Original Article

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Association of Bicarbonate level in Stage 3 and Stage 4 of Chronic Kidney Disease (CKD) Patients

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ABSTRACT

Background and Objectives: Chronic kidney disease (CKD) disrupts acid-base balance, leading to metabolic acidosis. The impaired kidneys cannot remove acid effectively or reabsorb enough bicarbonate, resulting in low bicarbonate levels and metabolic acidosis. To evaluate the association of bicarbonate in patients among chronic kidney disease (CKD) stage 3 and stage 4. To evaluate the metabolic acidosis in the progression of chronic kidney disease (CKD).

METHODOLOGY: A retrospective study was conducted in the Department of Nephrology, Sheikh Zayed Hospital, Lahore, Punjab. The study was conducted during the 3 months from May to July, 2023. The study included a total of 150 patients diagnosed with chronic kidney illness. Among these individuals, 74 were found to have stage 3 CKD, while the remaining 76 were evaluated to have stage 4 CKD. Cobas C-311 and Microlab 300 were used to analyze bicarbonates level. A self-designed Performa was used to collect the patient data. Data were entered and analyzed by using excel and displayed by using Tables and Bar Charts.

RESULTS: In chronic kidney disease (CKD) stage 3, results indicated that 45% of male patients and 32% of female patients had normal serum bicarbonate levels ranging from 22 to 29 mEq/L, while the level was less than 22 mEq/L in 55% of males and 68% of females. According to the results from chronic kidney disease (CKD) stage 4, 15% of male and 14% of female patients had normal serum bicarbonate levels ranging from 22 to 29 mEq/L, and 85% of male and 86% of female patients had a serum bicarbonate level < 22 mEq/L.

CONCLUSION: In conclusion, individuals with CKD, especially those in late stages, frequently have metabolic acidosis, which is characterized by low blood bicarbonate levels. This condition has been associated with higher mortality rates and greater risk of kidney disease progression.

KEYWORDS: Chronic kidney disease (CKD), Nephrology, Metabolic acidosis, Bicarbonate.

INTRODUCTION

The kidneys, a pair of organs resembling beans, are positioned beneath the rib cage on both sides of the spine. To maintain body homeostasis, kidneys remove acid produced by cells and regulate the balance of water, salt, and minerals in the body(1). The kidneys have a crucial role in upholding the balance of various electrolytes (bicarbonates and phosphate ions) in the body, thereby contributing to the maintenance of overall body homeostasis(2). In mitochondrial energy production, pyruvate is oxidized into acetyl CoA and CO2 in the presence of pyruvate dehydrogenase. As CO2 is metabolized by carbonic anhydrase enzyme, it becomes carbonic acid. As carbonic acid dissociates into bicarbonate, it forms bicarbonate. As a labile molecule, bicarbonate increases pH causing alkalosis, and removing it causes acidosis(3). In human body bicarbonate play important role in pH buffering system (maintaining homeostasis). Bicarbonate is an anionic chemical compound consisting of a carbon atom bonded to three oxygen, along with a hydrogen atom

How to cite this: Sahar T, Bibi A, Ali A, Rasool F A, Hussain R. Awareness of Digital Eye Strain and Its Effects on the Ocular Health among Young Individuals, International Journal of Healthcare Profession. 2024; 1(2):3-7

Vol. 01, Issue 03, July-September, 2024

attached to one of those oxygen atoms(4).

When the kidneys are unable to effectively filter blood, they develop chronic kidney disease (CKD), which makes them work harder just to survive. It is the most prevalent, slowly progressive and irreversible condition of the kidneys which usually remains asymptomatic(5). Chronic kidney disease can cause different levels of illness as it indicates the abnormal kidney structure or function(6). The risk factors for developing chronic kidney disease may include age, gender, family history, hypertension, anemia or obesity(7). Common symptoms of chronic kidney disease are edema, pain, fatigue, nausea, restlessness and shortness of breath(8). Other than dialysis, chronic kidney disease can be controlled at early stage by controlling other health issues like diabetes and blood pressure(9).

End-stage renal disease (ESRD) refers to renal failure treated by kidney transplant or dialysis. Chronic kidney disease complications include metabolic acidosis. In dialysis patients, metabolic acidosis manifests as low serum bicarbonate levels and is associated with high death ratio(10). According to the National Kidney Foundation, kidney disease is classified into five stages based on the severity of the condition. In the case of CKD, these stages are defined as follows: Stage 1, normal or high GFR (GFR > 90 mL/min); Stage 2, mild CKD (GFR = 60-89 mL/min); Stage 3A, moderate CKD (GFR = 45-59 mL/min); Stage 3B, moderate CKD (GFR = 30-44 mL/min); Stage 4, severe CKD (GFR = 15-29 mL/min); and Stage 5 is end stage of CKD(11). In developing countries, the prevalence of chronic kidney disease is 11%-13%(12). Epidemiologic investigations have revealed a weak link of serum bicarbonate with poor renal outcomes, and death. The kidneys continuously lose the ability to release hydrogen ions and orchestrate smelling salts as renal function declines. Consequently, patients with lower eGFRs are more prone to having reduced bicarbonate levels, with approximately 19% of individuals in CKD stages 4 and 5 exhibiting serum bicarbonate levels below 22 mmol/L(13).

Bicarbonate levels in the blood are significant prognostic markers for all patients, even those with typical qualities. Regardless of kidney failure movement and mortality, a low serum bicarbonate level raises the chance of developing diabetes. The GFR is the principal factor impacting serum bicarbonate levels, however there are additionally different elements that assume a significant part. Stage 3 and 4 CKD patients are likely to have low serum bicarbonate if they have diabetes, smoke, have low hemoglobin, or have low serum egg white levels(14).

METHODOLOGY

It was a retrospective study. Data was collected from the Department of Nephrology, Sheikh Zayed Hospital, Lahore, Punjab. Total of 150 samples of chronic kidney disease patients of stage 3 and stage 4 was collected. (CKD) Chronic kidney disease patients of stage 3 and stage 4 were included.

A Performa were used to collect patient data of chronic kidney disease patients. Aseptic phlebotomy procedures were used to obtain intravenous blood samples from chronic kidney disease patients. The methods and instruments we used for analysis were; Microlab 300 and Cobas C 311. Both Cobas C 311 and Microlab 300 works on the principles of spectrophotometry, particularly the Beer-Lambert Law. As stated by this law, the level of light absorbed by a sample corresponds directly to the concentration of the substance it contains. In addition to spectrophotometry, Cobas C 311 also follows the principles of potentiometry and ion selective electrode (ISE).

Data were entered and analyzed by using excel for statistical analysis. Tables and Bar charts were used to display the data.

RESULTS

We identified 150 patient diagnosed along with chronic kidney disease (CKD) stage 3 and stage 4 from the department of nephrology in Shaikh Zayed Hospital Lahore. There were 76 individuals with stage 4 CKD and 74 patients with stage 3 CKD. 34 individuals with stage 2 and 40 patients with stage 3 CKD were included. Similarly, stage 4 chronic kidney disease (CKD) includes the 34 male and 42 female patients.

Table 1 Gender based distribution of CKD stage 3 and stage 4

Gender	CKD Stage 3	CKD Stage 4	Total Number of patient
Male	40	34	74
Female	34	42	76
Total	74	76	150

The data indicates that among the patients with chronic renal disease stage 3, there were 40 male and 34 female patients. Among the male patients, 45% (n=18) had normal serum bicarbonate levels, while 55% (n=22) had low serum bicarbonate levels. Comparable to male patients, 68% (n=23) of female patients had low serum bicarbonate levels, whereas 32% (n=11) of female patients had normal serum bicarbonate levels.

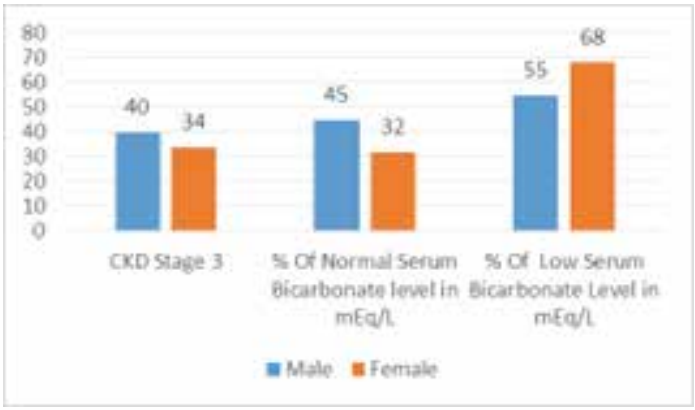

Figure 1 Gender based association of serum bicarbonate in CKD stage 3

Results demonstrates that there were 40 male and 34 female individuals with stage 3 chronic renal disease; of them, 22 male with an average age of 55 and 23 female with an average age of 53 were diagnosed with metabolic acidosis.

Table 2 Gender based progression of metabolic acidosis in CKD stage 3

Gender	CKD Stage 3	Average of age in year	Metabolic Acidosis
Male	40	55	22
Female	34	53	23

Patients with stage 4 chronic renal disease included 34 men and 42 female, with 15% (n=5) of the male being diagnosed with normal blood bicarbonate level and 85% (n=29) of the male being diagnosed with low level of serum bicarbonate. Similar to the male patient, 86% (n=36) of the female patient had low serum bicarbonate levels, while 14% (n=6) of the female patient had normal serum bicarbonate levels.

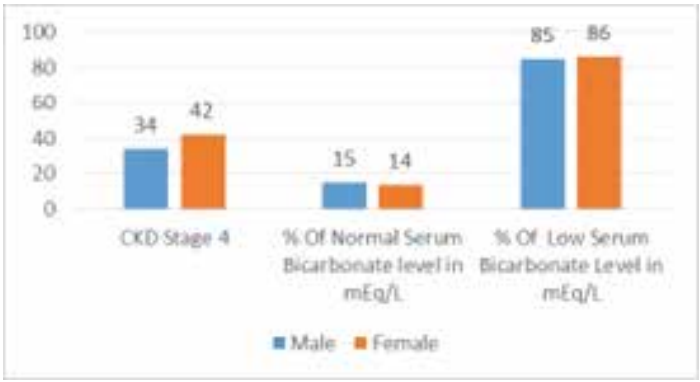

Figure No.2 Gender based association of serum bicarbonate in CKD stage 4

There were 34 male and 42 female patients with stage 4 chronic kidney disease, out of whom 29 patients who are male and, on average, 52 were diagnosed with metabolic acidosis and 36 average age of 51 for female patients.

Table No.3 Gender based progression of metabolic acidosis in CKD stage 4

Gender	Count of patient	Average of age in year	Metabolic Acidosis	Non-Metabolic Acidosis
Male	34	52	29	5
Female	42	51	36	6

Comparing the association between the amount of serum bicarbonate and the advancement of metabolic acidosis in stages 3 and 4 of chronic kidney disease (CKD), 40 male and 34 female patients along with stage 3 chronic renal disease were included. The average level of serum bicarbonate in males and females was 22 mEq/L, and 55% and 68%, respectively, of both genders were found to be progressing into metabolic acidosis.

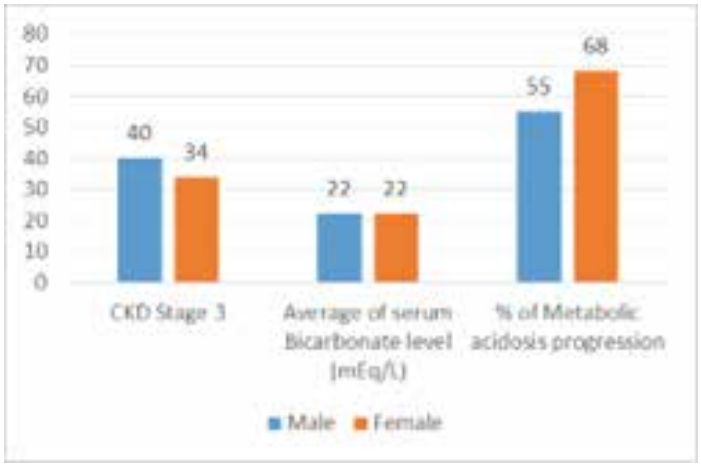

Figure 3 Gender Base Average of Serum Bicarbonate Level and Metabolic Acidosis Progression in CKD Stage 3

Chronic kidney disease stage 4 were includes the 34 male and 42 female patients. The average of serum bicarbonate level in male and female were remain 19 mEq/L and 18 mEq/L accordingly and the progression of metabolic acidosis in male and female were found 85% and 86% respectively.

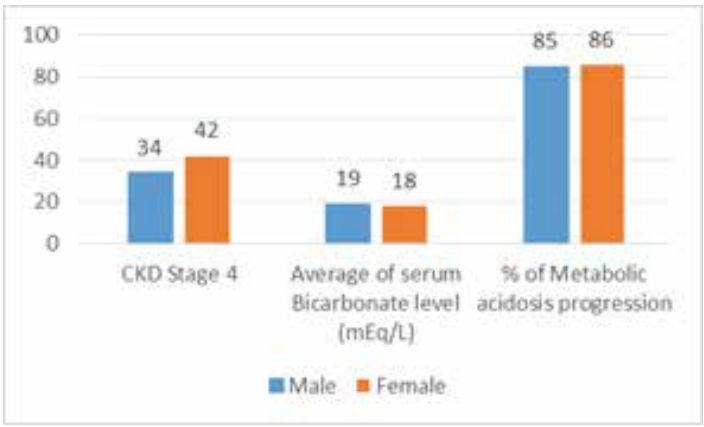

Figure No.4 Gender Base Average of Serum Bicarbonate Level and Metabolic Acidosis Progression in CKD Stage 4

DISCUSSION

Kidneys maintain the body's homeostasis by removing acid and regulating water, salt, and mineral levels. They are responsible for maintaining the levels of various substances in the body. Patients among chronic kidney disease (CKD) mostly experience metabolic acidosis, due to this condition, the blood level of bicarbonate is low. The mortality rate among patients receiving dialysis has been associated with this condition.

Hoorn, E wout J et al. research has been done on how sodium bicarbonate affects CKD patients' systolic blood pressure. The study included 60 participants (SD 10), whose systolic blood pressure was 136 (SD 17) mm Hg, glomerular filtration rate (eGFR) was 38 (SD 10) milliliters/minute, and serum bicarbonate level was 22 (SD 4). A meta-analysis found that sodium bicarbonate supplementation had no significant effect on systolic blood pressure in individuals with CKD stages G1-5. In addition, sodium bicarbonate recipients did not significantly increase their use of antihypertensive medication or diuretics, while sodium bicarbonate recipients decreased their use of antihypertensive medication(15). Mirela Dobre MD, et al. studied the risk of heart failure in chronic kidney disease patients. 3586 patients were involved, out of them, the patients who have had higher bicarbonate levels develop heart failure(18).

Hyo Jin Kim studied the impact of metabolic acidosis on CKD development in Korean individuals. There were four groups of patients based on their serum bicarbonate levels: (With total carbon dioxide concentrations of 22 to 26, 26.1 to 29.9, and 30 mmol/l, respectively) Low and Lower Normal and Higher Normal, and High. An individual with metabolic acidosis has a serum bicarbonate level below 22 mmol/l. Renal events can be defined as either a twofold increase in serum creatinine levels, a diagnosis of end stage renal disease, a 50% decrease in glomerular filtration rate (GFR) from baseline values, or the occurrence of other significant changes in renal function. The findings demonstrated that, in comparison to the group with lower normal bicarbonate levels, the group with low bicarbonate levels exhibited a considerably quicker fall in (GFR). Furthermore, among Korean patients CKD who were not yet receiving dialysis, a higher incidence of kidney failure events and a fast decline in kidney function found both fervently connected with metabolic acidosis(19).

Michal L. Melamed et al. studied on the multicenter randomized, placebo-controlled, randomized trial of sodium bicarbonate in CKD Stages 3 and stage 4. They have concluded that in these patients, sodium bicarbonate therapy is beneficial. There were 149 patients included with CKD stages 3 and stage 4 at three centers in Cleveland, OH, and the Bronx, NY, between July 2011 and April 2016. The mean serum bicarbonate level and estimated glomerular filtration rate were both 24.0 x 2.2 mEq/L and 36.3 x 11.2 mL/min/1.73 m, respectively, furthermore did not differ among intervention also placebo groups. The intervention group had consistently higher mean serum bicarbonate levels than the placebo group throughout all stages of the follow-up (P 0.001). There were no significant differences found in these two groups in levels of glomerular filtration rate, blood pressure, or levels of muscle gene expression(20).

Our results are comparable to these researches as In chronic kidney disease (CKD) stage 3, results indicated that 45% of male patients and 32% of female patients had normal serum bicarbonate levels ranging from 22 to 29 mEq/L, while the level was less than 22 mEq/L in 55% of males and 68% of females. According to the results from chronic kidney disease (CKD) stage 4, 15% of male and 14% of female patients had normal serum bicarbonate levels ranging from 22 to 29 mEq/L, and 85% of male and 86% of female patients had a serum bicarbonate level < 22 mEq/L.

CONCLUSION

In conclusion, According to study, individuals with CKD, especially those in late stages, frequently have metabolic acidosis, which is characterized by low blood bicarbonate levels. This condition has been associated with higher mortality rates and greater risk of kidney disease progression. The risk of developing CKD generally increases with age. Older adults are more likely to have Diabetes and hypertension are two illnesses that are major contributors to CKD.

Sources of Support:
No funding was received for this article.

Data Availability:
All raw and processed data is available.

Disclaimer:
The views expressed in this manuscript are those of the authors and not those of the institutions they are affiliated with.

ACKNOWLEDGEMENT: None
CONFLICT OF INTEREST: None
GRANT SUPPORT AND FINANCIAL DISCLOSURE: None.

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Authors Contributions:

Taha Sahar and Alia Bibi: Substantial contributions to the conception and design of the work.

Asad Ali and M.Faiz Rasool: Design of the work and the acquisition. Drafting the work.

Rizwan Hussain: Final approval of the version to be published.

Submitted for publication: 03-07-2024
Accepted after revision: 08-08-2024