis (T), and cellular/fibrocellular crescent (C). On immunofluorescence microscopy, the severity of mesangial deposition of IgA, immunoglobulin G (IgG), immunoglobulin M (IgM), complement component 3 (C3), and complement component 1q (C1q) was coded as five grades of 0 to 5 according to 0, ±, 1+, 2+, 3+, and 4+.

Statistical analysis

For continuous variables, data with normal distributions were described as means with standard deviations and compared using a one-way analysis of variance (ANOVA) test. Skewed data were expressed as the median (lower quartile, upper quartile), and the Kruskal–Wallis test was used to identify differences among the three groups. Categorical data were expressed as numbers (percentages) and assessed

using the chi-squared test. The Kaplan–Meier survival curve with the log-rank test, restricted cubic splines, and Cox regression model were used to analyze the association of serum phosphorus with IgA nephropathy progression. All tests were two-tailed, and p values < 0.05 were considered statistically significant. The data analysis was performed using IBM SPSS Statistics 22.0 [IBM Corp. (2013) IBM SPSS Statistics for Windows, Version 22.0. IBM Corp, Armonk, NY].

Results

Baseline characteristics of the study population

A total of 162 IgA nephropathy patients were included in our study, and males were predominant, accounting for 61.7% of the cohort. The mean age of the whole cohort was 37 ± 11 years, and the baseline serum phosphorus was 1.13 ± 0.18 mmol/L. The median (lower quartile, upper quartile) baseline eGFR was 66.43 (48.37–93.40) mL/min/1.73 m^2. The proportion of patients with CKD stage 1–4 was 25.9%, 30.2%, 37.7%, and 6.2%, respectively.

According to tertiles of serum phosphorus, the clinical data and pathological characteristics of patients were shown in Tables 1 and 2. Comparing with men, women's serum phosphorus levels were higher. In the high tertile of serum phosphorus group, patients' serum hemoglobin and serum albumin were lower than in the low tertile group (all $P < 0.05$). Next, we assessed the correlation between serum phosphorus and pathological characteristics among 162 IgA nephropathy patients. There was no statistically significant difference among the three groups in the Oxford classification and the severity of mesangial deposition of IgA, IgG, IgM, complement C3, and C1q on immunofluorescence microscopy (all $P > 0.05$).

Serum phosphorus and renal outcomes

During a median 16 month follow-up, 15 patients reached the composite outcome. There were statistically significant different among the three groups (log-rank test $P = 0.005$) by Kaplan–Meier survival analysis (shown in Fig. 1). Patients of the high tertile of serum phosphorus group was with a poor renal prognosis compared with the low tertile group patients (log-rank test $P = 0.003$).

The restricted cubic splines showed that there was a positive correlation between baseline serum phosphorus and hazard ratio of adverse renal outcomes, which meant higher

Table 1 Clinical characteristics of study population

| Characteristics	Tertile 1 (n = 54)	Tertile 2 (n = 54)	Tertile 3 (n = 54)	P value
Age (year)	36.02 ± 9.14	38.19 ± 11.73	36.85 ± 12.09	0.592
Female (%)	14 (25.9)	18 (33.3)	30 (55.6) *	0.004
Body mass index (Kg/m^2)	25.40 ± 4.02	25.11 ± 3.99	24.45 ± 3.66	0.428
Systolic blood pressure (mmHg)	133.41 ± 16.00	135.15 ± 16.02	137.61 ± 16.43	0.399
Diastolic blood pressure (mmHg)	84.94 ± 12.83	82.93 ± 12.91	86.22 ± 13.11	0.413
Mean arterial pressure (mmHg)	101.10 ± 13.05	100.33 ± 13.09	103.35 ± 13.23	0.464
Medication use (%)				
Glucocorticoid	5 (9.3)	6 (11.1)	14 (25.9)	0.032
Other immunosuppressants	3 (5.6)	2 (3.7)	9 (16.7)	0.035
ACEI/ARB	31 (57.4)	30 (55.6)	26 (48.1)	0.594
Hemoglobin (g/L)	138.70 ± 18.49	132.78 ± 19.12	127.85 ± 20.88*	0.017
UACR (g/g)	1.22 (0.55, 2.05)	1.42 (0.65, 2.11)	1.33 (0.66, 2.93)	0.468
Plasma albumin (g/L)	40.54 ± 5.04	37.24 ± 6.95 *	36.90 ± 7.11*	0.006
Cholesterol (mmol/L)	4.73 (4.16, 5.85)	5.29 (4.32, 6.32)	5.23 (4.56, 6.12)	0.144
Triglyceride (mmol/L)	1.80 (1.23, 2.55)	1.57 (1.10, 2.41)	1.90 (1.37, 2.69)	0.398
Uric acid (umol/L)	407.50 (264.00, 459.25)	382.00 (320.75, 472.25)	378.00 (335.75, 434.50)	0.858
Serum creatinine (umol/L)	113.00 (80.75, 148.00)	115.50 (81.75, 134.25)	110.00 (74.00, 177.00)	0.963
eGFR (mL/min/1.73m^2)	71.64 (51.86, 98.00)	63.30 (53.80, 87.80)	64.04 (39.79, 99.27)	0.332
Serum phosphorus (mmol/L)	0.95 (0.88, 1.01)	1.13 (1.07, 1.16)	1.33 (1.25 1.39)	<0.001

ACEI angiotensin-converting enzyme inhibitor, *ARB* angiotensin II receptor blockers, *UACR* urine albumin to creatinine ratio, *eGFR* estimated glomerular filtration rate

*P value < 0.05 compared with first tertile

Table 2 Pathological characteristics of study population

Characteristics	Tertile 1 (n = 54)	Tertile 2 (n = 54)	Tertile 3 (n = 54)	P value
Immunofluorescence microscopy				
IgA Mesangial deposit	3.24 ± 1.13	3.37 ± 0.68	3.40 ± 0.72	0.611
IgG Mesangial deposit	0.13 ± 0.55	0.20 ± 0.63	0.21 ± 0.60	0.745
IgM Mesangial deposit	0.59 ± 0.98	0.69 ± 1.01	0.92 ± 1.25	0.314
C3 Mesangial deposit	1.37 ± 1.57	1.43 ± 1.63	1.19 ± 1.56	0.722
C1q Mesangial deposit	0.41 ± 0.86	0.24 ± 0.80	0.34 ± 0.78	0.566
Oxford classification				
M0 (%)	29 (53.7)	24 (44.4)	30 (55.6)	
M1 (%)	25 (46.3)	30 (55.6)	24 (44.4)	0.465
E0 (%)	29 (53.7)	27 (50.0)	26 (48.1)	
E1 (%)	25 (46.3)	27 (50.0)	28 (51.9)	0.841
S0 (%)	2 (3.7)	4 (7.4)	9 (16.7)	
S1 (%)	52 (96.3)	50 (92.6)	45 (83.3)	0.057
T0 (%)	26 (48.1)	19 (35.2)	28 (51.9)	
T1 (%)	25 (46.3)	31 (57.4)	18 (33.3)	
T2 (%)	3 (5.6)	4 (7.4)	8 (14.8)	0.089
C0 (%	40 (74.1)	33 (61.1)	32 (38.9)	
C1 (%)	12 (22.2)	21 (38.9)	19 (35.2)	
C2 (%)	2 (3.7)	0 (0.0)	3 (5.6)	0.214

IgA immunoglobulin A, *IgG* immunoglobulin G, *IgM* immunoglobulin M, *C3* complement component 3, *C1q* complement component 1q, *M* mesangial hypercellularity; *E* endocapillary hypercellularity, *S* segmental glomerulosclerosis, *T* tubular atrophy/interstitial fibrosis, *C* cellular/fibrocellular crescent
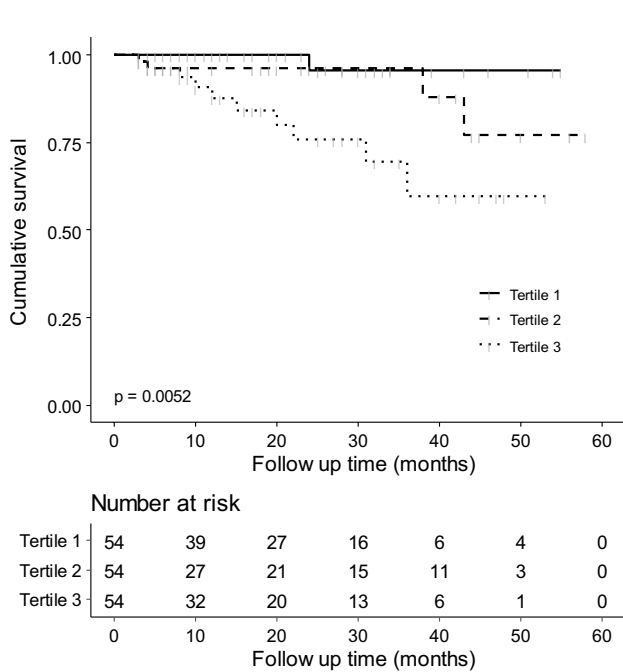
Fig. 1 Kaplan–Meier survival analysis among three tertiles of serum phosphorus groups
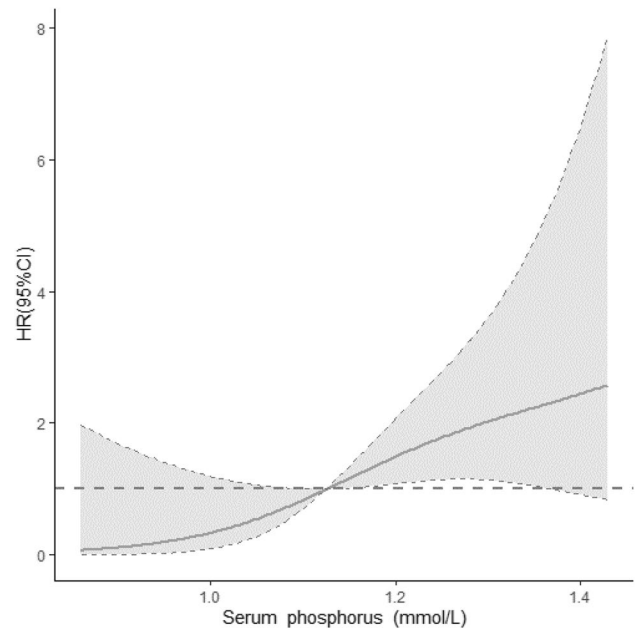
Fig. 2 Restricted cubic spline curve of hazard ratio (HR) of serum phosphorus for IgA nephropathy progression. The solid line represents the estimated HR, the shaded area represents the 95% confidence interval (CI), and the dashed lines on it are the upper and lower limits of the 95% CI, the horizontal dashed line represents HR equal to 1

Table 3 Unadjusted Cox regression analysis affecting the prognosis of patients with IgA nephropathy

Characteristics	P value	HR	95%CI
Serum phosphorus (mmol/L)	0.003	63.510	(3.953, 1020.284)
Serum phosphorus as categorical variable (mmol/L)			
Tertile 1: 0.73–1.04	Reference	Reference	Reference
Tertile 2: 1.04–1.21	0.206	4.120	(0.459, 36.997)
Tertile 3: 1.21–1.60	0.018	11.895	(1.522, 92.993)
Hemoglobin (g/L)	0.003	0.966	(0.945, 0.988)
Age (year)	0.537	1.013	(0.972, 1.057)
Female	0.861	0.912	(0.324, 2.564)
ACEI/ARB treatment	0.888	1.078	(0.382, 3.037)
Glucocorticoid treatment	0.233	2.008	(0.639, 6.312)
Body mass index (Kg/m^2)	0.776	0.984	(0.878, 1.102)
Mean arterial pressure (mmHg)	0.007	1.045	(1.012, 1.078)
UACR (g/g)	0.061	1.197	(0.992, 1.446)
Plasma albumin (g/L)	0.097	0.943	(0.879, 1.011)
Cholesterol (mmol/L)	0.710	1.059	(0.782, 1.434)
Triglyceride (mmol/L)	0.562	0.894	(0.612, 1.306)
Uric acid (umol/L)	0.157	1.003	(0.999, 1.008)
Serum creatinine (umol/L)	0.000	1.028	(1.018, 1.037)
eGFR (mL/min/1.73m^2)	0.000	0.923	(0.887, 0.961)
M1	0.157	2.294	(0.726, 7.253)
E1	0.329	1.671	(0.596, 4.683)
S1	0.703	1.484	(0.195, 11.294)
T1–T2	0.009	7.362	(1.651, 32.830)
C1–C2	0.134	2.174	(0.788, 5.998)

ACEI angiotensin-converting enzyme inhibitor, *ARB* angiotensin II receptor blockers, *UACR* urine albumin to creatinine ratio, *eGFR* estimated glomerular filtration rate, *M* mesangial hypercellularity; *E* endocapillary hypercellularity, *S* segmental glomerulosclerosis, *T* tubular atrophy/interstitial fibrosis, *C* cellular/fibrocellular crescent, *HR* hazard ratio, *CI* confidence interval

serum phosphorus levels may result in poor renal outcomes (shown in Fig. 2).

In an unadjusted Cox proportional hazard model (shown in Table 3), baseline serum phosphorus as a continuous variable was associated with increased risk for adverse renal outcomes (HR = 63.510, 95% CI = 3.953–1020.284, P = 0.003), and the high tertile of serum phosphorus group had an increased risk of the composite outcome by using the low tertile group as the reference (HR = 11.895, 95% CI = 1.522–92.993, P = 0.018). In addition, mean arterial pressure, hemoglobin, eGFR and tubular atrophy/interstitial fibrosis ≥ 25% were also associated with poor renal prognosis. After adjustment for initial mean arterial pressure, hemoglobin, eGFR, tubular atrophy/interstitial fibrosis ≥ 25% and other traditional risk factors such as age, sex, and UACR, the high tertile of serum phosphorus group significantly related

to IgA nephropathy progression compared with the low tertile group (HR = 9.424, 95%CI = 1.019–87.165; P = 0.048) (shown in Table 4).

Discussion

Disorders of calcium and phosphorus metabolism are common complications in patients with ESKD. An increasing body of evidence suggested that higher serum phosphorus levels were strongly associated with increased mortality in patients with CKD [10, 15]. Serum phosphorus is also a risk factor associated with increased cardiovascular events in the general population [16]. Several studies have explored the association of serum phosphorus with kidney disease outcomes in patients with CKD. However, the association of serum phosphorus with IgA nephropathy progression is still uncertain.

Norris et al. [17] found that serum phosphorus was directly associated with adverse renal events in African American Study of Hypertension and Kidney Disease. In the prospective Ramipril Efficacy In Nephropathy (REIN) trial, Zoccali et al. [18] found that serum phosphate levels could aggravate CKD progression and attenuate the renoprotective effect of ACEI. In a Spanish study, they found that time-averaged serum phosphorus levels (serum phosphorus levels averaged over the follow-up time) were independently associated with a more rapid decline of renal function in patients with advanced CKD [19]. This effect does not seem to be limited to hyperphosphatemia. Chang et al. [20] used propensity score analysis to evaluate the causal effects of the normal range serum phosphorus on the incidence of ESKD, and they discovered that the relative higher baseline phosphorus levels were associated with clinical parameters consistent with the advancement of CKD, and the patients with the higher time-averaged phosphorus showed significantly higher HRs for ESKD. Furthermore, in prospective studies of the general population, serum phosphorus levels in the upper-normal range were associated with a doubling in the risk of developing incident CKD and ESKD [21]. More controversially, the largest cohort study of early CKD failed to validate the independent association of serum phosphorus with risk of death or progression to ESKD [22], and the possible explanations were that serum phosphorus levels were measured only once and the follow-up period years were relatively short in this study.

There are few pieces of research regarding the relationship between serum phosphorus and the progression of IgA nephropathy, and the relationship between normal-range serum phosphorus and poor renal outcomes in IgA nephropathy has not been explored. In our study, we included 162 primary IgA nephropathy patients with normal serum phosphorus levels at the renal biopsy, and

Table 4 Hazard ratio of serum phosphorus for IgA nephropathy progression with Cox proportional hazard models

Serum phosphorus	Model 1	Model 2	Model 3
As continuous variable, mmol/L, HR (95% CI)	66.342 (4.466, 985.404)	8.485 (0.531, 135.646)	8.535 (0.525, 138.806)
P value	0.002	0.130	0.132
As categorical variable, mmol/L, HR (95% CI)			
Tertile 1: 0.73–1.04	Reference	Reference	Reference
Tertile 2: 1.04–1.21	4.205 (0.466, 37.957)	3.062 (0.286, 32.807)	3.215 (0.286, 36.171)
P value	0.201	0.355	0.344
Tertile 3: 1.21–1.60	13.301 (1.664, 106.321)	8.968 (1.025, 78.439)	9.424 (1.019, 87.165)
P value	0.015	0.047	0.048
P value for trend	0.003	0.024	0.024

UACR urine albumin to creatinine ratio, *eGFR* estimated glomerular filtration rate, *HR* hazard ratio, *CI* confidence interval. Model 1: adjusted for age and sex; Model 2: Model 1 + adjusted for initial mean arterial pressure, UACR, hemoglobin, eGFR; Model 3: Model 2 + adjusted for tubular atrophy/interstitial fibrosis ≥ 25%

focused on the effects of normal-range serum phosphorus on IgA nephropathy progression. We found relative higher serum phosphorus as a categorical variable was significantly associated with poor renal survival, whether in crude analysis or multivariable Cox proportional hazard model. This was consistent with previous reports that the higher serum phosphorus within the normal range may be a risk factor for the progression of CKD [11, 20, 21]. Yu et al. [23] first indicated disorders of phosphorus metabolism were associated with IgA nephropathy progression in patients without dialysis and found the fourth phosphorus quartile (1.33–2.24 mmol/L) had higher risk for renal progression (HR = 2.62, 95%CI = 1.44–4.77, *P* < 0.002) compared with those in the bottom quartile (0.35–1.07 mmol/L), serum phosphorus levels (1.33–2.24 mmol/L) of the top quartile were mostly within the normal range, while the adverse effect on the renal outcome was observed. Our study was conducted in patients with normal-range serum phosphorus and excluded those with hyperphosphatemia, therefore, the mean serum phosphorus levels at baseline were relatively low. These results suggested that we should pay attention not only to the harm of hyperphosphatemia but also to the potential adverse effects of the relative higher serum phosphorus even in normal range. In addition, according to analysis of pathology types and serum phosphorus levels, there was no correlation between the two factors.

However, our study is only an observational study and cannot elucidate the causality. We should be aware that a slight tubular dysfunction may be represented as relatively higher serum phosphorous level, leading to the worse prognosis in the high tertile group. Namely, serum phosphorous may not affect kidney function but reversely, less healthy kidney may exhibit as high serum phosphorous. Our patients'

serum phosphorus levels were within the normal range, however, normal-range serum phosphorous may less likely to cause vascular calcification. Animal models showed that overload phosphate induced podocyte injury via type III Na-dependent phosphate transporter [24]. Furthermore, several studies showed that fibroblast growth factor 23 (FGF23) was closely associated with CKD progression [25, 26]. FGF23 is elevated prior to the appearance of high phosphorus levels and maintains serum phosphorus within the normal range by increasing the rate of phosphate excretion per nephron [27], potentially causing calciprotein particle formation in the tubular lumen, interstitial fibrosis, and tubular injury [28], these seem to indirectly suggest that higher serum phosphorus levels within the normal range can lead to an unfavorable renal prognosis, however, the hypothesis of causality still needs to be tested by high-quality randomized controlled studies.

Currently, phosphorus-lowering treatment focuses on patients with overt hyperphosphatemia in clinical practice, and normophosphatemia may not be an indication to start phosphate-lowering treatment due to concerns about the efficacy and safety of phosphate binders in the Kidney Disease: Improving Global Outcomes Clinical Practice Guidelines [29]. Although our study suggests that normal range serum phosphorus is associated with poor renal outcomes in patients with IgA nephropathy, whether appropriate phosphorous management is important in IgA nephropathy needs additional study.

Study limitation

This research was a retrospective study with small sample size and a short follow-up period. In this study, we only

explored the relationship between baseline serum phosphorus levels and renal outcomes in patients with IgA nephropathy by multifactorial regression analysis, despite unavoidable confounding factors were remained. The relationship between time-averaged phosphorus and renal outcomes was not considered in the analysis. Large-scale prospective studies are still needed to explore this in the future.

Conclusion

In summary, our study showed that relatively higher serum phosphorus levels within the normal range were significantly associated with the progression of IgA nephropathy.

Data availability The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Informed consent The research was granted an exemption from requiring written informed consent by the Ethics Committee of Qilu Hospital of Shandong University.

References

1. Nugent RA, Fathima SF, Feigl AB, Chyung D (2011) The burden of chronic kidney disease on developing nations: a 21st century challenge in global health. Nephron Clin Pract 118(3):c269–c277. https://doi.org/10.1159/000321382
2. Zhang L, Wang F, Wang L, Wang W, Liu B, Liu J et al (2012) Prevalence of chronic kidney disease in China: a cross-sectional survey. Lancet 379(9818):815–822. https://doi.org/10.1016/S0140-6736(12)60033-6
3. Li LS, Liu ZH (2004) Epidemiologic data of renal diseases from a single unit in China: analysis based on 13,519 renal biopsies. Kidney Int 66(3):920–923. https://doi.org/10.1111/j.1523-1755.2004.00837.x
4. Roberts IS (2014) Pathology of IgA nephropathy. Nat Rev Nephrol 10(8):445–454. https://doi.org/10.1038/nrneph.2014.92
5. Pattrapornpisut P, Avila-Casado C, Reich HN (2021) IgA nephropathy: core curriculum 2021. Kidney Dis 78(3):429–441. https://doi.org/10.1053/j.ajkd.2021.01.024
6. Rudnicki M, Siwy J, Wendt R, Lipphardt M, Koziolek MJ, Maixnerova D et al (2021) Urine proteomics for prediction of disease progression in patients with IgA nephropathy. Nephrol Dial Transplant 37(1):42–52. https://doi.org/10.1093/ndt/gfaa307
7. Berthoux F, Mohey H, Laurent B, Mariat C, Afiani A, Thibaudin L (2011) Predicting the risk for dialysis or death in IgA nephropathy. J Am Soc Nephrol 22(4):752–761. https://doi.org/10.1681/ASN.2010040355
8. Lee K, Shin J, Park J, Hwang S, Jang HR, Huh W et al (2018) First-year GFR slope and long-term renal outcome in IgA nephropathy. Eur J Clin Invest 48(6):e12936. https://doi.org/10.1111/eci.12936
9. D'Amico G (2000) Natural history of idiopathic IgA nephropathy: role of clinical and histological prognostic factors. Am J Kidney Dis 36(2):227–237. https://doi.org/10.1053/ajkd.2000.8966
10. Da J, Xie X, Wolf M, Disthabanchong S, Wang J, Zha Y et al (2015) Serum phosphorus and progression of CKD and mortality: a meta-analysis of cohort studies. Am J Kidney Dis 66(2):258–265. https://doi.org/10.1053/j.ajkd.2015.01.009
11. Xu D, Lv J, Wang J, Zhang L, Zhang H (2017) Association between plasma phosphorus and renal outcome: a prospective cohort of patients majorly with glomerulonephritis. Nephrology (Carlton) 22(1):43–48. https://doi.org/10.1111/nep.12724
12. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI et al (2009) A new equation to estimate glomerular filtration rate. Ann Intern Med 150(9):604–612. https://doi.org/10.7326/0003-4819-150-9-200905050-00006
13. Yang X, Jiang N, Huang J, Gu A, Lin A, Zhang L et al (2014) Clinical factors associated with hyperphosphatemia in peritoneal dialysis patients. Chin J Nephrol 30(1):29–34. https://doi.org/10.3760/cma.j.issn.1001-7097.2014.01.006
14. Trimarchi H, Barratt J, Cattran DC, Cook HT, Coppo R, Haas M et al (2017) Oxford classification of IgA nephropathy 2016: an update from the IgA nephropathy classification working group. Kidney Int 91(5):1014–1021. https://doi.org/10.1016/j.kint.2017.02.003
15. Palmer SC, Hayen A, Macaskill P, Pellegrini F, Craig JC, Elder GJ et al (2011) Serum levels of phosphorus, parathyroid hormone, and calcium and risks of death and cardiovascular disease in individuals with chronic kidney disease: a systematic review and meta-analysis. JAMA 305(11):1119–1127. https://doi.org/10.1001/jama.2011.308
16. Dhingra R, Sullivan LM, Fox CS, Wang TJ, D'Agostino RB Sr, Gaziano JM et al (2007) Relations of serum phosphorus and calcium levels to the incidence of cardiovascular disease in the community. Arch Intern Med 167(9):879–885. https://doi.org/10.1001/archinte.167.9.879
17. Norris KC, Greene T, Kopple J, Lea J, Lewis J, Lipkowitz M et al (2006) Baseline predictors of renal disease progression in the African American Study of Hypertension and Kidney Disease. J Am Soc Nephrol 17(10):2928–2936. https://doi.org/10.1681/ASN.2005101101
18. Zoccali C, Ruggenenti P, Perna A, Leonardis D, Tripepi R, Tripepi G et al (2011) Phosphate may promote CKD progression and attenuate renoprotective effect of ACE inhibition. J Am Soc Nephrol 22(10):1923–1930. https://doi.org/10.1681/ASN.2011020175
19. Caravaca F, Villa J, García de Vinuesa E, Martínez del Viejo C, Martínez Gallardo R, Macías R et al (2011) Relationship between serum phosphorus and the progression of advanced chronic kidney disease. Nefrologia 31(6):707–715. https://doi.org/10.3265/Nefrologia.pre2011.Sep.11089
20. Chang WX, Xu N, Kumagai T, Shiraishi T, Kikuyama T, Omizo H et al (2016) The impact of normal range of serum phosphorus on the incidence of end-stage renal disease by a propensity score analysis. PLoS One 11(4):e0154469. https://doi.org/10.1371/journal.pone.0154469
21. O'Seaghdha CM, Hwang SJ, Muntner P, Melamed ML, Fox CS (2011) Serum phosphorus predicts incident chronic kidney disease

and end-stage renal disease. Nephrol Dial Transplant 26(9):2885–2890. https://doi.org/10.1093/ndt/gfq808

22. Mehrotra R, Peralta CA, Chen SC, Li S, Sachs M, Shah A et al (2013) No independent association of serum phosphorus with risk for death or progression to end-stage renal disease in a large screen for chronic kidney disease. Kidney Int 84(5):989–997. https://doi.org/10.1038/ki.2013.145

23. Yu G, Cheng J, Jiang Y, Li H, Li X, Chen J (2021) Serum phosphorus and calcium levels, and kidney disease progression in immunoglobulin A nephropathy. Clin Kidney J 14(9):2108–2113. https://doi.org/10.1093/ckj/sfab002

24. Sekiguchi S, Suzuki A, Asano S, Nishiwaki-Yasuda K, Shibata M, Nagao S (2011) Phosphate overload induces podocyte injury via type III Na-dependent phosphate transporter. Am J physiol Renal physiol 300(4):F848–F856. https://doi.org/10.1152/ajprenal.00334.2010

25. Scialla JJ, Astor BC, Isakova T, Xie H, Appel LJ, Wolf M (2013) Mineral metabolites and CKD progression in African Americans. J Am Soc Nephrol 24(1):125–135. https://doi.org/10.1681/ASN.2012070713

26. Lundberg S, Qureshi AR, Olivecrona S, Gunnarsson I, Jacobson SH, Larsson TE (2012) FGF23, albuminuria, and disease progression in patients with chronic IgA nephropathy. Clin J Am Soc Nephrol 7(5):727–734. https://doi.org/10.2215/CJN.10331011

27. Isakova T, Wahl P, Vargas GS, Gutiérrez OM, Scialla J, Xie H et al (2011) Fibroblast growth factor 23 is elevated before parathyroid hormone and phosphate in chronic kidney disease. Kidney Int 79(12):1370–1378. https://doi.org/10.1038/ki.2011.47

28. Kuro-o M (2013) Klotho, phosphate and FGF-23 in ageing and disturbed mineral metabolism. Nat Rev Nephrol 9(11):650–660. https://doi.org/10.1038/nrneph.2013.111

29. Ketteler M, Block GA, Evenepoel P, Fukagawa M, Herzog CA, McCann L et al (2018) Diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder: synopsis of the kidney disease: improving global outcomes 2017 clinical practice guideline update. Ann Intern Med 168(6):422–430. https://doi.org/10.7326/M17-2640