

# Can Peripheral Venous Gases Replace Arterial Gases in a Patient with Chronic Kidney Disease?

# Jose Lucas Daza<sup>1</sup>, Yaroslad de la Cruz<sup>1</sup>, Gerardo Gutierrez<sup>1</sup>, Luis Puello, Victor Aldana<sup>2</sup>, Antonio Vasquez<sup>3</sup>, Orlando Ariza<sup>4</sup>, Alexander Ariza<sup>5</sup>, Andres Cardenas<sup>6</sup>

<sup>1</sup>Department of Internal Medicine, Nephrology, University of Buenos Aires, Buenos Aires, Argentina <sup>2</sup>Department of Internal Medicine, Cardiology and Epidemiology, School of Medicine, Universidad de Los Andes, Bogotá, Colombia

<sup>3</sup>Department of Internal Medicine, University of Buenos Aires, Buenos Aires, Argentina

<sup>4</sup>Department of Internal Medicine, Cardiology, University of Buenos Aires, Buenos Aires, Argentina

<sup>5</sup>Department of Internal Medicine, Hematology, University of Buenos Aires, Buenos Aires, Argentina

<sup>6</sup>Department of General Medicine, University Cooperativa, Santa Marta, Colombia

Email: montelucaz@gmail.com

How to cite this paper: Daza, J.L., de la Cruz, Y., Gutierrez, G., Puello, L., Aldana, V., Vasquez, A., Ariza, O., Ariza, A. and Cardenas, A. (2023) Can Peripheral Venous Gases Replace Arterial Gases in a Patient with Chronic Kidney Disease?. *Open Journal of Nephrology*, **13**, 150-160. https://doi.org/10.4236/ojneph.2023.132015

**Received:** April 12, 2023 **Accepted:** June 27, 2023 **Published:** June 30, 2023

Copyright © 2023 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0). http://creativecommons.org/licenses/by/4.0/ Abstract

**Introduction:** Metabolic acidosis (MA) is a frequent alteration in chronic kidney disease (CKD) that is associated with numerous complications, which is why its correction is recommended. Oral sodium bicarbonate is currently the treatment of choice. Objective: The objective is to determine if venous bicarbonate is equal to arterial bicarbonate in the follow-up of a patient with chronic kidney disease. Materials Methods: Single-center Cross-sectional studies in a cohort of adult patients with stage 4 - 5 CKD. Samples were taken between January 2022 and January 2023, in a Clinic in the city of Ibague/ Colombia obtained from the radial artery. The inclusion criteria were: not being treated with alkaline at the time of inclusion. Results: A total of 71 patients were included, 73.2% male (52) and 26.8% female (19), with different stages: stage 3 with 5.6% (4), stage 4 with 60.6% (43), stage 5 with 33.8% (23). 66.2% were diabetic, 88.7% had arterial hypertension, and 15.5% of the patients presented hematoma as a complication and pain associated with arterial puncture. The result of mean venous bicarbonate was 18.8 with a standard deviation of 2.3, arterial bicarbonate a mean of 19.4 with a standard deviation of 2.1 with a value of P 0.46, venous pH with a mean of 7.37 with a standard deviation of 0.48 and a mean arterial pH of 7.38 with a standard deviation of 0.48 with a P value of 0.01. Values of venous bicarbonate compared to arterial bicarbonate showed no statistically significant difference in patients with chronic kidney disease, but there were more complications such as hematoma and

pain in patients in the arterial puncture cohort, because of this result venous bicarbonate corresponds to arterial bicarbonate, but has less risk of complications associated with the procedure. **Conclusion:** Metabolic acidosis is a frequent alteration in advanced chronic kidney disease, these results showed that the values of arterial and venous bicarbonate have no statistically significant differences, but there is a greater risk of complications with arterial blood gases, due to this, venous bicarbonate could be a useful tool for patients with chronic kidney disease.

## **Keywords**

MA (Metabolic Acidosis), CKD (Chronic Kidney Disease), GFR (Glomerular Filtration Rate)

# **1. Introduction**

Metabolic acidosis (MA) is a frequent alteration in chronic kidney disease (CKD) [1] [2]. The deterioration of renal function reduces the net excretion of acids and causes a positive balance of hydrogen ions, in such a way that when the glomerular filtration rate falls below 20 - 25 ml/min, a reduction in blood bicarbonate [3] begins to be observed, although with more sensitive biochemical analyses, such as urinary ammonium [4] and citrate [5] excretion, it can be shown that this metabolic defect begins in less advanced stages of the disease.

The negative effects of MA in CKD have been the subject of numerous investigations that have shown its association with bone, metabolic and inflammatory [6] [7] endocrine [8] [9] complications, progression of CKD [10] [11] and mortality [12] [13]. More interestingly, the MA correction improves or reverses many of these side effects, [14] [15] these results supporting the recommendation to treat it actively.

The development of metabolic acidosis depends on two factors, the excretory capacity of the kidneys and the endogenous or exogenous acid load. In chronic kidney disease, metabolic acidosis develops when the kidneys are unable to excrete the daily acid load of non-volatile acids is usually in the order of 50 to 100 mEq/d, which leads to a positive  $H^+$  balance and a low CO<sub>2</sub> concentration (Figure 1).

Acid loading with ammonium chloride (NH<sub>4</sub>Cl) for 4 days increases urinary ammonium (NH<sub>4</sub><sup>+</sup>) excretion in healthy individuals, maintaining serum total carbon dioxide (tCO<sub>2</sub>) in the normal range. In chronic kidney disease (CKD), ammonium excretion is not increased, leading to metabolic acidosis. Adapted from Welbourne *et al.* (J Clin Invest. 1972; 51(7):1852-1860).

To assess arterial gases a procedure named arterial puncture must be performed regularly, this procedure requires experience and produces limitations for the patient, since it can be painful [16] and can cause complications such as arterial injury, thrombosis with distal ischemia, hemorrhage, aneurysm formation, median nerve damage, and rarely, reflex sympathetic dystrophy [17] [18].

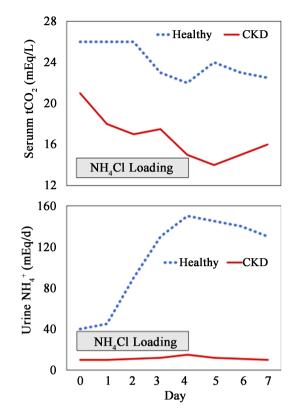


Figure 1. Urinary ammonium excretion in healthy subjects vs patients whit renal disease.

The objective of this study is to determine if the bicarbonate taken from venous gases does not differ from arterial bicarbonate in patients with chronic kidney disease, which can lead to reduce the risk of complications that arterial puncture can generate.

## 2. Materials and Methods

Venous and arterial gases, pH and bicarbonate determinations were analyzed in a patient with chronic kidney disease. These samples were taken between January 2022 and January 2023, in a Clinic in the city of Ibague/Colombia in patients using a renal unit. The samples were obtained from the radial artery, the modified Allen maneuver was performed with the objective of knowing if the radial and ulnar arteries were permeable and the puncture was performed prior to disinfection of the anatomical site.

All the samples and biochemical analyzes were extracted and carried out in the same central laboratory by conventional methods and were processed minutes after extraction, the samples were obtained with pre-heparinized syringes, at the end of the procedure the syringe was withdrawn and the puncture site was compressed with clean gauze for approximately 2 minutes, when extracting the arterial blood sample, the syringe was shaken to achieve a homogeneous mixture and avoid the formation of clots.

The determination of serum bicarbonate was carried out in less than 15 minutes, from the venous or arterial extraction. The arterial gas analyzer used was a Gasometer model ABL flex 800, prior to introducing the sample into the receptacle it was confirmed that the syringe was free of bubbles.

Qualitative descriptive statistical analysis was calculated. Analysis was made through relative and absolute frequencies, the quantitative variables with arithmetic mean, standard deviation and 95% prediction intervals, venous bicarbonate vs. arterial bicarbonate, venous pH and arterial pH differences were made through X<sup>2</sup> and p value.

The demographic and clinical data were obtained from the medical records, the physical examination and the anamnesis. The patients were classified with chronic kidney disease according to (KDOQUI 2012) guidelines and the glomerular filtration rate was calculated using the abbreviated formula (CKD/ EPI).

Informed written consent was obtained in compliance with research standards for human research for all patients in accordance with the Helsinki Declaration.

Inclusion criteria: 1) Chronic kidney disease with filtration less than 30 ml/min; 2) Not taking alkali.

Exclusion criteria: 1) Anticoagulated; 2) Upper limb amputations.

## 3. Results

Regarding bicarbonate, our study had a mean difference (MD) for arterial and peripheral venous  $HCO_3$  of 0.6 with 95% limits of agreement. The total group with chronic kidney disease included a total of 71 patients, 73.2% male (52) and 26.8% female [19], with different stages, stage 3 with 5.6% (4), stage 4 60.6% (43), stage 5 33.8% (23), 66.2% were diabetic, 88.7% arterial hypertension, 15.5% of the patients presented hematoma and pain associated with arterial puncture as a complication (Table 1).

Mean venous bicarbonate 18.6 mEq/L with a standard deviation of 2.3, arterial bicarbonate an average of 19.2 mEq/L, with a standard deviation 2.1 with a P value of 0.46, the venous pH with a mean of 7.37 with a standard deviation of 0.48 and a mean arterial Ph of 7.38 with a standard deviation of 0.048 with a P value 0.01 (Table 2).

In the present study, there was also demonstrated that there is a significative bivariable correlation between arterial and venous gases (Table 3).

The results of this study show that there were no statistically significant differences between venous and arterial bicarbonate values and also venous sampling for blood gas analysis were less painful for patients and had fewer complications.

Previous studies have shown an arteriovenous mean difference for bicarbonate ranging from 1.88 to 0.52 [19]. Our results suggest venous bicarbonate values may be an acceptable substitute for arterial measurement in the patient with chronic kidney disease (Figure 2).

There is a positive linear correlation between the variable of venous bicarbonate and arterial bicarbonate. This is shown by a straight regression line with an upward slope  $R^2$  is greater than 0.80 ( $R^2$  0.98). Reduced glomerular filtration rate is the most important risk factor for metabolic acidosis (**Table 4**), particularly when the GFR falls to <40 mL/min/1.73m<sup>2</sup>.

**Table 1.** Sociodemographic characteristics (n = 71).

Variable	<b>Median (p25 - p75)</b> 71 (61 - 81)	
Age		
Sex N (%)		
• Female	19 (26.76)	
• Male	52 (73.24)	
Chronic Kidney Disease N (%)		
• Stage 3	4 (5.63)	
• Stage 4	43 (60.56)	
• Stage 5	24 (33.80)	
Diabetic N (%)		
• Yes	47 (66.20)	
• No	24 (33.80)	
Systemic Arterial Hypertension N (%)		
• Yes	63 (88.73)	
• No	8 (11.27)	
Bruise/Pain N (%)		
• Yes	11 (15.49)	
• No	60 (84.51)	
Arterial pH	7.39 (7.38 - 7.41)	
Venous pH	7.38 (7.37 - 7.40)	
Arterial Bicarbonate	19.2 (18.3 - 20.8)	
Venous Bicarbonate	18.6 (17.9 - 20.1)	

#### Table 2. Correlation between arterial and venous gases.

N		Mean	Std. Deviation	P Value
Arterial pH	71	7.3832	0.04831	0.01
Venous pH	71	7.3710	0.04894	0.01
Arterial HCO <sub>3</sub>	71	19.4958	2.18792	0.46
Venous HCO <sub>3</sub>	71	18.8845	2.33951	0.91

#### Table 3. Correlation of gasometry.

Parameter	Correlation	P Value
Arterial Bicarbonate/Venous Bicarbonate	0.98	<0.001
Arterial pH/Venous pH	0.99	<0.001

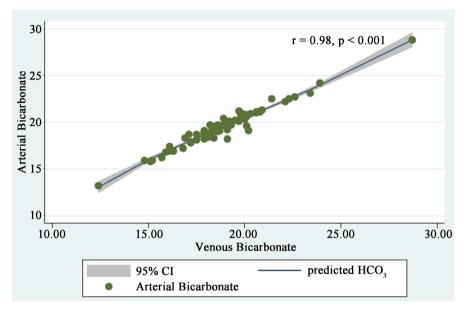


Figure 2. Graphic correlation between arterial bicarbonate and venous bicarbonate in CKD.

Table 4. Risk factors for metabolic acidosis in chronic kidney disease.

Reduced GFR Hyperkalemia Reduced Urinary Acid Excretion Albuminuria Smoking Anemia Higher Serum Albumin Concentration Nonuse of a Diuretic

Angiotensin Converting Enzyme Inhibitor/Angiotensin Receptor Blocker Use

For example, those with stage 4 CKD are 7 times more likely and those with stage 3 CKD are 2 times more likely to have metabolic acidosis than those with stage 2 CKD [20] [21] (**Figure 3**).

# 4. Discussion

Evidence-based medicine currently promotes interpreting data to improve decision-making and conduct in patients. In chronic kidney disease patients, it can economically benefit health systems in order to reduce the number of studies requested in this high-cost pathology in our country, a phenomenon that is shared with different populations worldwide who do not have the human, technological and economic resources available, being this item a limitation for this study.

Chronic renal failure is a disease with a high cost worldwide and the distributed

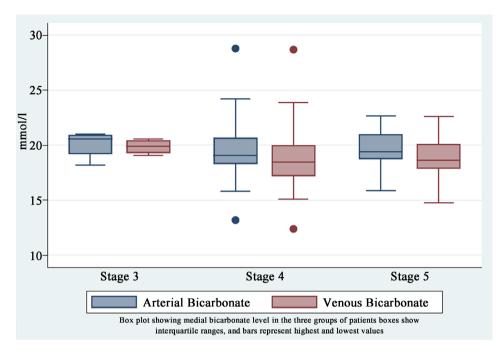


Figure 3. Value of bicarbonates in chronic kidney disease.

public spending for management is too high for both pre-dialysis and dialysis patients, since a large number of laboratories are required periodically to adequately interpret these patients, situation that may not be the most appropriate from the cost-effective point of view for the public health of each country.

In the case of the internal environment of patients with chronic renal failure, the frequency of presentation of acid-base disorders secondary to the progression of their underlying pathology, leads to a continuous evaluation of the internal environment, and sometimes even more frequently when there are other secondary factors that can alter it, such as the use of nephrotoxic drugs, acute conditions that precipitate renal failure such as infections, metabolic decompensation, among others.

Bicarbonate concentration is a widely used measure to assess the acid-base status of patients and can be measured directly or derived from Henderson-Hasselbalch equation. Bicarbonate ions constitute 95% of total plasma carbon dioxide [22] therefore, they have been used interchangeably.

Bone buffering is an important response to excess acid, either in the setting of overt metabolic acidosis or high dietary acid intake. Bone buffering leads to hypercalciuria, negative calcium balance, and loss of bone mineral content. In vivo studies demonstrated that extracellular acidification increases osteoclast activity and inhibits osteoblast activity. These effects contribute to the reduction of bone mineral density in patients with and without kidney disease [23] [24].

Results from large cohort studies have found that metabolic acidosis is also associated with increased all-cause mortality in CKD; it is also associated with malnutrition, inflammation, and oxidative stress [25] [26].

Dietary strategies should be considered in the management of metabolic aci-

dosis in CKD. This may include a combined approach to reduce acid-producing foods and beverages and increase base-producing ones. In addition to providing alkali, the potassium, fiber, and other nutrients in fruits and vegetables may be beneficial for CKD. Serum potassium should be <4.5 mEq/L if fruits and vegetables are recommended and should be closely monitored. Reducing protein in the diet also increases serum CO<sub>2</sub> concentration and can be incorporated into dietary recommendations [27] [28] [29].

Metabolic acidosis is a common complication of CKD and is associated with a number of clinically important adverse outcomes. These include increased risks of CKD progression, mortality, and impaired musculoskeletal health [30].

Currently there is little evidence about the correlation between the use of venous or arterial gases for monitoring patients with chronic renal failure since the medical literature has focused on patients in intensive care units and data from those studies are extrapolated towards the renal population. This correlation is important due to the possible complications that arterial puncture brings to obtain a sample for blood gases, which are less for venous extraction. Also, the cost-effective extraction of arterial samples is much higher and requires trained personnel, so the use of venous blood can represent a reduction in expenses in patients with advanced chronic renal failure.

The human resource that performs the extraction of arterial blood must have suitable training that improves the effectiveness indices in sampling with the aim of reducing pain and complications from multiple punctures, such as pseudoaneurysms, damage to the vascular bed, neurological damage, among others. On the contrary, venous punctures require less complexity in the extraction technique and the supplies used in some cases may be of less value.

The aim of this study was to investigate the correlation between venous bicarbonate and arterial bicarbonate samples in a patient population of patients with chronic kidney disease of diverse etiologies, finding that venous bicarbonate levels can be correlated with their arterial equivalents.

## **5.** Conclusions

Venous gas sampling becomes a valuable, simple, low-risk, and minimalcomplication tool for the diagnosis of metabolic disorders or acid-base status in patients with chronic kidney disease, and could replace arterial blood gases in this age group in the evaluation of serum bicarbonate levels.

Larger-scale studies, with a larger population in subgroups with specific pathologies, are needed to determine the usefulness of monitoring patients and carrying out interventions based on these results.

There are no interests or disputes of any investigators and there was no fund support in this article.

## **Conflicts of Interest**

The authors declare no conflicts of interest regarding the publication of this paper.

## References

- Goraya, N., Simoni, J., Sager, L.N., Pruszynski, J. and Wesson, D.E. (2018) Acid Retention in Chronic Kidney Disease Is Inversely Related to GFR. *American Journal of Physiology-Renal Physiology*, **314**, F985-F991. https://doi.org/10.1152/ajprenal.00463.2017
- Kraut, J.A. and Madias, N.E. (2016) Metabolic Acidosis of CKD: An Update. American Journal of Kidney Diseases, 67, 307-317. https://doi.org/10.1053/j.aikd.2015.08.028
- [3] Moranne, O., Froissart, M., Rossert, J., Gauci, C., Boffa, J.J., Haymann, J.P., *et al.* (2009) NephroTest Study Group Timing of Onset of CKD-Related Metabolic Complications. *Journal of the American Society of Nephrology*, **20**, 164-171. <u>https://doi.org/10.1681/ASN.2008020159</u>
- [4] Raphael, K.L. (2018) Metabolic Acidosis and Subclinical Metabolic Acidosis in CKD. *Journal of the American Society of Nephrology*, 29, 376-382. <u>https://doi.org/10.1681/ASN.2017040422</u>
- [5] Goraya, N., Simoni, J., Sager, L.N., Madias, N.E. and Wesson, D.E. (2019) Urine Citrate Excretion as a Marker of Acid Retention in Patients with Chronic Kidney Disease without Overt Metabolic Acidosis. *Kidney International*, 95, 1190-1196. https://doi.org/10.1016/j.kint.2018.11.033
- [6] Kalantar-Zadeh, K., Mehrotra, R., Fouque, D. and Kopple, J.D. (2004) Metabolic Acidosis and Malnutrition-Inflammation Complex Syndrome in Chronic Renal Failure. *Seminars in Dialysis*, 17, 455-465. <u>https://doi.org/10.1111/j.0894-0959.2004.17606.x</u>
- [7] Eustace, J.A., Astor, B., Muntner, P.M., Ikizler, T.A. and Coresh, J. (2004) Prevalence of Acidosis and Inflammation and Their Association with Low Serum Albumin in Chronic Kidney Disease. *Kidney International*, 65, 1031-1040. <u>https://doi.org/10.1111/j.1523-1755.2004.00481.x</u>
- [8] Mak, R.H.K. (1998) Effect of Metabolic Acidosis on Insulin Action and Secretion in Uremia. *Kidney International*, 54, 603-607. https://doi.org/10.1046/j.1523-1755.1998.00023.x
- [9] Esche, J., Shi, L., Sánchez-Guijo, A., Hartmann, M.F., Wudy, S.A. and Remer, T. (2016) Higher Diet-Dependent Renal Acid Load Associates with Higher Glucocorticoid Secretion and Potentially Bioactive Free Glucocorticoids in Healthy Children. *Kidney International*, **90**, 325-333. <u>https://doi.org/10.1016/j.kint.2016.02.033</u>
- [10] Dobre, M., Yang, W., Chen, J., Drawz, P., Hamm, L.L., Horwitz, E., et al. (2013) Association of Serum Bicarbonate with Risk of Renal and Cardiovascular Outcomes in CKD: A Report from the Chronic Renal Insufficiency Cohort (CRIC) Study. American Journal of Kidney Diseases, 62, 670-678. https://doi.org/10.1053/j.aikd.2013.01.017
- [11] Shah, S.N., Abramowitz, M., Hostetter, T.H. and Melamed, M.L. (2009) Serum Bicarbonate Levels and the Progression of kidney Disease: A Cohort Study. *American Journal of Kidney Diseases*, 54, 270-277. <u>https://doi.org/10.1053/j.ajkd.2009.02.014</u>
- [12] Raphael, K.L., Zhang, Y., Wei, G., Greene, T., Cheung, A.K. and Beddhu, S. (2013) Serum Bicarbonate and Mortality in Adults in NHANES III. *Nephrology Dialysis Transplantation*, 28, 1207-1213. <u>https://doi.org/10.1093/ndt/gfs609</u>
- [13] Navaneethan, S.D., Schold, J.D., Arrigain, S., Jolly, S.E., Wehbe, E., Raina, R., *et al.* (2011) Serum Bicarbonate and Mortality in Stage 3 and Stage 4 Chronic Kidney Disease. *Clinical Journal of the American Society of Nephrology*, 6, 2395-2402. https://doi.org/10.2215/CJN.03730411

- [14] Kraut, J.A. and Madias, N.E. (2017) Adverse Effects of the Metabolic Acidosis of Chronic Kidney Disease. Advances in Chronic Kidney Disease, 24, 289-297. <u>https://doi.org/10.1053/j.ackd.2017.06.005</u>
- [15] Dubey, A.K., Sahoo, J., Vairappan, B., Haridasan, S., Parameswaran, S. and Priyamvada, P.S. (2018) Correction of Metabolic Acidosis Improves Muscle Mass and Renal Function in Chronic Kidney Disease Stages 3 and 4: A Randomized Controlled Trial. *Nephrology Dialysis Transplantation*, **35**, 121-129. https://doi.org/10.1093/ndt/gfv214
- Giner, J., Casan, P., Belda, J., Gonzalez, M., Miralda, R.M. and Sanchis, J. (1996)
   Pain during Arterial Puncture. *Chest*, **110**, 1443-1445. https://doi.org/10.1378/chest.110.6.1443
- [17] Malatesha, G., Singh, N., Bharija, A., Rehani, B. and Goel, A. (2007) Comparison of Arterial and Venous pH, Bicarbonate, pCO<sub>2</sub> and pO<sub>2</sub> in Initial Emergency Department Assessment. *Emergency Medicine Journal*, 24, 569-571. https://doi.org/10.1136/emj.2007.046979
- [18] Criscuolo, C., Nepper, G. and Buchalter, S. (1995) Reflex Sympathetic Dystrophy Following Arterial Blood Gas Sampling in the Intensive Care Setting. *Chest*, **108**, 578-580. <u>https://doi.org/10.1378/chest.108.2.578</u>
- [19] Brandenburg, M.A. and Dire, D.J. (1998) Comparison of Arterial and Venous Blood Gas Values in the Initial Emergency Department Evaluation of Patients with Diabetic Ketoacidosis. *Annals of Emergency Medicine*, **31**, 459-465. <u>https://doi.org/10.1016/S0196-0644(98)70254-9</u>
- [20] Raphael, K.L., Carroll, D.J., Murray, J., Greene, T. and Beddhu, S. (2017) Urine Ammonium Predicts Clinical Outcomes in Hypertensive Kidney Disease. *Journal of the American Society of Nephrology*, 28, 2483-2490. https://doi.org/10.1681/ASN.2016101151
- [21] Raphael, K.L., Zhang, Y., Ying, J. and Greene, T. (2014) Prevalence of and Risk Factors for Reduced Serum Bicarbonate in Chronic Kidney Disease. *Nephrology* (*Carlton*), **19**, 648-654. <u>https://doi.org/10.1111/nep.12315</u>
- [22] Meza García, M. (2011) Acid-Base Disturbances in Critically Ill Patients. Acta Medica Peruana, 28, 46-55.
- [23] Krieger, N.S., Frick, K.K. and Bushinsky, D.A. (2004) Mechanism of Acid-Induced Bone Resorption. *Current Opinion in Nephrology and Hypertension*, 13, 423-436. <u>https://doi.org/10.1097/01.mnh.0000133975.32559.6b</u>
- [24] Reaich, D., Price, S.R., England, B.K. and Mitch, W.E. (1995) Mechanisms Causing Muscle Loss in Chronic Renal Failure. *American Journal of Kidney Diseases*, 26, 242-247. <u>https://doi.org/10.1016/0272-6386(95)90179-5</u>
- [25] Dobre, M., Yang, W., Pan, Q., et al. (2015) Persistent High Serum Bicarbonate and the Risk of Heart Failure in Patients with Chronic Kidney Disease (CKD): A Report from the Chronic Renal Insufficiency Cohort (CRIC) Study. *Journal of the American Heart Association*, 4, e001599. https://doi.org/10.1161/JAHA.114.001599
- [26] Kovesdy, C.P. anderson, J.E. and Kalantar-Zadeh, K. (2009) Association of Serum Bicarbonate Levels with Mortality in Patients with Non-Dialysis-Dependent CKD. *Nephrology Dialysis Transplantation*, 24, 1232-1237. https://doi.org/10.1093/ndt/gfn633
- [27] Goraya, N., Simoni, J., Jo, C.H. and Wesson, D.E. (2013) A Comparison of Treating Metabolic Acidosis in CKD Stage 4 Hypertensive Kidney Disease with Fruits and Vegetables or Sodium Bicarbonate. *Clinical Journal of the American Society of Nephrology*, 8, 371-381. <u>https://doi.org/10.2215/CJN.02430312</u>

- [28] Goraya, N. and Wesson, D.E. (2017) Management of the Metabolic Acidosis of Chronic Kidney Disease. Advances in Chronic Kidney Disease, 24, 298-304. <u>https://doi.org/10.1053/j.ackd.2017.06.006</u>
- [29] Remer, T. and Manz, F. (1995) Potential Renal Acid Load of Foods and Its Influence on Urine pH. *Journal of the American Dietetic Association*, **95**, 791-797. <u>https://doi.org/10.1016/S0002-8223(95)00219-7</u>
- [30] Raphael, K., Wei, G., Baird, B., Greene, T. and Beddhu, S. (2011) Higher Serum Bicarbonate Levels within the Normal Range Are Associated with Better Survival and Renal Outcomes in African Americans. *Kidney International*, **79**, 356-362. <u>https://doi.org/10.1038/ki.2010.388</u>