## **Original Research Article**

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20163779

# Study of association of serum bicarbonate levels with mortality in chronic kidney disease

# Kumar S.1\*, Nikethan D.2

**Received:** 26 August 2016 **Revised:** 30 August 2016 **Accepted:** 27 September 2016

## \*Correspondence:

Dr. Kumar S.,

E-mail: kumarsrinivasan67@gmail.com

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

#### **ABSTRACT**

**Background:** Chronic kidney disease has been recognized as a major global public health problem. The approximate prevalence of CKD in India is 800 per million population. Metabolic acidosis is a feature of CKD due to the reduced capacity of the kidney to synthesise ammonia and excrete hydrogen ions. This may be corrected by oral bicarbonate supplementation or by increasing the bicarbonate concentration in the dialysate fluid during dialysis. Studies have shown that low serum bicarbonate is associated with progression of kidney disease and increased mortality. Due to the limited availability of studies done in Indian population this study was undertaken to assess the serum bicarbonate levels in different stages of CKD and its effect.

**Methods:** Prospective data of 100 patients with various stages of chronic kidney disease admitted and treated in vims hospital in department of medicine and nephrology between January 2014 to June 2015 were studied.

**Results:** out of 100 cases 71 were male and 29 were female. Highest numbers of cases were found in the age group of 51 to 60 years followed by 41 to 50yrs. Most common cause of chronic kidney disease in our study group were diabetes, hypertension, nephrotic syndrome PCKD. Most patients were in stage 4 followed by stage 2, and Many patients had low serum bicarbonate level and only 07 patients had high serum bicarbonate level who were in stage 3 and stage 4. Of the 21 mortality 14 patients had low serum bicarbonate level (10-14 meq/l) and 07 patients had high serum bicarbonate level (mean value 25 meq/l). More death were noticed in the stage 5 followed stage 4 and stage 3 in 6th decade. Out of 100 cases, 68 cases were on dialysis and 32 cases were not on dialysis. Hence present study determines the association of serum bicarbonate levels as a risk factor for mortality in chronic kidney disease.

**Conclusions:** low serum bicarbonate levels are associated with high mortality in chronic kidney disease. Hence it is essential to optimise serum bicarbonates with oral supplementation.

**Keywords:** Chronic kidney disease, Metabolic acidosis, Serum bicarbonates

## INTRODUCTION

Chronic kidney disease has been recognized as a major global public health problem. The approximate prevalence of CKD in India is 800 per million population. Prevalence of CKD patients will continue to rise, reflecting the growing elderly population and

increasing number of patients with diabetes and hypertension. 1,2 Metabolic acidosis is a feature of CKD due to the reduced capacity of the kidney to synthesize ammonia and excrete hydrogen ions. This may be corrected by oral bicarbonate supplementation or by increasing the bicarbonate concentration in the dialysate fluid during dialysis. 3 Normally an approximate of 15,000

<sup>&</sup>lt;sup>1</sup>Associate Professor, Department of General Medicine, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India

<sup>&</sup>lt;sup>2</sup>Department of General Medicine, Vydehi Institute of Medical Sciences and Research Centre, Bangalore, Karnataka, India

mmol of carbon dioxide and 50 to 100 mleq of nonvolatile acid is produced each day. Acid-base balance is maintained by elimination of carbon dioxide by the lungs and excretion of nonvolatile acid by the kidneys which affects the plasma bicarbonate concentration.<sup>4</sup> The hydrogen ion concentration of the blood is determined by the ratio of the pCO<sub>2</sub> and plasma bicarbonate concentration. Metabolic acidosis can be due to one or more of the following pathophysiologic processes such as increased production of nonvolatile acids, increased loss of bicarbonate and decreased renal excretion of acid.<sup>5</sup> In chronic kidney disease metabolic acidosis occurs due to an impairment of ammonium excretion as a result of decreased functioning nephrons where the total ammonium excretion begins to fall when the glomerular filtration rate (GFR) is below 40 to 50 mL/min. The retained acid is buffered by bicarbonate in the extracellular fluid, by tissue buffers, and by bone. Usually the anion gap remains normal until late stages of CKD when it begins to widen due to the retention of anions such as phosphate, sulfate, urate, and hippurate. Renal replacement therapy improves metabolic acidosis due to the additional base load delivered in the dialysate.6,7

Studies have shown that low serum bicarbonate is associated with progression of kidney disease and increased mortality. Due to the limited availability of studies done in Indian population this study was undertaken to assess the serum bicarbonate levels in different stages of CKD and its effect.

## **METHODS**

Prospective data of 100 patients with various stages of chronic kidney disease admitted and treated in VIMS&RC hospital in department of Medicine and Nephrology between January 2014 to June 2015 were studied as per proforma and after obtaining their consent. The institutional ethics committee approved the study.

## Objective

Patients were observed for levels of serum bicarbonate at various stages of CKD and their association with mortality during the hospital stay.

### Inclusion criteria

All CKD patients aged > eighteen years stage-2-4 with or without dialysis.

## Exclusion criteria

Patients> eighteen, pregnant patients, patients with renal transplant, chronic heart disease and cancer were excluded from our study. Statistical analysis was done using SPSS 11.

#### **RESULTS**

Out of 100 cases 71 were male and 29 were female. Highest numbers of cases were found in the age group of 51 to 60 years, followed by 41 to 50 years. Most common cause of chronic kidney disease in our study group were diabetes, hypertension, nephrotic syndrome, Poly Cystic Kidney Disease. Most patients were in stage 4 followed by stage 2, and Many patients had low serum bicarbonate level and only 07 patients had high serum bicarbonate level who were in stage 3 and stage 4. Of the 21 mortality, 14 (66.64%) patients had low serum bicarbonate level (10-14meg/l) and 07 (33.36%) patients had high serum bicarbonate level (mean value 25meq/l). More death were noticed in the stage 5 followed stage 4 and stage 3 in the 6<sup>th</sup> decade. Out of 100 cases, 68 cases were on dialysis and 32 cases were not on dialysis. Hence present study determines the association of serum bicarbonate levels as a risk factor for mortality in chronic kidney disease. The following were the observation made from the study of 100 cases of CKD admitted under Nephrology and Medicine Department in Vydehi Institute of Medical Science and Research Centre, Bengaluru.

Table 1: Age distribution in the study group.

| Ago in woons | No of cases | % Percentage  |
|--------------|-------------|---------------|
| Age in years | No of cases | 76 rercentage |
| 20-30        | 06          | 6%            |
| 31-40        | 21          | 21%           |
| 41-50        | 23          | 23%           |
| 51-60        | 27          | 27%           |
| 61-70        | 17          | 17%           |
| 71-80        | 03          | 03%           |
| >80          | 03          | 03%           |

Total number of cases studied is 100; Mean age =58.9 years, Age range = 20 to >80 years.

Table 2: Gender distribution in the study group.

| Sex    | No of Cases | Percentage |
|--------|-------------|------------|
| Male   | 71          | 71%        |
| Female | 29          | 29%        |

Table 3: Gender distribution across age group.

| Age      | Female | Percentage | Male | Percentage |
|----------|--------|------------|------|------------|
| (years)  |        |            |      |            |
| 20 to 30 | 02     | 6.8%       | 04   | 5.6%       |
| 31 to 40 | 08     | 27.5%      | 13   | 18.3%      |
| 41 to 50 | 08     | 27.5%      | 15   | 21.1%      |
| 51 to 60 | 05     | 17.2%      | 22   | 30.9%      |
| 61 to 70 | 05     | 17.2%      | 12   | 16.9%      |
| 71 to 80 | 01     | 3.44%      | 02   | 2.81%      |
| >80      | 0      | 0%         | 03   | 4.2%       |

Maximum incidence of CKD occurred in the age group of 51-60 years followed by in the age group of 41-50 years.

Majority of cases were about 71% seen in male patients, when compared to 29% seen in female patients.

The common causes in the present study were diabetes mellitus, hypertension, and nephrotic syndrome.

Table 4: Causes of chronic kidney disease in the study group.

| Diagnosis          | No of cases | Percentage |
|--------------------|-------------|------------|
| Diabetes           | 76          | 76%        |
| Hypertension       | 67          | 67%        |
| DM+HTN             | 52          | 52%        |
| Nephrotic syndrome | 08          | 08%        |
| Drug induced       | 01          | 01%        |
| PCKD               | 07          | 07%        |

Table 5: Stages of CKD in the study group.

| Stage of CKD | No of cases | Percentage |
|--------------|-------------|------------|
| Stage 2      | 26          | 26%        |
| Stage 3      | 19          | 19%        |
| Stage 4      | 31          | 31%        |
| Stage 5      | 24          | 24%        |

In our study majority of patients admitted are in stage 4 followed by stage 2.

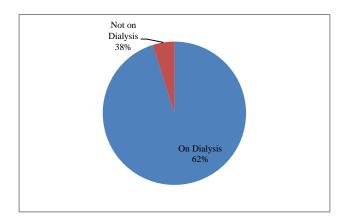


Figure 1: Patients on dialysis.

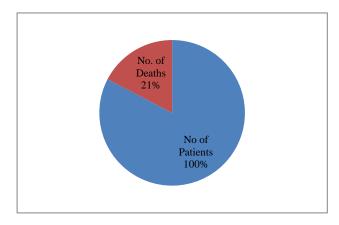


Figure 2: Mortality.

In present study majority of patients admitted are with in bicarbonate range of 10-14 meq/lt.

Table 6: Bicarbonate level in the present study.

| HCO3 level in meq/l | No. of cases | Percentage |
|---------------------|--------------|------------|
| 21 -25              | 31           | 31%        |
| 15-20               | 31           | 31%        |
| 10-14               | 33           | 33%        |
| <10                 | 05           | 05%        |

Table 7: Mortality in relation to age.

| Age intervals in years | No. of death | Percentage |
|------------------------|--------------|------------|
| 20-30                  | 0            | 0%         |
| 31-40                  | 01           | 4.7%       |
| 41-50                  | 01           | 4.7%       |
| 51-60                  | 05           | 23.8%      |
| 61-70                  | 10           | 47.6%      |
| 71-80                  | 01           | 4.7%       |
| >80 Yrs                | 03           | 14.2%      |

Maximum number of deaths occurred in 6<sup>th</sup> decade.

Table 8: Relationship between HCO<sub>3</sub> level and mortality.

| HCO <sub>3</sub> level | Mortality | Percentage |
|------------------------|-----------|------------|
| 21 to 25               | 05        | 23.8%      |
| 15 to 20               | 02        | 9.5%       |
| 10 to 14               | 10        | 47.6%      |
| <10 meq/l              | 04        | 19.04%     |

Maximum numbers of deaths were noticed in patients with bicarbonate range of 10-14 meg/lt.

Table 9: Relationship between mortality and stages of CKD.

| Stages of CKD | No of death | Percentage |
|---------------|-------------|------------|
| Stage 2       | 0           | 0%         |
| Stage 3       | 04          | 19.04%     |
| Stage 4       | 04          | 19.04%     |
| Stage 5       | 13          | 61.9%      |

Maximum numbers of deaths were noticed in patients with stage 5.

## **DISCUSSION**

Low serum bicarbonate levels are associated with high mortality in chronic kidney disease. The optimal management of metabolic acidosis in chronic kidney disease patients including the monitoring or administration of bicarbonate has not been established yet. However various guidelines have recommended serum bicarbonate levels to be maintained at or above twenty two mleq/ltr bicarbonate replacement therapy in

chronic kidney disease is possible and easy to use making it a good option. 4,5,16 Hence it is essential to optimize serum bicarbonates with oral supplementation. According to present study it was noted that the incidence of Chronic Kidney Disease varied from minimum age of 20 years to maximum age of 88 years (Table 1). In the present study, maximum cases were found in 6th decade followed by 5<sup>th</sup> decade (Table 2). Seventy one were male. Patients in the age group of fifty one to sixty years and twenty nine female patients were in the age group of thirty one fifty years. Most common cause of Chronic Kidney Disease in our study includes diabetes followed by hypertension. Other causes were nephrotic syndrome and Poly Cystic Kidney Disease (Table 4). Most of the patient presented in our study group were stage 4 followed by stage 5 followed by stage 2 (Table 5). Sixty eight patients in our study underwent hemodialysis and the other thirty eight did not (Figure 7). According to our study, low serum bicarbonate levels were found in the stage 5 followed by stage 4, thirty eight patients had low serum bicarbonate (Table 6). Navaneethan et al., study stated that low serum bicarbonate level are associated with increased mortality among stage 3 patients. <sup>6,7,9</sup> In our study, there is increased mortality in stage 3 patients associated with low serum bicarbonate level. Same study concluded that high serum bicarbonate level are associated with increased mortality in the stage 3 and stage 4. In our study, there was increased mortality in stage 3 and stage 4 with high serum bicarbonate level (Table 8). Eliichiro Kanda et al, study stated that patient with the lowest quartile of serum bicarbonate level show a high risk of chronic kidney disease progression compared with patients with high serum bicarbonate levels. 10-15 In present study group, many patients were in stage 4 and stage 5 have low serum bicarbonate level. Many patients in the study group had low serum bicarbonate level and only 07 patients were having high serum bicarbonate level who were in stage 3 and stage 4. Out of 100 cases, 21 patients expired (Figure 2). In this 14 patients had low serum bicarbonate level (10-14meq/l) and 07 patients had high serum bicarbonate level(mean value 25 meq/l). More death were noticed in the stage 5 followed stage 4 and stage 3 (Table 9) More death noted on 6th decade (Figure 7). Hence present study determines the association of serum bicarbonate level with mortality in chronic kidney disease.

## **CONCLUSION**

Low serum bicarbonate levels are associated with high mortality in chronic kidney disease. Bicarbonate replacement therapy in chronic kidney disease is cost effective and easy to administer. Hence it can be used as a modality to optimize serum bicarbonates with iv/oral supplementation.

Funding: No funding sources Conflict of interest: None declared

Ethical approval: The study was approved by the

Institutional Ethics Committee

#### REFERENCES

- 1. Kanda E, Ai M, Yoshida M, Kuriyama R, Shiigai T. High serum bicarbonate level within the normal range prevents the progression of CKD in elderly CKD patients. BMC Nephrology. 2013;14:4.
- Goraya N, Simoni J, Jo CH, 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.
- 3. Yaqoob MM. Treatment of acidosis in CKD. Clin J Am Soc Nephrol. 2013;8:342.
- 4. Saikumar JH, Kovesdy CP. Bicarbonate therapy in end-stage renal disease: current practice trends and implications. Semin Dial. 2015;28:370.
- 5. Kovesdy CP. Metabolic acidosis and kidney disease: does bicarbonate therapy slow the progression of CKD? Nephrol Dial Transplant. 2012;27:3056.
- 6. Raphael KL, Zhang Y, Wei G. Serum bicarbonate and mortality in adults in NHANES III. Nephrol Dial Transplant. 2013;28:1207.
- 7. Navaneethan SD, Schold JE, Arrigain S. Serum bicarbonate and mortality in stage 3 and stage 4 chronic kidney disease. Clin J Am Soc Nephrol. 2011;6(10):2395-402.
- Dobre M1, Yang W, Chen J, Drawz P, Hamm LL, Horwitz E, et al. Association of serum bicarbonate with risk of renal and cardiovascular outcomes in CKD: a report from the Chronic Renal Insufficiency Cohort (CRIC) study. Am J Kidney Dis. 2013;62;670.
- 9. Menon V, Tighiouart H, Vaughn NS. Serum bicarbonate and long-term outcomes in CKD. Am J Kidney Dis. 2010;56:907.
- 10. Kanda E, Ai M, Kuriyama R, et al. Dietary acid intake and kidney disease progression in the elderly. Am J Nephrol 2014; 39:145.
- 11. Rebholz CM, Coresh J, Grams ME. Dietary acid load and incident chronic kidney disease: results from the ARIC study. Am J Nephrol 2015; 42:427.
- 12. Vallet M, Metzger M, Haymann JP. Urinary ammonia and long-term outcomes in chronic kidney disease. Kidney Int. 2015;88:137.
- Banerjee T, Crews DC, Wesson DE, Tilea AM, Saran R, Ríos-Burrows N, et al. High Dietary Acid Load Predicts ESRD among Adults with CKD. J Am Soc Nephrol. 2015;26:1693.
- 14. Driver TH, Shlipak MG, Katz R. Low serum bicarbonate and kidney function decline: the multiethnic study of atherosclerosis (MESA). Am J Kidney Dis. 2014;64:534.
- 15. Goldenstein L, Driver TH, Fried LF. Serum bicarbonate concentrations and kidney disease progression in community-living elders: the health, aging, and body composition (health ABC) study. Am J Kidney Dis. 2014;64:542

- 16. KDIGO. Management of progression and complications of CKD. Kidney Int Suppl. 2013;3:73.
- 17. Abramowitz MK, Melamed ML, Bauer C. Effects of oral sodium bicarbonate in patients with CKD. Clin J Am Soc Nephrol. 2013;8:714.

**Cite this article as:** Kumar S, Nikethan D. Study of association of serum bicarbonate levels with mortality in chronic kidney disease. Int J Res Med Sci 2016;4:4852-6.