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Review

Chronic Kidney Disease: role of diet for a reduction in the severity of the disease

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Abstract: Chronic kidney disease is a critical health crisis in the US, affecting about 37 million adults. Known as "the silent killer" because it is often undiagnosed until it has reached a stage of progression. Renal dysfunction causes many adverse effects to the body's biological mechanisms, such as fluid electrolyte and pH balance, blood pressure regulation, excretion of toxins and waste, vitamin D metabolism, and hormonal regulation. Many CKD patients experience hyperkalemia, hyperphosphatemia, chronic metabolic acidosis, bone deterioration, blood pressure abnormalities, and edema. Symptoms experienced may be minimized, and the disease's progression may be slowed through an appropriate diet, which is why medical nutrition therapy is a critical aspect of the medical intervention for CKD. The current KDOQI recommendations are proposed as well as the physiological mechanisms behind the recommendations. Current biological explanations of the effects of a whole foods plant-based diet are included for possible contrast with the current renal diet. Strong evidence continues to support the importance of proper nutrition in the prevention and progression of kidney disease.

Keywords: Diabetes; Chronic Kidney Disease; Proteinuria; Dialysis; Inflammation; Diet; Nutrition

1. Introduction

The kidneys control many biological mechanisms such as fluid, electrolyte, pH balance, blood pressure, excretion of toxins and waste, vitamin D metabolism, and hormone synthesis. About thirty-seven million US adults are estimated to have chronic kidney disease (CKD), which is more than one in seven adults [1] . Even More astonishing, nine in ten adults do not know they have the disease, and half of the adults with little kidney function who are not on dialysis are unaware they have CKD [1]. Chronic kidney disease is referred to as the "Silent Killer" because it often goes undiagnosed due to a lack of apparent symptoms. An estimated 94% with mild to moderate decline in renal function and about 48% of individuals with severe renal dysfunction go undiagnosed [2].

The National Kidney Foundation (NKF) defines CKD as either a decline in glomerular filtration rate (GFR) to <15mL/min/1.73m² or the presence of kidney damage persisting for at least three months [3]. Kidney damage refers to functional damage such as proteinuria and glomerulonephritis and structural damage as seen in polycystic kidneys [4]. CKD is divided into five stages depending on the severity of renal function measured by GFR; stage 5, also known as end-stage renal disease (ESRD), is when GFR is <15mL/min/1.73m² [4].

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Chronic kidney disease is commonly from a secondary health condition resulting from a preexisting health condition causing end-organ damage to the kidneys [5]. However, CKD may be primarily renal disease, such as polycystic kidney disease [6]. Diabetes mellitus (DM), hypertension, and glomerulonephritis are the leading causes of kidney failure [7], with DM as the most common cause [8]. Diabetes accounts for 30%-50% of ESRD in the US; conversely, 30-40% of DM patients develop diabetic nephropathy [9]. Patients with T1DM and T2DM are both at risk; however, since type-2 is significantly prevalent, it is associated with elevated CKD cases compared to type-1 [4]. Reducing CVD risk and maintaining glycemic and BP control are imperative therapeutic measures to reduce the risk for diabetic neuropathy [9].

Hypertension is a leading modifiable factor in preventing CVD, the number one cause of death in the US [10]. Hypertension is also a risk factor, as well as a cause of CKD [11]; is the second leading cause for nephropathy [4]. Hypertensive nephrosclerosis is associated with end-organ damage due to poorly managed hypertension [12].

The prevalence of diabetes and hypertension is growing exponentially, predicting that CKD will continue to rise [13]. CKD patients are at increased risks for other health conditions, including acute kidney injury (AKI), CVD, T2DM, and mortality [14]. Chronic kidney disease is nationally incorporated into health promotion and disease-prevention programs to reduce the prevalence of the disease [15]. The US Department of Health and Human Services Healthy People 2020 had a target goal to minimize CKD prevalence from 14.8% (2001-06) to 13.3% by 2020 [16].

Medical nutrition therapy is imperative for CKD patients because it may significantly slow the progression of the disease and relieve adverse symptoms experienced in CKD patients [7]. Although CKD is progressive, appropriate medical and nutrition intervention may slow the disease's progression by careful monitoring of protein, calcium, phosphorus, potassium, and sodium [17]. This review covers CKD pathophysiology, the most current diet recommendations, and their mechanisms for delaying the progression of the disease. In addition, the mechanisms of the newly explored whole food plant-based diet (WFPBD) are explained for its possibility of better managing the prevention and progression of CKD than the current renal diet.

2. Renal Functions

The kidneys are responsible for a series of life-sustaining mechanisms (**Figure 1**). The primary functions of the kidneys are to sustain and maintain fluid and electrolyte and metabolic acid-base balance, accomplished through solute and fluid regulation, conservation of nutrients, and excretion of metabolic bodily waste [18]. The kidneys have endocrine and exocrine functions regulating and maintaining critical biological mechanisms in the body [19]. The exocrine functions involve fluid and electrolyte balance [20], acid-base regulation [21], excretion of body waste [22], and blood pressure regulation [23]. The endocrine functions include vitamin D metabolism [24], and hormone synthesis [25].

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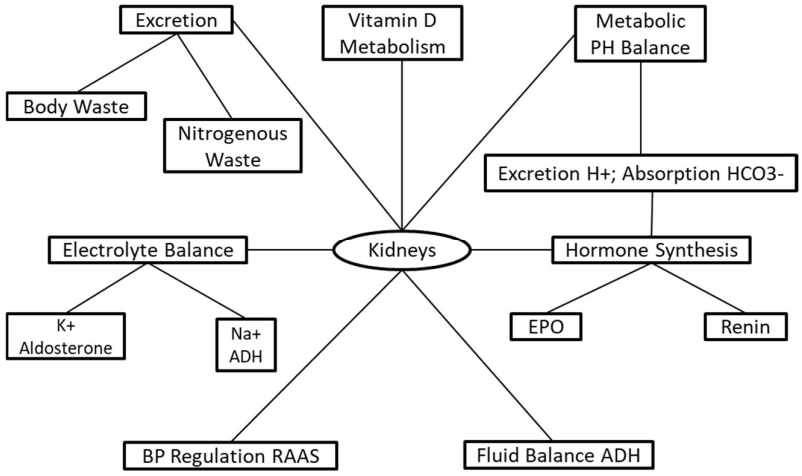
2.1 Fluid Balance and Blood Pressure

The renin-angiotensin-aldosterone system (RAAS) is the body's primary mechanism for regulating blood pressure through its effects on fluid and sodium balance [26].

Figure 1. The physiological role of kidneys.



Renin, a hormone synthesized in the kidney, is the rate-limiting step in the RAAS; the absence of renin inhibits the RAAS cascade [27]. RAAS is activated when the baroreceptors detect a critical change in pressure, which indicates low blood volume; blood volume raises through the production of angiotensin II (A-II); a potent vasoconstrictor [28]. The activation of vasopressin from A-II increases water reabsorption, and sodium is reabsorbed in the presence of aldosterone, subsequently leading to water retention—all of which work to increase blood volume. [29]. In CKD, the RAAS malfunctions by over secreting renin from the kidneys resulting in inappropriate activation of A-II, leading to hypertension [28]. Regulating and maintaining BP through dietary intake is critical, and adopting the Mediterranean Diet or the Diet Approaches to Stop Hypertension (DASH) may assist in improved health outcomes for CKD patients with or at risk for hypertension [17].

2.2 Anemia

Anemia is a common consequence of CKD, especially in advanced stages; more than 50% of ESRD patients have anemia [30]. A decline of erythropoietin (EPO) production is commonly experienced [31] due to a reduction in renal function [32]. Erythropoietin is a glycoprotein hormone unique among the hematopoietic growth factors because it is produced in the kidneys, not in the bone marrow [33]. EPO is synthesized by interstitial cells in the renal cortex's peritubular capillary bed; however, in diseased kidneys, these cells lose their function for producing EPO [34]. EPO influences several mechanisms that maintain sufficient iron levels, such as the body's ability to recycle and replenish iron by macrophage phagocytosis of destroyed RBCs [35]. Hepcidin is another regulator of iron metabolism [36]; it is a peptide hormone synthesized in the liver regulating intestinal iron absorption and iron release from iron stores [37]. The impairment of EPO production has adverse effects on iron absorption and utilization [38]. CKD is associated with increased hepcidin levels due to the clearing of the inflammatory cytokine IL-6 from circulation by renal filtration; hepcidin levels are inversely proportional to the severity of kidney dysfunction and further disturb iron levels [38].

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Erythropoiesis-stimulating agents (EAS) have been considered the best treatment for managing anemia in CKD patients since they became available in 1989 [30]. Although the use of ESAs has improved conditions in CKD, RCTs have questioned the safety of the duration in treatment and the use of high dose ESAs to normalize hemoglobin (Hb) levels [38]. The 2012 Kidney Disease Improving Global Outcomes (KDIGO) recommend that when prescribing iron therapy, to balance the therapy's potential benefits against the risk of harm the treatment may induce [39]. An increase in Hb without initiating ESAs is the desired goal; however, for CKD- non dialysis (ND) patients with a Hb concentration less than 10.0 g/dl, ESA treatment should be based on individual circumstances of the patient [39]. Individualized cases include the rate of decreasing Hb, the risks of needing a transfusion, response to prior treatment, the severity of anemic symptoms, and the potential risk related to ESAs [39]. The KDIGO guidelines are only recommendations with less than satisfactory evidence; however, there are no current clear guidelines, so the KDIGO guidelines serve as a significant point of reference for clinical use when determining how or when to treat anemic CKD patients with ESAs [30].

3. Inflammation and chronic kidney disease

An early sign of abnormal kidney function is albumin detection in the urine, known as albuminuria. A urinary albumin excretion rate of higher than 30mg/d defines albuminuria; however, albumin excretion higher than 300 mg/d is proteinuria [40]. Proteinuria indicates progressive kidney damage, even when the GFR has not yet declined [40]. Proteins in the urine promote inflammation and fibrotic effects, which cause chronic tubulointerstitial damage [40]. Occurring from initiation of tubular chemokine expression, activation of the complement system resulting in inflammatory cell infiltration in the interstitium, and sustained fibrogenesis [41]. Evidence suggests a switch of chemokine expression occurs during the phase changes from acute to chronic inflammation seen in CKD [42]. A transition from the expression of CXCL chemokines (IL-8/ CXCL8) to chemokines (MCP-1/CCL2, RANTES/CCL5) shown from an increase in urinary IL-8/CXCL8 levels in early stages and increasing levels of urinary MCP-1 with increasing renal injury [43]. In addition, cytokines released during inflammation further damage the kidneys by activating infiltrated macrophages [44]. The activated macrophages release cytokines IL-1, TNF-α, complement factors, and metalloproteinases, resulting in damage to the kidneys (**Figure 2A)** [45]. The progression leads to glomerular sclerosis [40], and the sclerotic areas cause damage to the Bowmans Capsule [41]. For diabetic patients, protein reabsorption in the proximal tubule may be interrupted by elevated blood glucose, 7GF-β, or angiotensin II [46]. The tubulointerstitial damage from proteinuria alters the excretion of urine protein by preventing tubule reabsorption of filtered proteins [46]. Albumin in tubular cells explicit inflammatory and fibrotic mediators such as interleukins, monocyte chemotactic protein 1, cytokines such as RANTES, and growth factors implementing changes to tubular morphology and tubulointerstitial damage [47]. The impairment of protein urine in the tubules increases inflammation and fibrotic effects; this vicious cycle leads to neuropathy [46]. Serum levels of these inflammatory molecules and the soluble forms of receptors, adhesion molecules have been shown to be independent risk factors (**Figure 2B**) for development and progression of CKD in both type-1 diabetes [48], [49], [44] and type-2 diabetes patients [50], [51].

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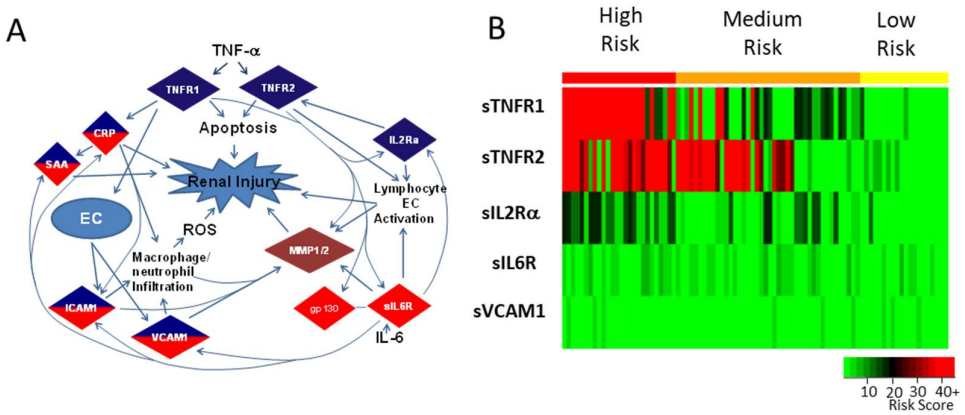

Figure 2. Inflammatory molecules and receptors involved in CKD. A: activation of TNF-α, IL-6 system leads to production of acutephase proteins, adhesion molecules, matrix metalloproteinases and reactive oxygen species damaging renal corpuscle. B: Soluble form of TNF-α receptors I and II (sTNFRI and sTNFRII), IL-2 receptor –α (sIL2Rα), IL-6 receptor (sIL6R) and vascular cell adhesion molecule-1 (sVCAM-1) in serum are risk factors to identify T1D patients with high, medium, and low risk for CKD.

4. Medical Nutrition Therapy

The NKF published the first Kidney Disease Outcomes Quality Initiative (KDOQI), a set of nutritional guidelines for patients with end-stage renal disease in 1996 [17]. Since then, the KDOQI guidelines have gone through revisions and expanded to include nutrition recommendations for each stage of CKD, dialysis, and pre/ post-kidney transplant [17]. Most suggestions provided in this review are from the recent *KDOQI Clinical Guideline for Nutrition in CKD: 2020 Update*, which was developed with the Academy of Nutrition and Dietetics.

4.1 Protein & Renal Function

The effects of a high protein diet (HPD) on renal health have been investigated since the 1920s when rats given a HPD presented an increase in kidney weight [52]. Conclusive data suggest that chronic protein intake (more than 1.2 g/kg/body wt/d) [53], leads to increased pressure and glomerular morphologic changes resulting in renal dysfunction (**Table 1**)[54]. Glomerular hyperfiltration is defined as modifying renal hemodynamics through glomerular capillary hyperemia and increasing intraglomerular pressure [53]. HPD induce glomerular hyperfiltration; hyperemia and increased hydraulic pressure result in vasodilation of the afferent arteriole [55]. HPDs contribute to progressive glomerular damage, which, combined with the renal deterioration from diseased kidneys, may contribute to a more rapid disease progression in renal patients. Oba et al. collected 43 healthy (non-diseased) kidneys from live human donors to examine the effect of a HPD on the single-nephron GFR (SNGFR) [55]. This study concluded that a HPD might increase SNGFR and induce glomerular hyperfiltration; however, this study is unique by identifying that the analysis of human SNGFR is an exemplary parameter to alterations in renal hemodynamics at the single-nephron level [55]. The exact mechanism for renal hemodynamic responses to heightened protein intake is not yet understood [56].

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Table 1: Protein & Energy requirements and recommendations for adult chronic kidney disease (CKD) patients.

Nutrients	Damage in CKD	Recommendation	Outcome	Ref
Protein	Proteinuria/glomerular sclerosis/ hyper-filtration/ intra-glomerular hypertension & hyper-perfusion	0.55–0.6 g/kg body wt./day	Reduce uremia, uremic toxins, & hyperfiltration. Improve organ function & renal hemodynamics.	[60],[53], [54]
CKD 3-5 patients. Not on Dialysis/ Without Diabetes				
CKD 3-5 Pts Not on Dialysis and w/ Diabetes	Proteinuria/glomerular sclerosis/ hyper-filtration/ intra-glomerular hypertension & hyper-perfusion	0.6 - 0.8 g/kg body wt./day	Reduce uremia, uremic toxins, & hyperfiltration. Improve organ function & renal hemodynamics.	[60],[54] [55]
HD and PD Pts w/ & Without Diabetes	Proteinuria/glomerular sclerosis/ hyper-filtration/ intra-glomerular hypertension & hyper-perfusion	1.0-1.2 g/kg body wt./day	Reduce uremia, uremic toxins, & hyperfiltration. Improve organ function & renal hemodynamics.	[60],[54][55]
Energy Intake	Inadequate intake ↑risk PEW, ↑risk malnutrition. Excessive intake ↑risk CVD, ↑risk diabetes	25-35 kcals/kg body wt./day	Maintain neutral nitrogen balance & body composition.	[60],[56]

Recommendations are for metabolically stable patients under strict clinical supervision

Low protein Diets (LPD) have been shown to improve hyperfiltration, reduce nitrogenous waste, and ease the renal workload by decreasing glomerular pressure [53]. Proteinuria declined by 20-50% in CKD patients who adhered to a LPD [54]. Although LPD provide direct benefits to CKD patients, healthcare professionals are concerned about protein-energy malnutrition and protein-energy-wasting (PEW) in CKD patients due to inadequate energy intake [54]. When determining estimated energy requirements for CKD patients, 30-35 kcal/kg/body wt./day is recommended to maintain energy and nitrogen balance and avoid risk for malnutrition [57].

4. 2 Very Low Protein Diet

Low protein diet and very low protein diets (VLPD) (0.28-0.43 g/kg/ body weight/ day) may be achieved with nutrition supplementation with essential amino-acids (EAAs) and keto-analogs [58] to safeguard against PEW. The KDOQI guidelines recommend restricting protein to slow ESRD progression and improve quality of life (QoL) by reducing symptoms for metabolically stable patients [59]. The NKF defines metabolically stable as being absent from inflammatory or infectious diseases, poorly controlled diabetes, consumptive diseases, antibiotics or immunosuppressive medications, significant short-term loss of body weight, and no hospitalizations within two weeks [60]. For patients with CKD stage3-5, a protein restriction providing 0.55-0.60 g/kg/body weight/ day or a VLPD with supplementation with ketoacid analogs is recommended [60]. Diabetic adults with CKD 3-5 are recommended a protein diet providing 0.6-0.8 g/kg/ body weight/ day, and patients on maintenance hemodialysis or periodontal hemodialysis with or without diabetes are recommended a protein intake providing 1.0-1.2 g/kg/ body weight/day [60]. Diet modifications such as reducing protein from heme sources and including more plant-based proteins protect against metabolic acidosis by lowering acid production; these effects are mostly seen with a VLPD (0.3-0.5 g/kg/body weight/day) plus supplementation

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with ketoacid analogs [60]. Although protein requirements are highly individualized, protein consumption of 0.6g/kg/body weight is recommended for non-dialysis patients [17].

4.3 Calcium

Calcium balance is regulated by intestinal calcium absorption, kidney reabsorption, and calciotropic hormones that activate calcium exchange from the bone when serum calcium levels are low [17]. Insufficient calcium absorption and chronic calcium deficiency results in increased risk for hyperthyroidism and osteitis [17]. However, excessive calcium poses an increased risk for calcification, resulting in comorbidities and higher mortality [17]. Alterations in calcium metabolism are multifactorial and include the use of active vitamin D analogs. Research shows that ingesting about 800-1000mg/d of calcium may be sufficient to maintain calcium balance for patients with CKD stages 3 and 4 in the absence of vitamin D analogs [17]. Maintaining calcium balance is more complicated for CKD patients on dialysis, and hypercalcemia is relatively standard (**Table 2**).

4.4 Phosphorus

Phosphorus plays a critical role in bone formation, acid-base balance, and energy production [60]. The body's ability to maintain phosphate balance is achieved by the excretion of excess phosphate in the urine. As CKD progresses, alterations in renal function decline the ability to excrete enough phosphorus to maintain homeostasis [17]. Traditionally, The NKF guidelines recommended CKD 3-5 and hemodialysis (HD) patients restrict dietary phosphate to prevent hyperphosphatemia (**Table 2**) [61]. Hyperphosphatemia may lead to critical pathogenic consequences, including renal osteodystrophy, cardiovascular and soft tissue calcification, secondary hyperthyroidism, cardiac disease, and mortality in ESRD patients [62]. It is currently understood that phosphorus requirements depend on the stage of renal failure combined with the consideration not to restrict phosphorus intake to the point of malnutrition, mainly relevant to HD patients [63]. These are some reasons for the KDOQI revision for its phosphorus recommendations changing to receive an intake level sufficient to maintain normal phosphate levels for CKD 3-5 and HD [17]. Choosing phosphorus-containing foods lower in bioavailability and without phosphate additives is recommended [17]. Animal-based food sources of phosphorus have a gastrointestinal absorption rate of 40-60%, while the absorption rate of plant-based phosphorus is 20-50% [64]. A study by Moe et al. that included CKD stage 4 patients reported lower phosphate levels in patients fed a 7-day vegetarian diet than patients fed a 7-day animal-based diet [65]. Sources containing only organic phosphorus are more nutrient-dense than foods with phosphate additives, usually processed and high in sodium [66].

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Table 2: Daily requirements for Electrolytes in chronic kidney disease (CKD) patients.

Electrolytes	Damage in CKD	Recommendation	Outcome	Ref
Total calcium CKD 3-4 w/ no use of taking active vitamin D analogs	Ca2+ deficiency ↑ risk secondary hyperparathyroidism & bone disorders. Excessive Ca2+ ↑ risk extraosseous calcification & CVD	800-1,000 mg/d/day	Maintain Ca2+ balance	[60], [67]
CKD 5 w/ use of active vitamin D analogs	Ca2+ deficiency ↑ risk secondary hyperparathyroidism & bone disorders. Excessive Ca2+ ↑ risk extraosseous calcification & CVD	Individualize Ca2+ restriction based on the use of vitamin D analogs & calcimimetics	Maintain Ca2+ balance & prevent hypercalcemeia	[60],[69]
Dietary Phosphorus* CKD 3-5	High dietary phosphorus intake associated w/ accelerated progression of disease & greater 5-year mortality risk	adjust dietary phosphorus intake to maintain normal serum phosphate levels between 3.4-4.5 mg/dl	Maintain Ca2+ & PTH balance. ↓ Secondary hyperparathyroidism mineral & bone disorders. Slow progression of CKD	[60],[68], [69]
Dietary Potassium CKD 3-5 or post-transplantation	Hyper/hypokalemia associated w/ muscular weakness, hypertension, ventricular arrhythmias, and death. Hypokalemia associated w/ peripheral neuropathy.	adjust dietary K+ intake to maintain serum potassium within 3.5-5.5 mEq/L	Slow progression of CKD. Prevention of peripheral neuropathy & other nerve related dysfunction.	[60],[70]
Sodium (Na+) CKD 3-5 or post transplantation	↑BP excessive fluid retention/ increased weight	2,300 mg/day	↓BP & normalize fluid balance/ weight reduction/ may ↓proteinuria	[60],[71], [72],[73]

*Phosphate recommendations recently changed, previously 800mg.

4.5 Potassium

Potassium is the most abundant intracellular ion with a concentration of about 98%; it has many biological functions such as cellular metabolism and acid-base homeostasis [74]. It is also vital for cardiac function, neural transmission, muscular contractions, and glucose metabolism [76]. One condition that alters potassium balance is an abnormally high level of serum potassium which develops into hyperkalemia (**Table 2**). Hyperkalemia is a severe metabolic condition that is often experienced in patients with CKD. The kidneys' ability to excrete potassium is inversely related to a decline in GFR [74]. Hyperkalemia alters the nervous system's mechanisms causing electrophysiological dysfunctions [76], presenting clinical manifestations such as muscle weakness, paresthesia, paralysis, nausea, hypotension, cardiac arrhythmias, and cardiac arrest [76]. As CKD progresses, potassium levels are monitored closely; patients are advised to limit dietary potassium intake to maintain serum potassium levels within normal range [17]. Potassium is rich in many foods such as vegetables, dark leafy greens, coffee and tea, and citrus fruits. Nutrition therapy for CKD recommends vegetables and fruits that are low in potassium and high in fiber and other nutrients, and to boil vegetables to lessen potassium concentration [17].

The ideal potassium intake is difficult to determine because of factors that influence serum potassium levels, such as medications, hydration level, acid-base status, glycemic

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control, adrenal function, and gastrointestinal complications [17]. It is essential to consider these factors when assessing the appropriate intake of potassium for a CKD patient, as the recommendations for potassium are individualized. Further research investigating the effect of a low potassium diet and the progression of renal disease are needed. It is unclear whether a potassium-restricted diet can slow CKD progression; however, research shows that it may reduce all-cause mortality in CKD [75].

4.6 Sodium

Hypertension and CKD are interrelated; the onset of one significantly increases the risk for developing the other, making close monitoring and early detection methods critical. Elevated BP is experienced in CKD, being related to salt sensitivity [76]. The efficacy of low sodium intake and the reduction in BP in hypertensive patients dates back to 1948 [77], currently reaching a worldwide understanding of the relationship between sodium and hypertension [78]. Patients with hypertension have a 75% increased risk of developing CKD than normotensive individuals [79], and a 25% increased risk of developing a decline in GFR among pre-hypertension patients [12]. Hypertension is a known risk factor to the progression and mortality of CVD; however, research identifying the effect of sodium on the advancement of CKD remains inconclusive [17].

Nonetheless, sodium restriction is protective for the onset of hypertension, a rationale for sodium-restricted diets as part of the medical nutrition therapy for disease management in CKD [79]. For CKD stages 3-5, the most recent sodium intake recommendation is a maximum of 2.3g/d and make sodium restriction a lifestyle to control fluid volume and maintain a desirable weight for CKD 3-5 with dialysis [17]. Effective habits for reducing sodium may be achieved by identifying high sodium foods such as processed foods, canned vegetables, pickled foods, soups, chips, salted nuts and seeds, and restaurant items. Simple modifications such as choosing unprocessed foods, choosing frozen over canned vegetables, avoiding soups and pickled foods, choosing unsalted nuts and seeds, and requesting no additional salt when ordering at a restaurant help meet the recommendations for sodium intake (**Table 2**).

4.7 Vitamin D

The primary role of vitamin D (VD) is to activate intestinal calcium reabsorption [80], but alterations to this biological mechanism occur in CKD. Low levels of active VD in ESRD patients are associated with increased bone reabsorption and reduced bone mineral density [81]. Studies report a progressive decline in VD at more than 80% from CKD 1-5, dialysis [82], and transplant patients [83]. Vitamin D metabolism is interrupted due to the inability for the second hydroxylation step of 25-hydroxyvitamin D ($25(OH)_2D$)OH to occur for it to convert to the active form $1,25(OH)_2$DOH, which takes place in the kidneys [84]. Inhibition of $1,25(OH)_2D$ induces hypocalcemia, which stimulates the parathyroid gland to release parathyroid hormone at persistent circulating levels [84]. Over time, this may result in renal osteodystrophy, including secondary parathyroidism, osteitis fibrosa, osteomalacia, and adynamic bone disease [80].

The current KDOQI guidelines for CKD nutrition states that ergocalciferol or cholecalciferol effectively treats VD deficiency/inefficiency; however, specific dosing should be individualized and derived through a step-by-step approach [17]. This step-by-step approach includes monitoring 25(OH)D serum levels and serum calcium and serum phosphorus; this helps the healthcare team recommend specific dosing veered to the patient's

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requirements [17]. Although there is a need for high-quality studies to confirm dosing, appropriate timing, and the most effective VD supplement [17], supplementation with ergocalciferol or cholecalciferol is essential in treating and preventing BMD disease in CKD [84].

4.7 Whole Food Plant-Based Diet

Studies report that a whole food plant-based (WFPB) diet reduces the risk for T2DM and CVD in CKD patients [2]. A WFPB diet is more restrictive than a vegan diet by exclusion of processed and refined foods such as isolated vegetable oils, bleached flours, and sugar; the diet focuses on fiber and nutrient-dense foods low in protein and energy [2]. Whole grains, nuts, seeds, legumes, monosaturated oils, fruits and vegetables, and tubers make up the foods in a WFPB diet [85].

WFPB diets provide about 75% of CHO, emphasizing dietary fiber [86]. Fiber intake of about 27g/day reduces serum urea and creatine in CKD; high serum urea and creatine indicate abnormal GFR [87]. High fiber intake shifts the gut microbiota by increasing the amount of gut microflora that breaks down and processes fiber; microflora binds to protein nitrogen, which decreases serum urea from an increase in nitrogen excretion [94]. Soluble fiber intake such as apples and oats reduce serum cholesterol, postprandial glucose, insulin response [88] and induce satiety from delayed gastric emptying[89]. Insoluble fiber such as whole grains and legumes increases motility and transit time by softening stool, promoting regular bowel movement, especially critical for CVD and CKD patients because they commonly experience slowed colonic transit time [90]. WFPB diets are significantly higher in fiber than other diets resulting in several health benefits for just fiber alone [91].

For health reasons already mentioned, protein restriction is a primary aspect of the renal diet. However, this has led to PEW in CKD patients, which increase CKD progression and adversely effects the patient's overall health [92]. An alternate protein source may be more beneficial to the patients' health than restricting the amount of protein alone; the protein source may be of greater importance than the quantity [58]. Plant proteins are typically ingested along with fiber, phytonutrients, and antioxidants, though animal proteins are ingested along with saturated fat and cholesterol [2]; this may be the rationale as to why plant proteins are associated with a vaster decline in blood pressure compared to animal protein [93]. Additionally, animal protein is associated with decreased insulin sensitivity, increased ROS [94], and induces hyperfiltration [95]; ingesting an equal amount of plant protein does not promote the same effects [96].

WFPB diets do not restrict fat intake; however, the foods promoted are made up of monounsaturated and polyunsaturated fats and limit processed oils and saturated fat [2]. Previous studies show a daily caloric intake of lipids to be less than 15% in WFPB diets, protective against CVD [93]. It is well established that omega-3 fatty acids reduce inflammation [97], blood pressure and increase HDL cholesterol [98]. Plant-based omega-3's are in foods such as flaxseeds, chia seeds, walnuts, olives, and some dark green vegetables [2]. Consumption of 1.5-3g/day of omega-3's is associated with CVD prevention in CKD patients [99].

It is challenging for patients to comply with a restricted phosphorus diet because it is found in most foods [64]. Many fruits and vegetables contain a slight phosphorus trace, while its content is higher in seeds, nuts, and legumes; and even higher in animal products

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[66]. However, plant foods contain phytates that limit phosphorus's gastrointestinal absorption, decreasing the bioavailability of phytate-based phosphorus [66]. Additionally, a WFPB diet restricts processed foods and sugar, including restructured meat and soft drinks, which contain inorganic phosphorus-based additives for preservation. Inorganic phosphorus has the highest absorption rate, at more than 90% [100]. These additives generally go unnoticed due to their complex and unrecognizable names [101].

A WFPB diet is naturally low in sodium due to the restriction of processed foods, assisting the patient to maintain appropriate sodium levels. Additionally, WFPB diets are generally lower in energy and may be beneficial for weight management. However, caution and careful planning are critical to avoid inadequate energy intake and PEW, which could worsen the patient's health increasing their risk for morbidity and mortality [63]. A wide variety of plant-based foods need to make up the diet and increased consumption of starchy vegetables, fruits, and legumes to meet the RDAs for protein and energy [2]. A drawback in the WFPB diet is the need to supplement with vitamin B12 because sufficient vitamin B12 intake is only met through the consumption of animal-based foods [2]. The KDOQI guidelines state that there is insufficient evidence to recommend a protein source regarding the effects on nutritional status, phosphorus levels, or blood lipid profile [17]. Although evidence is growing that support the positive health benefits of WFPB diets, there is a need for more research to determine any nutritional deficiencies or other adverse health effects from a WFPB diet in a clinical population with CKD patients [2].

5. Conclusions

Chronic kidney disease is a growing health crisis in the U.S. Diabetes and hypertension are the leading causes of CKD development; as the US is experiencing an increasing prevalence of both, CKD is expected to remain a critical national health issue. At ESRD, the kidneys have lost their ability function, and as a result, a series of malfunctions occur that lead to adverse health problems and health outcomes. Once diagnosed with ESRD, the patient either will be on dialysis for the rest of their life or receive a kidney transplant. Medical nutrition therapy is a critical aspect in the intervention for CKD because it is almost solely through nutrition that aids in the delay of the disease's progression and the prevention of comorbidities and mortality.

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