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CHRONIC KIDNEY DISEASE

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Background; Vascular calcification has emerged as an independent risk factor for cardiovascular morbidity and mortality, especially in chronic kidney disease**.**
Vitamin K is a composite term referring to a group of fat-soluble vitamins that function as a cofactor for the enzyme -glutamyl carboxylase (GGCX), which activates a number of vitamin K-dependent proteins (VKDPs) involved in haemostasis and vascular and bone health.
Keywords; glutamyl carboxylase (GGCX), vitamin K-dependent proteins (VKDPs) and chronic kidney disease (CKD).

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Vitamin K is a composite term referring to a group of fat-soluble vitamins that function as a cofactor for the enzyme -glutamyl carboxylase (GGCX), which activates a number of vitamin K-dependent proteins (VKDPs) involved in haemostasis and vascular and bone health. (**1**)

Vascular calcification has emerged as an independent risk factor for cardiovascular morbidity and mortality, especially in chronic kidney disease. Deficiencies in calcium-regulatory proteins directly relate to development of calcifications. McCabe and colleagues report that vitamin K is a key regulator of vascular calcification, via carboxylation of vitamin K-dependent proteins such as matrix Gla protein. Knowledge about vitamin K status may propel therapeutic strategies to prevent and treat vascular calcification with high vitamin K supplementation (**2**)

Accumulating evidence demonstrates that chronic kidney disease (CKD) patients suffer from subclinical vitamin K deficiency, suggesting that this represents a population at risk for the biological consequences of poor vitamin K status. This deficiency might be caused by exhaustion of vitamin K due to its high requirements by vitamin K-dependent proteins to inhibit calcification (**3**)

Vitamin K is as a substrate for an enzyme, the vitamin K-dependent carboxylase that converts specific glutamic acid residues of a small number of proteins to glutamic carboxyl (Gla) residues by the addition of a CO2. Vitamin K is necessary to introduce carboxyl groups into glutamic acid residues in blood coagulation factors (II, VII, IX, X) to yield Gla residues; Gla-containing proteins include osteocalcin (OC), synthesized by the osteoblasts in bone, and matrix Gla protein (MGP), synthesized by chondrocytes and vascular smooth muscle cells (VSMCs), involved in bone mineralization and inhibition of vascular calcifications, respectively (**4**)

Considering that vitamin K is essential for the activation of matrix Gla protein (MGP), a powerful inhibitor of tissue calcification, functional vitamin K deficiency may contribute to high vascular calcification (VC) burden in haemodialysis patients; this is process in which mineral is pathologically deposited in blood vessels, mainly in large elastic and muscular arteries such as the aorta and the coronary, carotid, and peripheral arteries. The presence of VC is directly related to increased cardiovascular morbidity and mortality in dialysis patients (**5**)

Chronic kidney disease is a progressive condition characterized by structural and functional changes to the kidney due to various causes. Chronic kidney disease is typically defined as a reduction in kidney function, an estimated glomerular filtration rate (eGFR) of less than 60 mL/min per 1·73 m^2, or markers of kidney damage, such as albuminuria, hematuria, or abnormalities detected through laboratory testing or imaging and that are present for at least 3 months (appendix p 5) **(6).**

The global burden of chronic kidney disease is substantial and growing: approximately 10% of adults worldwide are affected by some form of chronic kidney disease, which results in 1·2 million deaths and 28·0 million years of life lost each year. By 2040, chronic kidney disease is estimated to become the fifth leading cause of death globally/one of the largest projected increases of any major cause of death **(7).**

The prevalence of different etiologies of chronic kidney disease varies considerably by region. There are many causes of chronic kidney disease, including those that are common and well researched, such as diabetes, glomerulonephritis, and cystic kidney diseases, but causation in chronic kidney disease is not yet fully understood. For instance, despite a close association between chronic kidney disease and hypertension, whether hypertension is a cause or a consequence of chronic kidney disease is controversial. As another example, chronic kidney disease of

unknown etiology and for which there is no known treatment is found in some agricultural communities in south Asia and central America; recurrent volume depletion has been speculated to be a cause, especially with the increasing frequency of climate change-related heat waves **(8).**

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