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Review Article

EMERGING ROLE OF DIET AND MICRONUTRIENTS IN CONSERVATIVE MANAGEMENT OF CKD NOT ON DIALYSIS

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A B S T R A C T

Though dietary factors are not directly involved in kidney damage, dietary habits significantly affect well-known risk factors for chronic kidney disease (CKD). Proper nutritional management in early CKD patients may positively influence modifiable risk factors such as hyperglycaemia, hypertension, and proteinuria as well as improve various metabolic alterations. Low protein diet helps in controlling uremic symptoms. Excess consumption of table sugars or beverages sweetened by sugar is associated with an increased risk of CKD. Dietary fibre intake helps lower blood pressure, serum lipid levels and level of inflammatory mediators and have protective cardiovascular effects. Patients with chronic kidney disease are recommended to consume diet low in sodium as well as to prevent retention of fluids and hypertension and reduce the risk of cardiovascular complications. It is essential to regulate dietary protein, fat and fibre intake and other micronutrient intake to reduce the rising incidence and prevalence of chronic kidney diseases.

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INTRODUCTION

Progressive and irreversible structural or functional renal impairment affecting multiple metabolic pathways for 3 or more months is defined as chronic kidney disease (CKD) as per KDIGO guidelines (Table1(a-c) [1]. According to population studies approximately 12% (25 million) people are estimated to have chronic kidney disease and approximately 0.2% (>500,000) is being treated by dialysis or transplantation for kidney failure [2, 3]. Chronic kidney disease has become a public health threat due to its rising prevalence, poor outcome and high treatment cost [4]. The clinical data is inconclusive on the nutritional outcomes achievable through dietary modification in patients of CKD.

Though dietary factors are not directly involved in kidney damage, dietary habits significantly affect well-known risk factors for CKD such as diabetes, hypertension, and obesity[5].A proper nutritional management in early CKD patients may positively influence modifiable risk factors such as hyperglycemia, hypertension, and proteinuria as well as improve various metabolic alterations; metabolic acidosis and hyperphosphatemia**.** It has been noticed that progressive reduction of nutritional intake due to anorexia, uremia and deranged hypothalamic output is related to worsened renal functions and upstaging of CKD.As a consequence of the symptoms of toxemia patients restrict their dietary intake leading to protein energy malnutrition (PEM).Studies have shown that it is important to supplement patients of CKD on conservative treatment with controlled dietary protein to compensate for loss of urinary proteins and inhibit CKD progression [6, 7]. In this review we discuss role of nutritional support in patients of CKD and its effect in progression to end stage renal disease (ESRD).

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Role of Proteins in diet

High protein intake increases the risk of CKD, has been debated for years now. Low protein diet helps in controlling uremic symptoms, reducing proteinuria and hyper filtration. Intake of more than 1.5g/ kg body weight per day may increase hyper filtration leading to kidney disease [8]**.**Professional guidelines advise a low protein diet (LPD) of 0.6–0.8 g protein/kg/day for CKD stages 3 and 4 [6, 9]. It is essential to supervise protein intake, as renal function declines, so do spontaneous protein intake increasing the risk of PEM.

The Modification of Diet in Renal Disease (MDRD) study showed that the progression of kidney disease is only minimally decelerated by a low-protein diet though other controlled trials have confirmed the beneficial effects of restricted protein intake [10, 11]**.**Recent studies in both experimental models and human kidney disease suggest that a low-protein di *et al* leviates proteinuria [8, 12].The amelioration of proteinuria is probably related to the reduction in intraglomerular pressure. Protein break down leads to persistently high blood urea levels i.e. azotemia, which causes oxidative stress, inflammation, and endothelial dysfunction

leading to cardiovascular disease[13].Reduction in protein intake leads to amelioration of azotemia by reducing production of nitrogenous compounds that act as uremic toxins [14]**.** A diet comprising of 0.6 to 0.8 g of protein per kilogram per day fulfills the dietary needs, especially if half the protein is from dairy products and other half from plant proteins.

Role of Carbohydrates in diet

Excess consumption of table sugars or beverages sweetened by sugaris also associated with an increased risk of CKD as fructose found in these promotes insulin resistance, dyslipidemia and hypertension [15, 16]**.**Along with this metabolism of fructose increases the production of uric acid, reactive oxygen species and chemokines. A diet restricted in sugars has been shown to reduce inflammatory markers such as intercellular adhesion molecule -1.

Table 1 (a) [39] Criteria for CKD (either of the following present for more than 3 months)

Markers of Kidney Damage	Albuminuria (AER≥30mg/24 hours; ACR ≥30mg/g[≥3mg/mmol])
	Urine sediment abnormalities due to tubular disorders
	Abnormalities detected by histology
	Structural abnormalities detected by imaging
	History of kidney transplantation
Decreased GFR	GFR <60ml/min/1.73m^2 (GFR categories G3a-G5)

Abbreviations: CKD, chronic kidney disease, GFR, glomerular filtration rate

Table 1 (b) [39] GFR categories in CKD

GFR category	GFR (ml/min/1.73m^2)	Terms
G1	≥ 90	Normal or high
G2	60-89	Mildly decreased
G3a	45-59	Mildly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	<15	Kidney failure

Abbreviations: CKD, chronic kidney disease, GFR, glomerular filtration rate
In absence of evidence of kidney damage, neither GFR category G1 nor G2 fulfill the criteria for CKD.

Table 1 (c) [39] Albuminuria categories in CKD

Category	AER (mg/24hr)	ACR approximate equivalent		Terms
		(mg/mmol)	(mg/g)	
A1	<30	<3	<30	Normal to mildly increased
A2	30-300	3-30	30-300	Moderately increased
A3	>300	>30	>300	Severely increased

Abbreviations: AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease.

Table 2 [39, 40]

Protein	≤0.8 g/kg/day, increase plant source
Carbohydrate/fat	30 to 35 kcal/kg/day; <30% of total calories from fat and <10% of total fat from saturated fat
Fiber	25 to 38 g/day
Sodium/Salt	<2.3 g/day (<5 g/day of NaCl)
Potassium	Individualize to keep the serum potassium within a normal range
Calcium	1.5 g/day from both dietary and medication sources
Phosphorus	0.8 to 1 g/day

Role of Fats in diet

Derangements in lipoprotein metabolism are typically seen in CKD, replacing saturated with polyunsaturated fatty acids (PUFAs) reduces triglycerides and increases high-density lipoproteins (HDLs) leading to improvement in renal outcome. In a study by De Goeji *et al*, serum low-density lipoprotein levels (LDL) > 2.5 mmol/L, increased serum triglycerides and HDL/LDL ratio <0.4 are associated with an accelerated decline in renal functions [17]. A Mediterranean diet having high PUFAs and low in saturated fatty acids in pre-dialysis patients has shown to improve dyslipidemia and improvement in CKD patients with GFR <60ml/min/1.73m^2 [18]. Similar results were found in two other studies with cohorts of 2600 and 5316 adults respectively having GFR <60ml/min/1.73m^2 suggesting diet comprising of n-3PUFAs had a protective effect on renal function[19, 20]. The n-6 PUFAs such as arachidonic acids contributes to inflammatory processes whereas n-3 PUFAs oppose pro-inflammatory actions of saturated fatty acids [21]. Although randomized control trials on effect of supplementation of n-3 PUFAs in the diet of CKD patients are sparse, but the ones done show significant reduction in expression of inflammatory mediators and pro-inflammatory adipose tissue gene expression [22,23].

Role of Fibers in diet

Dietary fiber intake helps lower blood pressure, serum lipid levels and level of inflammatory mediators. They also have protective cardiovascular affects with a recommended intake of 12 to 33 g/ days from whole foods or up to 42.5 g/days from supplements[24]. Dietary fiber may reduce serum urea levels, due to increased intestinal nitrogen excretion. Goraya *et al* showed that a fruits and vegetables diet caused reduction in dietary acid load leading to significant decrease in systolic blood pressure (BP) and helpful in hypertensive kidney disease [25].National Health and Nutrition Examination Survey (NHANES) III showed that in patients with and without CKD, for each 10 g/day increase in total fiber intake elevated serum C-reactive protein levels decreased by 38 and 11% respectively also total fiber intake was inversely related to mortality risk in CKD but not significantly associated with mortality rate changes in the normal population [26]. Few clinical trials have optimized dietary fiber intake to approximately 19.8 ± 8.9 g/day for CKD patients [27]**.**

Role of Sodium and fluid intake in diet

Older individuals (55years or more) on high sodium diet (>4g/day) usually have high blood pressure. Patients with chronic kidney disease are recommended to consume diet low in sodium so as to prevent retention of fluids and hypertension and reduce the risk of cardiovascular complications as well [28].Although it is not proved that low sodium diet reduces the progression of chronic kidney disease but studies suggest that sodium restriction enhances the effects of low-protein diet reducing glomerular hyperfiltration and proteinuria.A longitudinal study by He j and Mills involving examination of 24-hour urinary protein of 3939 patients of chronic kidney disease showed higher mortality rate of approximately 45% in patients having ≥ 4.5g per day of urinary sodium excretion as compared to those having <2.7 g per day of urinary sodium excretion[29].A daily dietary sodium intake of <4 g is recommended for patients of chronic kidney disease and for management of proteinuria and sodium fluid retention as <3 g per day. However it is recommended to not consume diet less

that 1.5 g per day asthe risk of hypernatremia is high and such stringent salt restriction may be harmful in patients with salt-losing nephropathies Also patients of CKD stage 3 are isosthenuric, in order to avoid the risk of hyponatremia it is recommended to restrict the fluid intake to less than 1.5 liters per day [30].

Role of Vitamins and Trace elements in diet

Due to inadequate food intake, CKD patients may have imbalance several vitamins and trace elements leading to oxidative stress and release of inflammatory mediators. These include Vitamin C deficiency, Vitamin E deficiency, and deficient carotenoids. Patients with advanced renal disease become deficient in folate, vitamin K, and calcitriol. Iron deficiency is a common complication in chronic kidney disease patients. Recent studies have suggested that supplementation of folic acid along with enalapril leads to slower disease progression. Also Vitamin K supplementation may reduce the development of vascular calcification. Studies have recommended that persons at high risk of chronic kidney disease and with established renal disease should consume conventional doses of vitamins and trace elements [31, 32].

Role of Potassium in Diet

It is well established that higher dietary potassium with lower sodium intake is associated with lower incidences of hypertension, stroke, nephrolithiasis, and kidney disease. Many potassium-rich foods are considered healthy for consumption being high in fiber and vitamin content [33].A relatively high daily potassium intake, 4.7 g (120 mmol), is recommended for healthy adults as well as those at high risk for kidney disease. Patients with hyperkalemia are usually recommended a potassium restricted diet (approximately <3g per day) [34].

Role of Phosphorus in diet

In renal insufficiency there are high circulating and tissue levels of parathyroid hormone and fibroblast growth factor 23 (FGF-23) that in turn increase urinary phosphorus excretion , hence hyperphosphatemia is uncommon in earlier stages of chronic kidney disease[35]. Higher plasma phosphorus levels are associated with an increased risk of kidney disease [36].Elevated parathyroid hormone and FGF-23 levels can cause bone disease, cardiovascular complications in the form of left ventricular hypertrophy, vascular calcification, and increased progression of kidney disease from vascular injury[37]. A low-protein diet decreases phosphorus intake. The gastrointestinal absorption of phosphorus is lower from vegetarian diet as compared to diet rich in meat. Patients with moderate- to-advanced kidney should limit the phosphorus intake to less than 800mg per day (26mmolper day) and avoid consumption of processed foods [38].

CONCLUSION

Looking at the rising incidence and prevalence of chronic kidney diseases, nutritional management and dietary regulations are essential to help increase dialysis-free periods and patient longevity. It is essential to regulate dietary protein, fat and fiber intake and other micronutrient intake for the same.

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