

Original Paper

Clinical Correlation between Vitamin K Deficiency and Matrix Gla Protein (MGP) Levels in Patients Undergoing Hemodialysis

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ABSTRACT

Chronic kidney disease (CKD) is closely linked to low vitamin K levels. Two major consequences of chronic kidney disease (CKD) that raise the risk of death and morbidity are skeletal fragility and cardiovascular disease (CVD). Vascular calcification (VC), alterations in bone tissue and metabolism, hormonal and ionic disorders, and chronic renal disease are all linked in a complicated pathogenetic way in CKD-MBD. Chronic renal illness, bone issues, and cardiovascular disease appear to be significantly influenced by vitamin K deficiency. Phylloquinone, menaquinone, and menadione are the three forms of vitamin K that are now accessible. Examined the connections between plasma vitamin K and serum total matrix G protein (MGP) in hemodialysis (HD) patients. In a case-control study, thirty samples were taken from patients at Al-Kadhimiya Teaching Hospital who had chronic renal disease, and thirty samples were taken from healthy individuals who were in good condition and the same age and gender. Serum vitamin K levels and Total MGP were measured using the ELISA technique. Using a spectrophotometer and a colorimetric test, the amounts of creatinine and urea were measured. The results showed that there was no statistical significance in age. Urea, creatinine levels were high in control group while vitamin K low in patient group. In conclusion, serum vitamin K levels were lower in patient group compared to the control group, and increased Total MGP in HD.

KEYWORDS: *matrix Gla protein (MGP), vitamin K, phylloquinone, haemodialysis (HD), chronic kidney disease.*

1-INTRODUCTION

Several health complications, including mortality, ESRD, and CVD, can develop from chronic kidney disease (CKD) [1,2]. The likelihood of these consequences rises as CKD worsens, and complications and comorbidities such as CKD-mineral and bone disorder (MBD), renal anaemia, and hyperpotassia [3] become more prevalent and severe. Patients with CKD face significant financial and physical challenges [4,5]. Several risk factors must be controlled to delay the progression of CKD [6]. Finding high-risk patients and assessing their health are made easier with an accurate risk prediction of CKD progression, which also gives us potential treatment approaches that can be customised for each patient. [3, 7]. Nephrology has had a significantly smaller number of clinical studies than other medical specialties, it was noted [8].

CKD's complex pathophysiology, trial study design challenges, and the absence of surrogate indicators of CKD development are the primary causes. The U.S. Food and Drug Administration has suggested the eGFR slope and change as surrogate indicators of end-stage renal disease (ESRD) [9,10]. These surrogate markers, however, are not sufficiently flexible to accommodate different patient outcomes and situations. Furthermore, employing surrogate markers made from data from other nations frequently results in low accuracy, and they present certain challenges when sampling bias is present. New surrogate indicators for a range of outcomes that represent the complex pathophysiology of CKD and patient circumstances must be developed in order to supplement the current markers [12]. Smooth vascular muscle cells and chondrocytes are the primary sources of matrix Gla protein (MGP), a potent local inhibitor of vascular calcification [1]. However, MGP has to be phosphorylated and carboxylated in order to be active; this carboxylation is reliant on vitamin K, and MGP secretion requires phosphorylation.

Proteins that contain γ -carboxyglutamate (Gla) residues cannot function properly without vitamin K. Notable coagulation factors that rely on vitamin K and are mostly produced in the liver are known as Gla proteins. Two types of extrahepatic Gla proteins are matrix Gla protein (MGP), which is produced in cartilage and blood vessels, and osteocalcin (OC), which is produced in bone. For Gla proteins to function, they must contain Gla residues, which are

created through a posttranslational carboxylation reaction that relies on vitamin K. Uncarboxylated (or inactive) proteins are produced when vitamin K is not consumed enough in the diet. [11]

2-METHODS

A case-control investigation. At Al-Kadhimiya Teaching Hospital, 30 samples were taken from patients who had been diagnosed with chronic renal disease by specialists. Furthermore, 30 samples were taken from healthy people who were in good general health and who were matched in terms of age and gender. From 1/4/2023 to 1/12/2024, the age and gender of every participant were documented. Five millilitres of blood were extracted from each participant, placed in a gel tube, and left to clot at room temperature for fifteen minutes. The combination was then centrifuged for 15 minutes at 3000 revolutions per minute, which separated the blood serum. After separation, the serum was kept frozen until it was required. ELISA was used to test serum vitamin K levels using the Chemoimmunoassay method (kit Cat. No. E2175Hu; BT-Laboratory, China). All subjects' levels of creatinine and urea were measured using colorimetric techniques and a spectrophotometer.

Statistical analysis:

SPSS version 26 was used for statistical analysis. After the data were dispersed, the T-test was selected as the suitable test type. The p-value, mean, and standard deviation were used to compare the outcomes.

3-RESULTS

The findings showed that age differences between the patient and control groups were not statistically significant ($P = 0.074$).

Table 1: Comparison of the patient and control groups' ages

Parameters	Control Mean± SD	Patients Mean± SD	P. value
Age (year)	31.13 ± 8.31	36.88 ± 9.63	0.074 ^{NS}

The results showed that while the sick group had lower levels of vitamin K than the control group, their levels of urea, creatinine, and T MGP were considerably greater ($P = <0.0001$).

Table 2: An analysis of the patient group's renal performance in comparison to the control group

Parameters	Control Mean ± SD	Patients Mean ± SD	P. value
Urea (mg/dl)	36.741 ± 11.388	85.679 ± 11.45	<0.0001
Creatinine (mg/dl)	0.825 ± 0.368	3.12 ± 1.089	<0.0001
Vitamin k (ng/L)	15.919 ± 5.212	6.031 ± 0.927	<0.0001
T MGP (pg/ml)	6.975 ± 2.664	16.346 ± 4.077	<0.002

Analysis of the correlation between Vitamin K and other parameters was found to have a strong negative correlation and a positive correlation in both patients and controls.

Table 3: The Correlations between all biomarkers in this study

		Correlations			
		TMGP	VIT K	urea	creat
TMGP	Pearson Correlation	1	-.632**	.785**	.674**
	Sig. (2-tailed)		.000	.000	.000
VIT K	Pearson Correlation	-.632**	1	-.754**	-.685**
	Sig. (2-tailed)	.000		.000	.000
urea	Pearson Correlation	.785**	-.754**	1	.885**
	Sig. (2-tailed)	.000	.000		.000
creat	Pearson Correlation	.674**	-.685**	.885**	1
	Sig. (2-tailed)	.000	.000	.000	

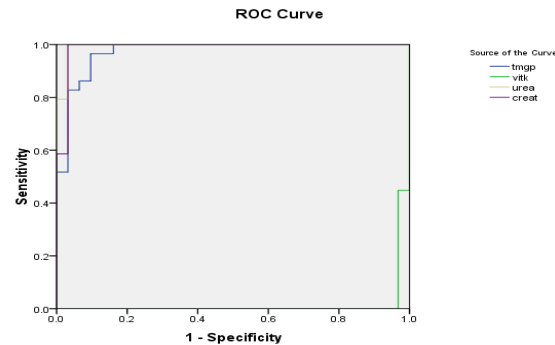
****.** Correlation is significant at the 0.01 level (2-tailed).

The connection is statistically significant at the 0.05 level (2-tailed).

The diagnostic performance of TMGP, vitamin K, urea, and creatinine among the groups under investigation was evaluated using ROC curve analysis. With area under the curve (AUC) values of 0.972, 0.993, and 0.987, respectively, TMGP, urea, and creatinine indicated outstanding diagnostic accuracy, as shown in Table 4. Additionally, these measures demonstrated great specificity (0.968) and 100% sensitivity, demonstrating their potent capacity to distinguish between the groups. Vitamin K, on the other hand, has a very low AUC value (0.014), indicating that this model has little predictive utility and poor diagnostic capability.

Table 4: ROC Curve Analysis Showing the Diagnostic Accuracy of TMGP, Vitamin K, Urea, and Creatinine in the Studied Groups

Test Result Variable(s)	Area	Sensitive	Specify
TMGP	.972	1.000	0.968
VIT K	.014	0.968	1.000
urea	.993	1.000	0.968
creat	.987	1.000	0.968



4-DISCUSSION

One feature of individuals with chronic kidney disease (CKD) is low vitamin K levels [13]. The most common causes of vitamin K deficiency in individuals with chronic kidney disease (CKD) are dietary restrictions, uraemia-associated dysbiosis, and certain drugs [14–15]. Dietary restrictions caused by the high potassium content of most green vegetables high in vitamin K worsen its scarcity [16]. Together with dietary intake, vitamin K is recycled by the "vitamin K cycle," which is comprised of g-glutamylcarboxylase, DT-diaphorase, and vitamin K epoxide reductase. Vitamin K recycling was reduced in CKD-affected rats, likely due to g-glutamyl-carboxylase's lower activity, and it functioned similarly to coumarins [17,18]. It is well recognised that individuals with chronic kidney disease (CKD) are more likely to experience bone fractures and vascular calcification (VC) [19], both of which raise the morbidity and mortality rate in CKD patients [20]. Vitamin K2 may be important in the pathophysiology and prevention of those severe consequences, according to a number of reports [21, 22].

A study including 387 hemodialysis patients evaluated the connection between vitamin K stores, vertebral fractures, and vascular calcifications [23]. Vitamin K antagonists (VKA), the phosphate binder sevelamer, and hemodialysis therapy are the three primary iatrogenic causes of vitamin K deficiency in people with chronic renal failure [24]. To reduce the risk of stroke in patients with atrial fibrillation (AF), VKA medicines are commonly prescribed to chronic kidney disease (CKD) patients, especially those undergoing haemodialysis. There are two ways in which warfarin can raise the risk of fragility fractures and vascular calcification. Firstly, it prevents the carboxylation of osteocalcin and other bone matrix proteins. Secondly, warfarin users tend to eat fewer foods that are rich in vitamin K, which increases the risk even more [25]. More people with atrial fibrillation are using non-vitamin K oral anticoagulants (NOACs) than vitamin K antagonists to avoid stroke and cardioembolic consequences. They are no longer advised for use in patients with severe chronic kidney disease (CKD) or end-stage renal disease (ESRD) [26]. Low peripheral vitamin K status has been associated with proteinuria and the development of chronic renal disease in previous studies [27]. Dialysis patients seem to have low amounts of vitamin K both in their blood and in their tissues [10, 11]. One possible explanation for low intake is the strict restriction of sodium, potassium, green vegetables, and dairy that is common in dialysis diets [12]. In addition, uremia can change vitamin K metabolism by

affecting γ -glutamyl carboxylase activity and interfering with lipoprotein-mediated transport [13, 14]. Vitamin K concentrations can be affected by some drugs that dialysis patients often take. Warfarin and other anticoagulants are vitamin K antagonists that have been shown to raise the risk of vascular calcifications [15]. Phosphate binders like sevelamer have been linked to changes in vitamin K status, such as an MK-4 deficit and elevated dp-ucMGP levels [16]. Subclinical vitamin K insufficiency may occur in patients treated with proton pump inhibitors and statins, according to clinical and experimental studies [13]. Another possible mechanism that could explain why dialysis patients have different vitamin K levels is gut dysbiosis [17]. The calcification inhibitor MGP is said to need the activation of vitamin K. Growing interest in vitamin K supplementation for HD patients' vascular calcification and calciphylaxis, as well as the potential for vitamin K antagonist therapy to exacerbate these conditions (28)

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