

Alkaline Diet

A Novel Nutritional Strategy in Chronic Kidney Disease?

Zahra Yari,¹ Parvin Mirmiran²

¹Department of Clinical Nutrition and Dietetics, Faculty of Nutrition and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Science, Tehran, Iran

²Nutrition and Endocrine Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Keywords. chronic kidney disease, alkaline diet, metabolic acidosis, dietary acid load, glomerular filtration rate

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.

IJKD 2018;12:204-8
www.ijkd.org

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}

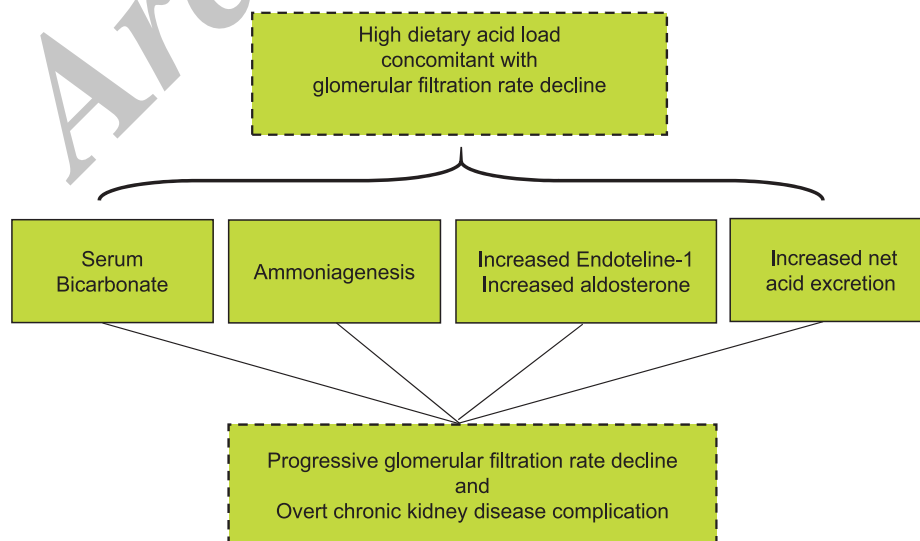
It is apparent that diet can prominently affect body acid-base balance, subclinical metabolic acidosis, age-related kidney function decline and chronic kidney disease progression.^{13,33,40,44} It seems that lowering dietary acid ash via more consumption of fruits and vegetables can have a greater effect 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.

REFERENCES

- Jha V, Garcia-Garcia G, Iseki K, et al. Chronic kidney disease: global dimension and perspectives. *Lancet*. 2013;382:260-72.
- Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Annals Intern Med*. 2003;139:137-47.
- Najafi I, Attari F, Islami F, et al. Renal function and risk factors of moderate to severe chronic kidney disease in Golestan Province, northeast of Iran. *PLoS One*. 2010;5:e14216.
- Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C-y. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *New Engl J Med*. 2004;351:1296-305.
- Phisitkul S, Khanna A, Simoni J, et al. Amelioration of metabolic acidosis in patients with low GFR reduced kidney endothelin production and kidney injury, and better preserved GFR. *Kidney Int*. 2010;77:617-23.
- Verove C, Maisonneuve N, El Azouzi A, Boldron A, Azar R. Effect of the correction of metabolic acidosis on nutritional status in elderly patients with chronic renal failure. *J Ren Nutr*. 2002;12:224-8.
- Kopple JD, Kalantar-Zadeh K, Mehrotra R. Risks of chronic metabolic acidosis in patients with chronic kidney disease. *Kidney Int*. 2005;67:S21-S7.
- Kopple JD. National kidney foundation K/DOQI clinical practice guidelines for nutrition in chronic renal failure. *Am J Kidney Dis*. 2001;37:S66-S70.
- Kraut JA, Madias NE. Metabolic Acidosis of CKD: An Update. *Am J Kidney Dis*. 2016;67:307-17.
- Goraya N, Simoni J, Jo C-H, Wesson DE. Treatment of metabolic acidosis in patients with stage 3 chronic kidney disease with fruits and vegetables or oral bicarbonate reduces urine angiotensinogen and preserves glomerular filtration rate. *Kidney Int*. 2014;86:1031-8.
- Nolan CR, Califano JR, Butzin CA. Influence of calcium acetate or calcium citrate on intestinal aluminum absorption. *Kidney Int*. 1990;38:937-41.
- Gaggi M, Cejka D, Plischke M, et al. Effect of oral sodium bicarbonate supplementation on progression of chronic kidney disease in patients with chronic metabolic acidosis: study protocol for a randomized controlled trial (SoBic-Study). *Trials*. 2013;14:196.
- Scialla JJ, Anderson CA. Dietary acid load: a novel nutritional target in chronic kidney disease? *Adv Chronic Kidney Dis*. 2013;20:141-9.
- Goraya N, Simoni J, Jo C, Wesson DE. Dietary acid reduction with fruits and vegetables or bicarbonate attenuates kidney injury in patients with a moderately reduced glomerular filtration rate due to hypertensive nephropathy. *Kidney international*. 2012;81:86-93.
- Murray CJ, Abraham J, Ali MK, et al. The state of US health, 1990-2010: burden of diseases, injuries, and risk factors. *JAMA*. 2013;310:591-606.
- Bailey JL. Metabolic acidosis: an unrecognized cause of morbidity in the patient with chronic kidney disease. *Kidney Int Suppl*. 2005;S15-23.
- Chen W, Abramowitz MK. Metabolic acidosis and the progression of chronic kidney disease. *BMC Nephrol*. 2014;15:55.
- Reddy ST, Wang C-Y, Sakhaee K, Brinkley L, Pak CY. Effect of low-carbohydrate high-protein diets on acid-base balance, stone-forming propensity, and calcium metabolism. *Am J Kidney Dis*. 2002;40:265-74.
- Schwalfenberg GK. The alkaline diet: is there evidence that an alkaline pH diet benefits health? *J Environ Public Health*. 2011;2012.
- Caso G, Garlick PJ. Control of muscle protein kinetics by acid-base balance. *Curr Opin Clin Nutr Metab Care*. 2005;8:73-6.
- Dawson-Hughes B, Harris SS, Ceglia L. Alkaline diets favor lean tissue mass in older adults. *The Am J Clin Nutr*. 2008;87:662-5.
- Park M, So R, Joo KW, Yoon HJ. Association between lower serum bicarbonate and renal hyperfiltration in the general population with preserved renal function: a cross-sectional study. *BMC Nephrol*. 2016;17:3.
- Adeva MM, Souto G. Diet-induced metabolic acidosis. *Clin Nutr*. 2011;30:416-21.
- Souto G, Donapetry C, Calvino J, Adeva MM. Metabolic acidosis-induced insulin resistance and cardiovascular risk. *Metab Syndr Related Disorder*. 2011;9:247-53.
- Yaqoob MM. Acidosis and progression of chronic kidney disease. *Curr Opin Nephrol Hypertens*. 2010;19:489-92.
- Nazar CM. Significance of diet in chronic kidney disease. *J Nephropharmacol*. 2013;2:37-43.
- Chauveau P, Rigotherier C, Combe C. Con: Higher serum bicarbonate in dialysis patients is protective. *Nephrol Dial Transplant*. 2016;31:1226-9.
- Banerjee T, Liu Y, Crews DC. Dietary Patterns and CKD Progression. *Blood Purif*. 2016;41:117-22.
- Trilok G, Draper H. Sources of protein-induced endogenous acid production and excretion by human

- adults. *Calcified Tissue Int.* 1989;44:335-8.
30. Remer T, Dimitriou T, Manz F. Dietary potential renal acid load and renal net acid excretion in healthy, free-living children and adolescents. *Am J Clin Nutr.* 2003;77:1255-60.
 31. Gannon RH, Millward DJ, Brown JE, et al. Estimates of daily net endogenous acid production in the elderly UK population: analysis of the National Diet and Nutrition Survey (NDNS) of British adults aged 65 years and over. *Brit J Nutr.* 2008;100:615-23.
 32. Ströhle A, Waldmann A, Koschizke J, Leitzmann C, Hahn A. Diet-dependent net endogenous acid load of vegan diets in relation to food groups and bone health-related nutrients: results from the German Vegan Study. *Ann Nutr Metab.* 2011;59:117-26.
 33. Scialla JJ, Appel LJ, Astor BC, et al. Estimated net endogenous acid production and serum bicarbonate in African Americans with chronic kidney disease. *Clin J Am Soc Nephrol.* 2011;6:1526-32.
 34. Frassetto LA, Todd KM, Morris RC, Jr., Sebastian A. Estimation of net endogenous noncarbonic acid production in humans from diet potassium and protein contents. *Am J Clin Nutr.* 1998;68:576-83.
 35. Remer T, Manz F. Estimation of the renal net acid excretion by adults consuming diets containing variable amounts of protein. *Am J Clin Nutr.* 1994;59:1356-61.
 36. Bahadoran Z, Mirmiran P, Khosravi H, Azizi F. Associations between Dietary Acid-Base Load and Cardiometabolic Risk Factors in Adults: The Tehran Lipid and Glucose Study. *Endocrinol Metab (Seoul).* 2015;30:201-7.
 37. Kanda E, Ai M, Kuriyama R, Yoshida M, Shiigai T. Dietary acid intake and kidney disease progression in the elderly. *Am J Nephrol.* 2014;39:145-52.
 38. Dobre M, Rahman M, Hostetter TH. Current status of bicarbonate in CKD. *J Am Soc Nephrol.* 2015;26:515-23.
 39. Goraya N, Wesson DE. Acid-base status and progression of chronic kidney disease. *Curr Opin Nephrol Hypertens.* 2012;21:552-6.
 40. Odermatt A. The Western-style diet: a major risk factor for impaired kidney function and chronic kidney disease. *Am J Physiol Ren Physiol.* 2011;301:F919-F31.
 41. Hannan MT, Tucker KL, Dawson-Hughes B, Cupples LA, Felson DT, Kiel DP. Effect of dietary protein on bone loss in elderly men and women: the Framingham Osteoporosis Study. *J Bone Miner Res.* 2000;15:2504-12.
 42. Appel LJ, Wright JT, Greene T, et al. Long-term Effects of Renin-Angiotensin System-Blocking Therapy and a Low Blood Pressure Goal on Progression of Hypertensive Chronic Kidney Disease in African Americans. *Arch Intern Med.* 2008;168:832-9.
 43. Goraya N, Simoni J, Jo C-H, Wesson DE. A comparison of treating metabolic acidosis in CKD stage 4 hypertensive kidney disease with fruits and vegetables or sodium bicarbonate. *Clin J Am Soc Nephrol.* 2013;8:371-81.
 44. Phisitkul S, Hacker C, Simoni J, Tran R, Wesson D. Dietary protein causes a decline in the glomerular filtration rate of the remnant kidney mediated by metabolic acidosis and endothelin receptors. *Kidney Int.* 2008;73:192-9.
 45. Goraya N, Wesson DE. Dietary management of chronic kidney disease: protein restriction and beyond. *Curr Opin Nephrol Hypertens.* 2012;21:635-40.
 46. Lindeman RD, Goldman R. Anatomic and physiologic age changes in the kidney. *Experiment Gerontol.* 1986;21:379-406.
 47. Garofalo C, Borrelli S, Minutolo R, Chiodini P, De Nicola L, Conte G. A systematic review and meta-analysis suggests obesity predicts onset of chronic kidney disease in the general population. *Kidney Int.* 2017;91:1224-35.
 48. Wahba IM, Mak RH. Obesity and obesity-initiated metabolic syndrome: mechanistic links to chronic kidney disease. *Clin J Am Soc Nephrol.* 2007;2:550-62.
 49. Chen S, Liu H, Liu X, et al. Central obesity, C-reactive protein and chronic kidney disease: a community-based cross-sectional study in southern China. *Kidney Blood Press Res.* 2013;37:392-401.
 50. Wesson DE, Simoni J, Broglio K, Sheather S. Acid retention accompanies reduced GFR in humans and increases plasma levels of endothelin and aldosterone. *Am J Physiol Ren Physiol.* 2011;300:F830-F7.
 51. de-Brito Ashurst I, O'Lone E, Kaushik T, McCafferty K, Yaqoob MM. Acidosis: progression of chronic kidney disease and quality of life. *Pediatr Nephrol.* 2015;30:873-9.
 52. Banerjee T, Crews DC, Wesson DE, et al. Dietary acid load and chronic kidney disease among adults in the United States. *BMC Nephrol.* 2014;15:137.
 53. Scialla JJ, Appel LJ, Astor BC, et al. Net endogenous acid production is associated with a faster decline in GFR in African Americans. *Kidney Int.* 2012;82:106-12.
 54. Banerjee T, Crews DC, Wesson DE, et al. High Dietary Acid Load Predicts ESRD among Adults with CKD. *J Am Soc Nephrol.* 2015;26:1693-700.
- Correspondence to:
 Parvin Mirmiran, PhD
 Department of Clinical Nutrition and Dietetics, Faculty of Nutrition and Food Technology, National Nutrition and Food Technology Research Institute, Shahid Beheshti University of Medical Science, Tehran, Iran
 E-mail: mirmiran@endocrine.ac.ir
- Received August 2017
 Accepted September 2017