

Alkaline Diet A Novel Nutritional Strategy in Chronic Kidney Disease?

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Chronic kidney disease is defined as a glomerular filtration rate lower than 60 mL/min/1.73 m², which is regarded as a public health priority and part of the growing burden of noncommunicable diseases. Reduced kidney function is concomitant with high levels of inflammatory factors, abnormal lipid profile, and anemia, as well as bone abnormalities, calcium deposition outside the bones, endothelial dysfunction, and cardiomyopathy. Furthermore, metabolic acidosis is a common complication in chronic kidney disease that is associated with secondary hyperparathyroidism and faster kidney disease progression. Effective preventive approaches may slow progression of chronic kidney disease and reduce the risk of subsequent morbidity and mortality. It seems that correction of metabolic acidosis slows down the decline in glomerular filtration rate and is one of the noble approaches. A diet rich in fruits and vegetables instead of bicarbonate therapy is feasible and economical and appears to have a positive effect on kidney hemodynamic function.

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INTRODUCTION

Chronic kidney disease (CKD) identification and staging rely on measurement of glomerular filtration rate and albuminuria.^{1,2} Chronic kidney disease incidence increases with age, obesity, diabetes mellitus, and hypertension, and affects 8% to 16% of adults worldwide.^{1,3} Due to multiple adverse outcomes and negative effects on quality of life, CKD universally recognizes as a health priority.^{1,4} Prevention and part of disease's control foremost are based on blood pressure monitoring, lipid-lowering therapy, and good glycemic control. In addition, correction of acidosis is thought to slow down the decline of glomerular filtration rate (GFR) over time.^{5,6}

Overt metabolic acidosis develops after a drop in GFR to less than approximately 25 mL/min/1.73 m².⁷ Current guidelines and the Kidney Disease Outcomes Quality Initiative recommend alkali therapy with sodium citrate or sodium

bicarbonate for CKD patients in whom serum total bicarbonate is less than 22 mEq/L,^{8,9} although it has been suggested that commencement of treatment when total bicarbonate is greater than 22 mEq/L can be more kidney protective.¹⁰ Although alkali treatment is effective in increasing plasma total bicarbonate and delaying GFR decline,⁵ sodium citrate promotes gastric aluminum absorption,¹¹ and sodium bicarbonate causes bloating and flatus.¹² Moreover, the added sodium may exacerbate fluid retention and increased blood pressure.¹⁰ The recent body of studies suggests that alkali treatment may hide the adverse effects of dietary acid ash by a normal serum bicarbonate concentration.¹³

Instead, non-sodium-based therapies such as base-inducing diet can reduce metabolic acidosis and urinary net acid excretion and are also kidney protective in CKD patients.^{10,14} On the other hand, diet is the leading CKD-related morbidity and

mortality risk factor¹⁵; thus, diet modification can be definitely effective. Regarding the limited data available on the association between dietary acid load and CKD and its related morbidity, in the present review, an attempt has been made to discuss the dietary elements of the acid load and to summarize the published literature on the role of alkaline diet in progression of CKD.

METABOLIC ACIDOSIS

Metabolic acidosis is defined as a low serum pH (less than 7.35), which occurs due to high production of hydrogen ions or low production of bicarbonate.^{9,16} Metabolic acidosis is a common complication of CKD, particularly when the glomerular filtration rate falls below 25 mL/min/1.73 m² to 30 mL/min/1.73 m².^{9,17}

Inapt and unbalanced diet such as high protein and low carbohydrate intake may cause mild metabolic acidosis.^{18,19} Metabolic acidosis is associated with muscle wasting and sarcopenia,^{20,21} metabolic syndrome components such as insulin resistance and hypertension,²²⁻²⁴ increased inflammatory mediators, high levels of corticosteroid and parathyroid hormones,²⁵ and increased risk of kidney calculi.¹⁸ Acidosis is a well-known risk factor for obesity, lipid disorders, and consequent cardiovascular disease.^{18,19} Furthermore, associations of acidemia with bone disorders, chronic kidney failure, and inappropriate nutritional status has been well recognized.^{26,27}

Elucidating the adverse effects of low serum bicarbonate is important for studying the relationship between dietary factors and CKD pathophysiology and for updating dietary guidelines for the management of CKD.

DIETARY ACID LOAD

For over a century, researchers have discovered the acid and alkaline nature of foods (Table), and diet is known as a major determinant of the body's acid load.^{5,28} Animal protein and cereal grains are considered to be acid-inducing foods, which are metabolized to acidic residues, mainly sulfuric acid. In contrast, fruits and vegetables are metabolized to alkaline residues, mainly potassium bicarbonate.^{21,29} The combination of acid- and base-inducing foods in diet determines dietary acid load (DAL).⁶ Diet transition, ie, lower intakes of magnesium and potassium as well as fiber and higher intakes of saturated fat, simple sugars, sodium, and chloride may induce metabolic acidosis.^{13,23}

The average daily DAL of the Western-style diet is approximately 1 mEq/kg, which is consistent with median estimations of DAL in several cohorts.³⁰⁻³³

DIETARY ACID-BASE LOAD INDICATORS

Two indicators of dietary acid-base load included potential renal acid load (PRAL) and protein-potassium ratio.¹⁸ The PRAL is calculated based on only 4 nutrients using the following equation:

$$\text{PRAL (mEq/d)} = 0.4888 \times \text{dietary protein (g/d)} + 0.0366 \times \text{dietary phosphorus (mg/d)} - 0.0205 \times \text{dietary potassium (mg/d)} - 0.0125 \times \text{calcium (mg/d)} - 0.0263 \times \text{magnesium (mg/d)}$$

Protein-potassium ratio is computed as the proportion of dietary protein (g/d) to dietary potassium (mg/d).^{18,34} A negative PRAL value means the food has an alkaline load; a positive value means the food has an acid load; in other words, upper values of PRAL and protein-potassium ratio confirm a higher dietary acid load.³⁵ Both indicators are associated with serum creatinine

Acid and Alkaline Nature of Foods

Food	Potentially Alkaline Foods	Neutral Foods	Potentially Acidic Foods
Fats	Butter, margarine, oils	...	Most of seeds such as pumpkin seeds, sesame seeds, sunflower seeds and walnuts, butternuts, and creamy salad dressings
Dairy	Milk
Carbohydrates		...	All types
Sweets	White sugar, honey	Sorghum syrup, brown sugar, molasses, and dry powder of cocoa	Gelatin and pudding
Proteins	All types
Vegetables and legumes	...	All types, except corn	...
Fruits	...	All types	...
Spices and herbs	...	All types	...

and CKD progression, independently.^{23,36,37}

METABOLIC ACIDOSIS AND CHRONIC KIDNEY DISEASE PROGRESSION

Metabolic acidosis is one of the initial complications of CKD. A body of recent literature proposes that acid-base disturbance mediates kidney failure progression,^{38,39} albeit the causative relationship between metabolic acidosis and risk of CKD in the general population is not yet perfectly elucidated (Figure).^{22,40} Both volatile and nonvolatile acids are produced in body's metabolic pathways, which are excreted through respiration as bicarbonate and by the kidney as ammonium and titratable acid, respectively.⁴¹

Most recent literature expressed that despite multiple therapies, GFR decline is progressive; hence, there is necessity for further adjuvant kidney-protective interventions.^{39,42} Additionally, continued evidence confirms that dietary acid reduction can be a potentially effective and economical approach, besides current treatments.^{14,43}

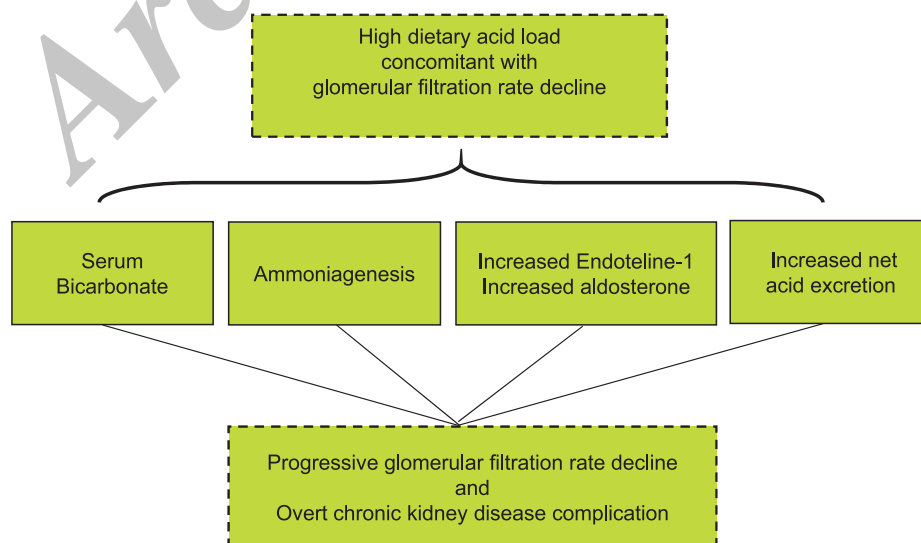
It is apparent that diet can prominently affect body acid-base balance, subclinical metabolic acidosis, age-related kidney function decline and chronic kidney disease progression.^{13,33,40,44} It seems that lowering dietary acid ash via more consumption of fruits and vegetables can have a greater effect than dietary protein restriction per se.⁴¹ The only drawback in alkaline diet administration is the probable risk of hyperkalemia in CKD patients.⁴⁵

CONCLUSIONS

In acidic diet and high animal protein intake, obesity and diabetes mellitus, the kidney is forced to excrete a high acid load, which results in renal hemodynamic changes and kidney hypertrophy.²³ Gradual loss of renal acid-base regulatory function with aging is undeniable.⁴⁶ Moreover, obesity is one of the most important risk factors for CKD,⁴⁷ maybe due to higher renal blood flow, renal lipotoxicity, higher net acid load, renal hemodynamic abnormalities, and inflammatory state.^{48,49} Pro-inflammatory adipokines elevation in central obesity is another hypothesis.⁴⁹ However, the contributory mechanisms of protective effects of alkaline diet in chronic kidney disease have not been clarified yet.

One possible mechanism is that high intake of fruits and vegetables and subsequent low dietary acid load decrease kidney injury markers such as urinary endothelin-1 and aldosterone levels.¹⁴ On the other hand, acid-inducing diets are supposed to hurt kidney through increased ammonium concentration and consequent tubular toxicity and by triggering the renin-angiotensin system.⁵⁰

Alkaline diet rich in fruits and vegetables has a low net acid load, hence not only exhibits favorable metabolic effects in patients with CKD, but also seems to be safe.^{13,19,25,28,51,52} Various studies by Goraya and colleagues have disclosed that reducing dietary acid load via high consumption of fruits and vegetables in CKD patients can result in lower level of kidney injury markers and urinary albumin



Metabolic acidosis and chronic kidney disease progression

excretion, without developing hyperkalemia.^{10,14,43} These findings are confirmed by that of Scialla and coworkers who mentioned an association between higher DAL and progressive GFR decline among African Americans with hypertensive nephropathy.⁵³ Furthermore, recent observational and cohort studies concluded that the higher dietary acid intake, the faster CKD progression would occur.^{37,54} Thus, according to the existing evidence, decreasing the acid residue through an alkaline diet may be an effective adjuvant kidney-protective therapy. Further large-scaled clinical trials are necessary to assert the effectiveness of alkaline diet in improving CKD patient's outcomes.

CONFLICT OF INTEREST

None declared.

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