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ABOUT COVER

Editorial board member of *World Journal of Diabetes*, Dr. José Carvalheira is an Associate Professor at the Campinas State University (UNICAMP, Brazil). Having received his Bachelor's degree from Pernambuco University College of Medicine in 1994, Dr. Carvalheira undertook his postgraduate training at UNICAMP, receiving his PhD in 2004. He became Chief Physician in the Clinical Oncology Division of the Hospital de Clínicas Affiliated to UNICAMP in 2014 and has held the position since. His ongoing research interests involve investigation of how body composition, energy homeostasis, and the underlying mechanisms of whole-body metabolism are linked to cancer survival outcomes. In particular, his studies aim to elucidate the regulatory role of insulin resistance and its attendant pathophysiological features in determination of cancer-mediated disturbances in systemic homeostasis and cancer prognosis. (L-Editor: Filipodia)

AIMS AND SCOPE

The primary aim of *World Journal of Diabetes* (*WJD*, *World J Diabetes*) is to provide scholars and readers from various fields of diabetes with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

  WJD mainly publishes articles reporting research results and findings obtained in the field of diabetes and covering a wide range of topics including risk factors for diabetes, diabetes complications, experimental diabetes mellitus, gestational diabetes, diabetic angiopathies, diabetic cardiomyopathies, diabetic coma, diabetic ketoacidosis, diabetic nephropathies, diabetic neuropathies, *etc.*.

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RESPONSIBLE EDITORS FOR THIS ISSUE

Case Control Study

Importance of serum phosphate in elderly patients with diabetes mellitus

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Abstract

BACKGROUND
Metabolic disturbances including changes in serum calcium, magnesium or phosphate (P) influence the prevalence of type 2 diabetes mellitus (DM). We assessed the importance of serum P in elderly patients with type 2 DM *vs* non-diabetes mellitus (non-DM) in relation to renal function.

AIM
To determine the association between serum P and serum glucose or insulin resistance in diabetic and non-diabetic patients.

METHODS
One hundred-ten subjects with a mean age of 69.02 ± 14.3 years were enrolled. Twenty-nine of the participants had type 2 DM (26.4%). The incidence of hypertension, smoking and receiving vitamin D (vitD) derivates were recorded. The participants were classified by both estimated glomerular filtration rate (eGFR) and albuminuria categories according to the Kidney Disease Improving Global Outcomes 2012 criteria.

RESULTS
We divided the patients in two groups according to the P cut-off point related to DM value. A comparison between high and low P showed that body mass index 30.2 ± 6.3 *vs* 28.1 ± 4.6 (*P* = 0.04), mean glucose 63.6 *vs* 50.2 (*P* = 0.03), uric acid 6.7 ± 1.6 *vs* 6.09 ± 1.7 (*P* = 0.05), mean intact-parathyroid hormone 68.06 *vs* 47.4 (*P* = 0.001), systolic blood pressure 147.4 ± 16.7 *vs* 140.2 ± 16.1 (*P* = 0.02), mean albuminuria 63.2 *vs* 50.6 (*P* = 0.04) and eGFR 45.6 ± 22.1 *vs* 55.4 ± 21.5 (*P* = 0.02) were significantly different. χ^2 tests showed a significant association between high P and DM, hypertension, receiving vitD, smoking and eGFR stage (χ^2 = 6.3, *P* =

0.01, χ^2 = 3.9, P = 0.03, χ^2 = 6.9, P = 0.009, χ^2 = 7.04, P = 0.01 and χ^2 = 7.36, P = 0.04, respectively). The adjusted model showed that older age, female gender and increased body mass index were significant predictors of type 2 DM when entering the covariates.

CONCLUSION
High serum P contributes to vascular and metabolic disturbances in elderly patients with type 2 DM and renal impairment.

Key Words: Serum phosphate; Diabetes mellitus; Renal disease; Old age; Albuminuria; Vitamin D

Core Tip: Despite high serum phosphate (P) being associated with hypertension, albuminuria, smoking, low estimated glomerular filtration rate and metabolic disorders, traditional factors including older age, female gender and high body mass index were proved to be potential predictors of type 2 diabetes mellitus. Serum P levels were similar in diabetic and non-diabetic patients and the association between serum P and serum glucose or insulin resistance was found to be non-significant in both diabetic and non-diabetic patients, which was discordant with previous reports, due to renal dysfunction.

INTRODUCTION

Patients with type 2 diabetes mellitus (DM) are a high risk group and metabolic disorders contribute to the prediction of morbidity and mortality in this population. Metabolic disturbances including changes in serum calcium, magnesium or phosphate (P) can explain why dyslipidemia, hyperglycemia and hyperuricemia, which are related to obesity, impact the progression to type 2 DM[1].

It has been reported that low serum levels of P are associated with increased insulin resistance in the healthy population[2]. Moreover, a previous experimental study using rats suggested that P depletion results in low insulin secretion by pancreatic beta cells, due to high intracellular calcium and inhibition of adenosine triphosphatase production[3]. Thus, it has been suggested that low serum P may disturb the regulation of serum glucose in non-DM with obesity[4].

Phosphate is essential for life, as it participates in the structure of cellular membranes as a material of nucleic acids, phospholipids and adenosine triphosphate. Additionally, P plays a crucial role in cellular signaling through reactions of phosphorylation. Homeostasis of P is affected by multiple interactions between the intestine, parathyroid glands, kidneys and bone.

Serum P levels are dependent on the absorption in the gut from dietary P, the excretion and reabsorption of P in the kidneys, and the movement of P between the extracellular and skeletal pools. Parathyroid hormone and fibroblast growth factor 23 play an important role in the regulation of serum P by mediating urinary P removal[5]. Elevated serum P is recognized as an independent predictor for advanced vascular disease in chronic kidney disease (CKD)[6]. However, epidemiological studies showed that all-cause mortality was independently related to increased serum P in all populations, even without CKD and serum P levels in the upper normal reference range[7,8].

In this study, we assessed the importance of serum P levels in elderly patients with type 2 DM compared to those without DM in relation to renal function clustering in CKD stages 1-4.

MATERIALS AND METHODS

Study subjects

This was a single-center cross-sectional study which included a total of one hundred-ten subjects. The participants were from the Department of Nephrology outpatient clinic of our Hospital, in which elderly non-dialysis patients are prevalent in accordance with most Nephrology Clinics worldwide. As the geriatric population continues to increase in most countries of the world (defined as age > 65 years) and the prevalence of renal disease rises with advancing age, nephrologists are usually confronted with an elderly patient population with co-morbidities and require ongoing care[9,10].

We studied sixty-seven males and forty-three females with a mean age of 69.02 ± 14.3 years after the exclusion of uncooperative patients and those who were younger than eighteen years of age. Subjects with established psychiatric symptomatology or dementia diagnosed by neuropsychologists were also excluded from the study, due mainly to invalid informed medical history or treatment.

Detailed individual medical histories and current pharmaceutical therapy were obtained from the participants. Twenty-nine of the participants had type 2 DM (26.4%) and eighty-one did not have DM (73.6%). The diabetics were taking the same hypoglycemic medications and both diabetics and non-diabetics were taking the same hypolipidemic medications. A total of seventy-five participants were hypertensive (68.2%) and thirty-five were non-hypertensive (31.8%). The hypertensive patients were receiving the same anti-hypertensive medications including beta-blockers, calcium channel blockers, and inhibitors of angiotensin II AT1 receptors. Forty subjects (36.4%) were taking vitamin D (vitD) and seventy (63.6%) were not taking vitD. None of the participants was taking P binders.

Demographic data including age, gender and lifestyle characteristics regarding physical activity, smoking and alcohol drinking were collected using a questionnaire. Fourteen of the participants were current smokers (12.7%), and ninety-six were non-smokers (87.3%). Non-drinkers were considered those who did not consume alcohol during the past month. The World Health Organization (WHO) recommendations for healthy adults were used to measure physical activity/inactivity[11].

Anthropometric measurements including body weight (to the nearest 0.1 kg) and height (to the nearest 0.1 cm) were recorded using an anthropometer (Seca, Hamburg, Germany). Body mass index (BMI) was calculated by dividing the body weight in kilograms by the square of the height in meters (kg/m^2) and categorized based on the WHO classification[12]. Waist circumference (WC), was measured from the midpoint between the top of iliac crest and the lower margin of the last palpable rib at the end of a normal expiration according to the WHO guidelines[13].

Biochemical measurements

Overnight fasting plasma glucose (normal range 65-110 mg/dL), creatinine (normal range 0.5-1.2 mg/dL), uric acid (normal range 2.6-6.0 mg/dL), calcium (normal range 8.1-10.4 mg/dL), P (normal range 2.5-4.5 mg/dL), triglycerides (normal range 40-150 mg/dL), low-density lipoprotein-cholesterol (normal range < 160 mg/dL) and high-density lipoprotein-cholesterol (normal range 35-80 mg/dL) were recorded from patient files using the latest results. A spectrophotometric technique using a Chemistry Analyzer (MINDRAY BS-200, Diamond Diagnostics, United States) was used for biochemical measurements.

The concentration of intact-parathyroid hormone (i-PTH) (normal range 18.5-88 pg/mL) and insulin (normal range 2.6-25 μU/mL) were measured by radioimmunoassays (CIS Bio International/France and BioSource Europe SA, Belgium, respectively). 25 hydroxyvitaminD$_3$ [25(OH) D$_3$] (normal range 30-100 ng/mL) was assessed using high-performance liquid chromatography[14].

The homeostasis model assessment of insulin resistance (HOMA-IR)[15] was used to calculate insulin resistance.

Urinary albumin and creatinine concentrations were measured by the Chemistry Analyzer using spot urine samples from the first morning void.

Definitions

Hypertension was defined as a mean systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 80 mmHg and/or participants who were taking antihypertensive therapy due to a pre-existing history of hypertension. We recommended the home two per day blood pressure measurements for SBP and DBP using an automatic sphygmomanometer (OMRON M4-I Co., Ltd., Kyoto, Japan).

Peripheral mean blood pressure (pMBP) was calculated as: pMBP = DBP + 0.4 (SBP - DBP). Pulse pressure was calculated as the difference between SBP and DBP.

The presence of CKD was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) 2012 criteria for a duration more than 3 mo[16]. The estimated glomerular filtration rate (eGFR) was calculated using the CKD Epidemiology Collaboration equation and classified in 4 categories (1 to 4) according to KDIGO 2012 criteria, as we did not include patients in the fifth stage of CKD. We also classified our participants in stages based on albuminuria, which was defined as urinary albumin-to-creatinine ratio (ACR) ≥ 30 mg/g according to KDIGO 2012[16]. As the ACR correlates well with 24-h urinary albumin excretion, calculation of ACR using a spot urine sample was considered acceptable[17]. Primary renal diseases included hypertensive nephrosclerosis, diabetic nephropathy, interstitial nephritis and other/unknown.

Central or visceral obesity was determined by a WC ≥ 94 cm in men and ≥ 80 cm in women using the International Diabetes Federation criteria for the diagnosis of metabolic syndrome[18].

Statistical analysis

Data were presented as absolute numbers and frequencies for binary and categorical variables. Data were expressed as mean ± SD or as median value (interquartile range) for data that showed skewed distribution. The differences between mean values for two groups were assessed using the unpaired *t*-test and data that showed skewed distributions were compared using the Mann-Whitney *U*-test. Bivariate correlations between variables were defined by Spearman coefficient and comparisons between categorical variables were defined by χ^2 tests. A *P* value < 0.05 was considered statistically significant. We built a model using logistic regression analysis in order to investigate the predictive role of serum P on the manifestations of DM by adjusting for covariates. Additionally, we built models using linear regression analysis to determine the relationship between serum P and serum glucose levels adjusting for covariates. The SPSS 15.0 statistical package for Windows (SPSS Inc., Chicago, IL, United States) was used for statistical analysis.

RESULTS

Correlations

Bivariate correlations defined by the Spearman coefficient showed a significant positive correlation between serum P and serum glucose (*r* = 0.204, *P* = 0.03), uric acid (*r* = 0.195, *P* = 0.04), albuminuria (*r* = 0.192, *P* = 0.04), i-PTH (*r* = 0.239, *P* = 0.01) and pMBP (*r* = 0.214, *P* = 0.02), although the relationship between P and eGFR was found to be significantly inverse in all subjects (*r* = -0.224, *P* = 0.01). When including diabetics and non-diabetics separately we observed that the correlation between serum P and both serum glucose and HOMA-IR was non-significant in both groups.

Comparisons

We determined the differences between diabetics and non-diabetics and observed similar serum P levels between these groups.

The patients were then divided into two groups according to the receiver operating characteristic curve P cut-off point related to a DM value equal to 3.65 mg/dL (greater, *n* = 43 or lower, *n* = 67 than 3.65 mg/dL). Characteristics and differences between the two groups of patients are listed in Table 1. The comparison between high and low P showed: BMI: 30.2 ± 6.3 *vs* 28.1 ± 4.6 (*P* = 0.04), mean glucose: 63.6 *vs* 50.2 (*P* = 0.03), uric acid: 6.7 ± 1.6 *vs* 6.09 ± 1.7 (*P* = 0.05), mean i-PTH: 68.06 *vs* 47.4 (*P* = 0.001), SBP: 147.4 ± 16.7 *vs* 140.2 ± 16.1 (*P* = 0.02), pMBP: 108.02 ± 9.8 *vs* 103.6 ± 7.8 (*P* = 0.01), mean albuminuria: 63.2 *vs* 50.6 (*P* = 0.04), eGFR: 45.6 ± 22.1 *vs* 55.4 ± 21.5 (*P* = 0.02), WC: 108.09 ± 15.9 *vs* 102.8 ± 14.3 (*P* = 0.07) and mean HOMA-IR: 56.8 *vs* 54.6 (*P* = 0.7).

Categorical associations

χ^2 tests showed significant associations between high P and DM, hypertension and receiving vitD (χ^2 = 6.3, *P* = 0.01, χ^2 = 3.9, *P* = 0.03 and χ^2 = 6.9, *P* = 0.009, respectively). χ^2 tests between high P and both eGFR and smoking also revealed significant associations (χ^2 = 7.36, *P* = 0.04 and χ^2 = 7.04, *P* = 0.01, respectively). The relationship between higher serum P and albuminuria or high insulin resistance defined by HOMA-IR was found to be non-significant.

Table 1 The differences between groups of patients according to serum phosphate higher or lower than the cut-off point related to diabetes mellitus equal to 3.65 mg/dL

Characteristic	Patients with serum P > 3.65 mg/dL (*n* = 43), mean ± SD	Patients with serum P < 3.65 mg/dL (*n* = 67), mean ± SD	P value
Age (yr)	71.2 ± 12.8	67.6 ± 15.2	0.2
BMI (kg/m^2)	30.2 ± 6.3[a]	28.1 ± 4.6	0.04
WC (cm)	108.09 ± 15.9	102.8 ± 14.3	0.07
Uric acid (mg/dL)	6.7 ± 1.2[a]	6.09 ± 1.7	0.05
LDL-C (mg/dL)	102.2 ± 29.5	110.1 ± 32.1	0.2
HDL-C (mg/dL)	44.5 ± 13.2	47.1 ± 9.8	0.2
Triglycerides (mg/dL)	137.7 ± 54.4	129.01 ± 60.1	0.4
Calcium (mg/dL)	9.5 ± 0.6	9.5 ± 0.5	0.9
P (mg/dL)	4.2 ± 0.4[a]	3.2 ± 0.3	0.001
i-PTH (pg/mL)	mean rank = 68.06[a]	47.4	0.001
25(OH)D3 (ng/mL)	18.9 ± 12.7	20.8 ± 9.2	0.3
Glucose (mg/dL)	mean rank = 63.6[a]	50.28	0.03
Insulin (μU/mL)	11.6 ± 7.4	11.9 ± 8.7	0.8
HOMA-IR (mmol/L)	mean rank = 56.8	54.6	0.7
SBP (mmHg)	147.4 ± 16.7[a]	140.2 ± 16.1	0.02
DBP (mmHg)	mean rank = 62.08	51.28	0.07
pMBP (mmHg)	108.02 ± 9.8[a]	103.6 ± 7.8	0.01
PP (mmHg)	65.7 ± 16.2	61.01 ± 17.7	0.1
ACR (mg/g)	mean rank = 63.2[a]	50.6	0.04
eGFR (mL/min/1.73 m^2)	45.6 ± 22.1[a]	55.4 ± 21.5	0.02
Category variables	*n* (%)	*n* (%)	
DM (yes/no)	17 (39.5)/26 (60.5)[a]	12 (17.9)/55 (82.1)	0.01
Hypertension (yes/no)	34 (79.1)/9 (20.9)[a]	41 (61.2)/26 (38.8)	0.03
Receiving vitD (yes/no)	22 (51.2)/21 (48.8)[a]	18 (26.9)/49 (73.1)	0.009
Smoking (yes/no)	10 (23.3)/33 (76.7)[a]	4 (6)/63 (94)	0.01
Alcohol consumption (yes/no)	13 (30.2)/30 (69.8)	16 (23.9)/51 (76.1)	0.3
Physical activity (yes/no)	17 (39.5)/26 (60.5)	34 (50.7)/33 (49.3)	0.1
Classification based on eGFR:			0.04
eGFR > 90 mL/min/1.73 m^2	3 (7)[a]	6 (9)	
eGFR = 60-90 mL/min/1.73 m^2	7 (16.3)	18 (26.9)	
eGFR = 30-60 mL/min/1.73 m^2	21 (48.8)	37 (55.2)	
eGFR = 15-30 mL/min/1.73 m^2	12 (27.9)	6 (9)	

[a]$P < 0.05$. P: Phosphate; BMI: Body mass index; WC: Waist circumference; LDL-C: Low density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol; i-PTH: Intact-parathyroid hormone; 25(OH)D$_3$: 25 hydroxyD$_3$; HOMA-IR: Homeostasis model assessment of insulin resistance; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; pMBP: Peripheral mean blood pressure; PP: Pulse pressure; ACR: Albumin-to-creatinine ratio; eGFR: Estimated glomerular filtration rate; DM: Diabetes mellitus.

Adjusted models

The logistic regression analysis model showed that older age, female gender and increased BMI were significant predictors for the manifestations of type 2 DM after entering hypertension, smoking, serum calcium and serum P levels as covariates (Table 2). Moreover, in non-diabetics we observed that only high BMI predicted

Table 2 Logistic regression analysis for predicting diabetes mellitus manifestations

Variables in model	*P* value	Odds ratio	Confidence interval
Age (yr)	0.003	1.07	1.02-1.13
Gender (male/female)	0.04	0.30	0.09–0.99
BMI (kg/m^2)	0.02	1.11	1.01–1.22
Hypertension (yes/no)	0.4	1.58	0.4–5.9
Smoking (yes/no)	0.08	3.7	0.8–17.02
Calcium (mg/dL)	0.2	1.6	0.7–3.7
P (mg/dL)	0.9	1.05	0.4–2.4

DM: Diabetes mellitus; BMI: Body mass index; P: Phosphate.

elevated serum glucose adjusting for age, gender, hypertension, smoking, eGFR, albuminuria, serum calcium and serum P (Table 3). In contrast, in diabetics we observed that only albuminuria can predict high serum glucose entering the same covariates (Table 4).

DISCUSSION

A previous study which included 162 patients with type 2 DM *vs* 82 hospitalized non-DM patients showed that serum P levels were lower in type 2 DM, due to the disturbance in metabolism[19]. In contrast, in the present study we did not observe reduced serum P in the diabetic group compared with the non-DM group. This discrepancy may be attributed to the fact that 69.1% of our subjects had low renal function defined by an eGFR less than 60 mL/min/1.73 m^2. The elimination of P depends on renal function, thus a positive P balance occurs in the early stage of renal dysfunction, although serum P levels mainly increase in advanced stages of CKD and remain elevated in patients in the end stage of renal disease without dialysis treatment. Indeed, as shown in Table 1, we noted a significant association between high serum P and eGFR and most of the patients with high serum P were classified in the third and fourth eGFR stage, although most of those with a low serum P were classified in the first, second and the third eGFR stage.

A previous study also reported a positive correlation between serum glucose and serum P in non-diabetics (*n* = 82), although in the type 2 diabetic group (*n* = 162) this correlation was found to be non-significant[19]. In contrast, we observed a positive correlation in all our subjects, but not separately in non-diabetics (*n* = 81) or diabetics (*n* = 29). Our findings are in agreement with those of the previous study regarding the diabetic patients, but not the non-diabetic patients, even though we included a similar number of non-diabetic participants to that in the previous study.

In addition, we noted a significant relationship between high serum P and the manifestations of DM divided according to the P cut-off point for DM. We also observed that the patients with higher serum P had more vascular and metabolic abnormalities than those with lower serum P, in agreement with previous reports[1,20]. The patients who had higher serum P had significantly higher blood pressure, BMI, uric acid, serum glucose, i-PTH, albuminuria and decreased eGFR in comparison to those with lower serum P. Furthermore, the relationship between high serum P and both hypertension and smoking was found to be significant. Indeed, it has already been noted that vascular calcification, arterial stiffness, cardiovascular mortality and progression of renal disease in patients with CKD or without CKD were correlated with higher serum P[21-23]. A previous study of the general population also showed that smokers have higher serum P levels[24].

It was observed that low serum P was combined with increased insulin resistance in the healthy population. A previous study of 881 non-diabetic subjects showed that low serum P levels were associated with high 2-h serum glucose and reduced insulin sensitivity[2]. However, in this study which included 81 non-diabetics we observed a non-significant correlation between serum P levels and insulin resistance defined by HOMA-IR. We also found mildly increased HOMA-IR combined with more central obesity in patients with higher serum P rather than in those with low serum P. We can

Table 3 Relation to serum glucose variables in our participants without diabetes mellitus (*n* = 81)					
Variables in model	Beta	*t*	Sig.	Lower	Upper
Age (yr)	-0.02	-0.17	0.8	-0.28	0.24
Gender (male/female)	-0.03	-0.3	0.7	-7.8	5.6
BMI (kg/m^2)	0.4	3.9	0.001	0.5	1.6
Hypertension (yes/no)	0.02	0.2	0.8	-6.5	8.2
Smoking (yes/no)	0.04	0.3	0.7	-8.4	12.09
eGFR value (mL/min/1.73 m^2)	- 0.2	- 1.6	0.1	-0.3	0.03
ACR (mg/g)	0.03	0.2	0.7	-0.007	0.01
Calcium (mg/dL)	0.13	1.2	0.2	-2.4	9.7
P (mg/dL)	0.1	0.9	0.3	-2.7	7.7

Dependent variable: serum glucose. DM: Diabetes mellitus; BMI: Body mass index; eGFR: Estimated glomerular filtration rate; ACR: Albumin-to-creatinine ratio; P: Phosphate.

Table 4 Relation to serum glucose variables in our patients with diabetes mellitus (*n* = 29)					
Variables in model	Beta	*t*	Sig.	Lower	Upper
Age (yr)	0.26	1.02	0.3	-1.06	3.1
Gender (male/female)	0.06	0.2	0.7	-30.5	39.8
BMI (kg/m^2)	0.3	1.2	0.2	-1.6	6.5
Hypertension (yes/no)	-0.2	-1.3	0.19	-70.04	15.5
Smoking (yes/no)	0.33	1.4	0.15	-12.7	74.4
eGFR value (mL/min/1.73 m^2)	- 0.06	-0.2	0.79	-1.1	0.86
ACR (mg/g)	0.4	2.2	0.03	0.003	0.09
Calcium (mg/dL)	0.2	1.1	0.2	-10.6	38.2
P (mg/dL)	-0.13	-0.6	0.5	-32.4	17.07

Dependent variable: serum glucose. DM: Diabetes mellitus; BMI: Body mass index; eGFR: Estimated glomerular filtration rate; ACR: Albumin-to-creatinine ratio; P: Phosphate.

explain this finding in our participants who had renal function impairment (69.1%) combined with a higher serum P. Decreased renal function itself is strongly associated with increased insulin resistance[25].

Moreover, in our study we observed a significant association between high serum P and receiving vitD, as it is known that vitD mediates the absorption and metabolism of P. However, it has been suggested that serum P changes during therapy with vitD derivates and the increase in P impedes and/or abolishes the beneficial effect of paricalcitol on endothelial function mostly in CKD patients[20].

Despite finding a significant non-adjusted association between high serum P and manifestations of DM, the adjusted model showed that older age, female gender and high BMI were significant predictors of DM manifestations, although high serum P was not. Furthermore, in the non-DM group, high BMI was revealed to be a unique significant predictor of high serum glucose levels, although in DM patients albuminuria was an important predictor of serum glucose including potential covariates as shown in Tables 3 and 4.

According to the findings of this study, despite the fact that high serum P was found to be associated with hypertension, albuminuria, smoking, low eGFR and metabolic disorders, the traditional factors including older age, female gender and high BMI were proved to be stronger predictors of type 2 DM manifestations rather than high serum P. Thus, those receiving vitD derivates require monitoring to prevent a rise in serum P resulting in the abolishment of the beneficial effect of vitD on

vascular endothelium.

Limitations
The main limitation of this study is the cross-sectional nature of the single-center design in combination with the small number of patients.

CONCLUSION
High serum P contributes to vascular and metabolic disturbances in elderly patients with type 2 DM and renal impairment. Serum P levels were similar in diabetics and non-diabetics and the relationship between serum P and serum glucose or insulin resistance was found to be non-significant in both diabetic and non-diabetic patients in contrast to previous reports, due to reduced renal function.

ARTICLE HIGHLIGHTS

Research background
Metabolic disorders contribute to the prediction of morbidity and mortality in patients with type 2 diabetes mellitus (type 2 DM). Changes in serum calcium, magnesium or P are related to the prevalence of type 2 DM mainly in combination with obesity.

Research motivation
We determined the importance of serum P levels in elderly patients with type 2 DM compared to those without DM in relation to renal function clustering in chronic kidney disease stages 1-4.

Research objectives
One hundred-ten subjects with a mean age of 69.02 ± 14.3 years were included. Twenty-nine participants had type 2 DM (26.4%).

Research methods
The participants were classified into both estimated glomerular filtration rate (eGFR) and albuminuria categories according to the Kidney Disease Improving Global Outcomes 2012 criteria. The incidence of hypertension, smoking and those receiving vitamin D derivates were recorded.

Research results
We divided the patients in two groups according to the P cut-off point related to type 2 DM. A significant association was observed between high P and type 2 DM, hypertension, receiving vitamin D, smoking and eGFR (χ^2 = 6.3, P = 0.01, χ^2 = 3.9, P = 0.03, χ^2 = 6.9, P = 0.009, χ^2 = 7.04, P = 0.01 and χ^2 = 7.36, P = 0.04, respectively). A multi-factorial model showed that older age, female gender and increased BMI were significant predictors of type 2 DM after entering the covariates.

Research conclusions
High serum P contributes to vascular and metabolic disturbances in elderly patients with type 2 DM and renal impairment.

Research perspectives
Compared with high serum P, traditional factors such as older age, female gender and high BMI were proved to be stronger predictors of type 2 DM.

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