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Managing Metabolic Acidosis in Chronic Renal Diseases

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ABSTRACT

One of the most common side effects of chronic kidney disease is metabolic acidosis (CKD). It is associated with the development of CKD and various other functional disorders. Metabolic acidosis can be a common complication associated with progressive loss of kidney function. The form can be a metabolic acidosis with a non-anion gap or metabolic acidosis with a high or mixed anion gap. Reduced kidney ability to maintain acid-base homeostasis results in acid accumulation, causing various complications such as decreased nutritional status such as wasting muscle-hypoalbuminemia, inflammation, uremic bone disease and its association with increased mortality. In addition to the side effects associated with acid retention, metabolic acidosis can also cause kidney damage, possibly through stimulation of adaptive mechanisms aimed at maintaining acid-base homeostasis in the event of decreased renal function. chronic kidney disease (CKD), and therefore offers an effective, safe and affordable reno-protective strategy. This paper will discuss the physiology and pathophysiology of acid-base homeostasis in CKD, namely the mechanism of metabolic acidosis capable of impairing kidney function, and its relation to the benefits of alkaline therapy. based on clinical trials.

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1. INTRODUCTION

One of the most common side effects in people with chronic kidney disease (CKD) is metabolic acidosis [1]. As this disease has been associated with a number of negative consequences, including bone demineralization [2], insulin resistance [3], muscle protein proteolysis [4], functional limits in the elderly [5], and cognitive impairment [6,] nephrologists should not ignore it in the clinical setting. The prevalence of metabolic acidosis depends on the definition of the entity and its principles increased with worsening CKD stage. On serum bicarbonate concentration < 22 meq/L in CKD individuals, estimated to occur in 2.3% - 13% of individuals with stage 3 CKD, and 19%-37% in individuals with stage 4 CKD.

Metabolic acidosis is a condition in which there is too much acid in the body. This condition can occur due to the body producing too much acid or due to the kidneys not removing normal amounts of acid. Acidosis consisting of several types distinguished from the causes. Generally, the body's pH level is 7-7.4, which means that the human body has a neutral or slightly alkaline pH. In conditions of metabolic acidosis, too much acid in the body causes the body's pH to decrease below a value of 7 (7 is a neutral pH) and indicates that the body's pH is abnormal.

One of the early symptoms of impaired kidney function is metabolic acidosis. Significant studies have shown that reduced renal acid clearance associated with CKD causes metabolic acidosis, which in turn

negatively impacts bone mineral content and promotes skeletal muscle breakdown. Metabolic acidosis has recently been associated with death and the development of CKD in an observational study. Several small-scale investigations conducted over the last ten years, mostly in hypertensive CKD, have found that treating metabolic acidosis with alkaline medications protects Glomerolus Filtrasi Rate (GFR) [7-9].

It is important to note that mortality and cardiovascular outcomes are also associated with metabolic acidosis in CKD patients [7-9]. Basic research reveals that activation of endothelin-1, renin-angiotensin-aldosterone system, and alternative complement pathways all contribute to renal tissue injury induced by acid retention induced by loss of nephrons or dietary acid load [10-13]. In contrast, it has been found in several clinical cohort studies that lower serum bicarbonate levels are associated with more rapid development of CKD [14-18]. Alkali therapy does have a beneficial effect on the progression of CKD to renal failure on replacement therapy (KFRT), according to randomized controlled studies and accompanying meta-analyses [19-24].

Current recommendations state that alkaline treatment should be initiated when the serum bicarbonate level is 22 mEq/L [25,26]. However, the only basis for this suggestion is the serum bicarbonate level. In addition, anion gap acidosis may have an important role in the development of CKD, according to clinical trials using veverimer, the newest revolutionary technique for treating metabolic acidosis. Our aim was to examine the impact of metabolic acidosis on the development of CKD from the standpoint of blood pH and anion gap in this review[19].

In the extracellular fluid, the normal concentration of H+ is about one millionth of the concentrations of N+, K+, Cl, and HCO3. Small H+ ions, on the other hand, have a better affinity for small and negatively charged molecular components than larger cations such as Na+ or K+. Therefore, for normal cellular processes, less oscillations in H+ concentration are required [27].

In CKD patients, Kajimoto et al. [31] assessed lung conditions including interstitial pneumonia or chronic obstructive pulmonary disease, and they calculated compensatory respiratory capacity using data from venous blood gas measurements. They use a large amount of blood gas information to assess the compensatory ability of breathing. Using a mixed effects model, we plot the carbon dioxide pressure against the amount of bicarbonate and determine the slope of the regression line. The compensatory respiratory capacity and the amount of carbon dioxide pressure that can be reduced for each 1 mmol/L decrease in bicarbonate are both represented by the slope of the regression line in this context[17-20].

Decreased kidney function causes increased acid retention, thus leading to deleterious consequences, such as protein catabolism and protein-energy loss, worsening of uremic bone disease and its associations with decreased functional capacity and with increased mortality in patients with end-stage renal disease (ESRD). Acid load of the daily diet can also lead to bad results, even in its absence real acidosis[20].

Apart from these complications, metabolic acidosis is also directly related with kidney damage and increased CKD damage, possibly through mechanisms associated with adaptive responses that aim to enhance acid excretion in the progressive decline of renal function. Based on the study that linking metabolic acidosis with the development of CKD, it appears that. Alkaline supplementation can repair kidney damage and can slow it down Progressive CKD. These studies have shown the possibility that giving sodium bicarbonate (or its alternatives) or other oral alkaline therapy may be used as a reno-protective strategy for various stages of non-dialytic CKD, and is expected can slow the progression of kidney disease.

2. CAUSES OF METABOLIC ACIDOSIS

The cause of metabolic acidosis is due to excess acid production or the result of the kidneys not being able to remove acid from the body. This condition is caused by several reasons that can directly affect the production of acid in the body or conditions that affect kidney health. In order to find out the various causes of metabolic acidosis such as diabetic acidosis Diabetic acidosis is a condition when acidic substances known as ketone bodies accumulate in the body. This condition most often occurs in people with uncontrolled type 1 diabetes. This condition may also be referred to as diabetic ketoacidosis.

In another hand causes of metabolic acidosis as Hyperchloremic acidosis Hyperchloremic acidosis is caused by the loss of sodium bicarbonate in the body in too large amounts. Sodium bicarbonate is a substance that is alkaline. This condition can occur as a result of severe diarrhoea. Lactic acidosis Lactic acidosis is acidosis due to the accumulation of lactic acid in the body. The causes of this type of acidosis range from intense exercise, alcohol consumption, liver failure, the effects of drugs such as salicylates, seizures, prolonged lack of oxygen (due to shock, heart failure, severe anemia), to cancer. Renal tubular acidosis Renal tubular acidosis is acidosis caused by kidney disease. There is distal renal tubular acidosis (renal tubular acidosis type 1) and proximal renal tubular acidosis.

Apart from the causes above, other causes of metabolic acidosis are poisoning with several types of drugs such as aspirin, ethylene glycol, or methanol and dehydration. Both of these conditions are conditions that can affect the kidneys. There are also several factors that can increase a person's risk of developing metabolic acidosis. Factors that put a person at high risk include: A diet high in fat and low in carbohydrates (potentially causing ketoacidosis) Kidney failure Obesity Dehydration Aspirin or methanol poisoning Diabetes Symptoms of Metabolic Acidosis Symptoms of metabolic acidosis may vary from person to person.

3. CLINICAL FEATURES OF METABOLIC ACIDOSIS

The severity of symptoms can also differ depending on the severity of the metabolic acidosis experienced and its triggers. However, some of the most common signs and symptoms of this condition are as follows: rapid breathing, rapid heart rate, headache. weakness tired, confusion decreased appetite, abdominal pain, vomitting, bad breath (a common symptom of diabetic ketoacidosis). Acute metabolic acidosis can lead to coma and death. On the other hand, some metabolic acidosis conditions can also be mild, but continuous or chronic (Figure 1).

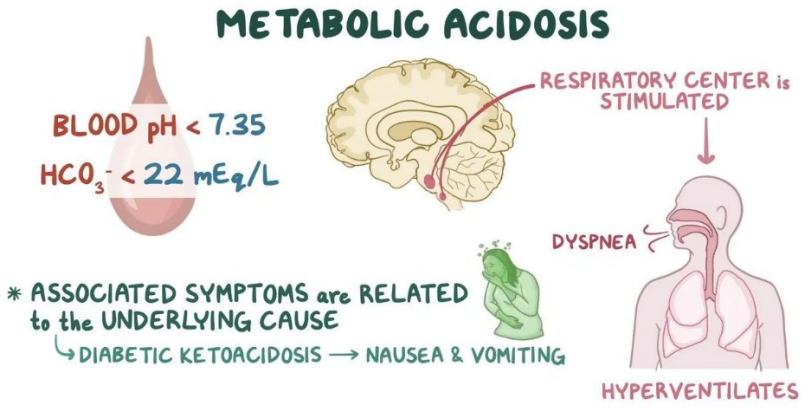

Fig. 1. Clinical Symptoms of Metabolic Acidosis

Patients with metabolic acidosis in CKD are often asymptomatic, and Acid-base disorders are usually recognized from blood chemistry tests. Concentration new serum bicarbonate decreases after a severe decrease in GFR. Average concentration serum bicarbonate is about 26.3 + 0.3 mEq/L at a serum creatinine <5 mg/dL, and decreased to <20 mEq/L after serum creatinine >10 mg/dL. Bicarbonate normal serum in CKD (in the absence of a process that is potentially increase in serum bicarbonate) showed no significant disturbance in the acid-base balance regulated by the kidney. The classification of the type of acidosis can be important for several reasons abnormalities associated with non-anion gap acidosis, eg renal disease tubulointerstitial and hyporeninaemic hypoaldosteronism. The disorder is also marked with hyperkalaemia, and have acidosis that is more severe than acidosis another with the same GFR such cases can be distinguished from acid cases.

4. DIAGNOSIS OF METABOLIC ACIDOSIS

Some symptoms of metabolic acidosis, a series of blood tests its necessary. Blood gas analysis is performed to determine the levels of oxygen and carbon dioxide in the blood, as well as the pH level in the blood. A basic metabolism panel is performed to check kidney function as well as pH balance. In addition, this examination is also carried out to determine levels of calcium, protein, blood sugar, and electrolyte levels in the body. Examinations carried out together can identify the type of acidosis. Assessment of suspects you have metabolic acidosis, the prior laboratory test is a urine sample. The pH level will be checked to see if acids and bases are properly excreted from the body. After that, additional tests may be carried out to determine the type of acidosis.

5. PREVENTION OF METABOLIC ACIDOSIS

The risk of developing metabolic acidosis can be reduced by carrying out various preventive measures. Here are some steps you can take to prevent you from getting metabolic acidosis: Make sure the body stays hydrated and not dehydrated. Meet fluid needs by drinking enough water or by consuming other fluids,

controling diabetes. Diabetics must be able to control their blood sugar to prevent ketoacidosis. Stop consuming alcoholic beverages because alcoholic beverages has the potential to cause a build-up of lactic acid.

6. TREATMENT OF METABOLIC ACIDOSIS

Treatment of metabolic acidosis can adjust to the type and also the cause of the acidosis. There are several types of treatment for metabolic acidosis such as oral sodium bicarbonate, used to treat hyperchloremic acidosis. The natirum citrate, used to treat acidosis caused by kidney disorders. Intravenous fluids and insulin, used to balance the pH in people with diabetes and ketoacidosis. Treatment for lactic acidosis is carried out according to the consequences so it can be in the form of bicarbonate supplements, intravenous fluids, oxygen, or antibiotics. Other treatment may be needed according to the severity of the cause of this condition. It should be noted that metabolic acidosis can cause complications if not treated properly. Complications that can occur include kidney stones, chronic kidney disorders, kidney failure, bone disease, and delayed growth.

Various methods are available for treating acidosis metabolism in CKD. Acid production increases primarily from digested protein, so that protein restriction will reduce the acid load and phosphate. Sodium bicarbonate Oral therapy is inexpensive and easy to administer. The bicarbonate reacts with protons in the stomach producing carbonic acid, which undergoes dissociates into carbon dioxide and water. This carbon dioxide can give rise sensation of fullness in the stomach. The target bicarbonate level that should be used is approx. 24 mEq/L. The maintenance dose of the base preparation should be adjusted so that the serum level bicarbonate around that value. Consider giving bicarbonate more aggressive in CKD, if abnormalities are found other diseases that cause it loss of base, for example profuse diarrhea, or the development of a large amount of acid load, for example: ketoacidosis

Treatment of metabolic acidosis can adjust veverimer, a non-absorbable hydrochloric acid binding polymer, recently underwent a series of clinical trials which yielded promising findings with regard to therapeutic approaches for metabolic acidosis in CKD [43-45]. As a treatment for metabolic acidosis in CKD patients, Veverimer (TRC101) was created. Hydrochloric acid binding is a revolutionary treatment idea for treating non-hazardous metabolic acidosis, unlike sodium or potassium. Veverimer is an oral hydrochloric acid binder, free of sodium and counterions. Apart from increasing serum bicarbonate, Veverimer specifically binds to and removes hydrochloric acid from the digestive system [44].

Treatment with veverimer improved renal outcome in a multicenter randomized controlled trial, defined as the occurrence of renal replacement therapy or a decrease in the estimated glomerular filtration rate (eGFR) of at least 50% over a 52-week period [43]. Chloride ion was predicted to increase with veverimer treatment in the initial study for the veverimer trial. However, Veverimer had no effect on chloride ion levels. Interestingly, at 5, 12, and 52 weeks after the start of the trial, veverimer treatment reduced the anion gap in CKD patients [43,44,46. These findings may imply that veverimer improves kidney function by reducing the anion gap.

A total of 374 of the 1058 CKD cohort patients—which were followed for a median of 3.0 years—developed KFRT. According to this study, 59% of CKD patients with similar HCO3 values were acidemic (pH 7.32) but 38% of them were with hypobicarbonatemia (HCO3 21.5). These results suggest that adequate respiratory compensatory capacity prevents acidemia in approximately 40% of CKD patients with hypobicarbonatemia (HCO3 21.5). This suggests that a significant percentage of individuals within the recommended target range for alkaline therapy do not display acidemia. Healthy participants in the Health ABC study were observed to make the same findings.

It was observed that 60% of people with low bicarbonate levels did not have acidemia [32]. The lowest bicarbonate quartile among CKD patients with acidemia (pH 7.32) has a 2.29-fold greater risk of KFRT compared to the highest bicarbonate quartile. The probability of KFRT in the lowest bicarbonate quartile of patients without acidemia (pH 7.32), however, did not differ substantially from that of the highest bicarbonate quartile. In conclusion, although many CKD patients with hypobicarbonatemia may not be candidates for KFRT, these patients should still be screened for alkaline therapy.

Previous physiological investigations demonstrated that NaHCO3 is more easily excreted than NaCl in relation to the potential increase in blood pressure and salt retention induced by alkali treatment because HCO3 is excreted mostly as NaHCO3, and not as KHCO3 [33]. Therefore, alkaline treatment (200 mEq/day, 16.8 g/day NaHCO3) did not cause changes in blood pressure or body weight in a small number of CKD patients when dietary salt consumption was limited to between 200 and 700 mg/day [33]. Nonetheless, intake of NaCl (100 mEq/day, 5.85 g/day) and NaHCO3 (100 mEq/day, 8.4 g/day) is balanced and still leads to weight gain and increased blood pressure [34]. Patients with CKD generally do not follow advice to apply very strict sodium restriction guidelines in clinical settings.

The average daily salt intake is 8 g, according to a recent study of CKD patients [35]. Indeed, patients with uncontrolled hypertension and/or congestive heart failure were excluded from the recent alkaline therapy trial [36], as were individuals with decompensated heart failure [22]. As a result, CKD patients who are eligible for alkaline therapy must be selected carefully. Study by Kajimoto et al. [31] may offer important suggestions for deciding which CKD patients might benefit from alkaline therapy. These studies suggest that patients with CKD who have low bicarbonate levels but no acidemia may not require sodium bicarbonate. The clinical importance of subclinical metabolic acidosis with normal serum bicarbonate, however, has only recently been recognized [37]. Alkali therapy has also resulted in improved renal function in patients with normal total venous CO2, according to a previous study [20].

7. ANION GAP LEVELS IMPACT THE PROGRESSION FOR CKD?

Metabolic Acidosis in CKD Acid base disorders are often found in CRF patients. Metabolic acidosis found in the majority of patients when the GFR falls to less than 20 – 50% of normal. The degree of acidosis is related to the severity of CKD, and usually more worse when the GFR is lower. The metabolic acidosis found is usually of the high anion-gap type, although the anion gap may be normal or only increased with CKD stage 4 or 5. In mild chronic renal insufficiency, metabolic acidosis occurs due to the inability of the kidneys to absorb bicarbonate, to excrete it ammonia, and to eliminate titrated acid excretion (hyperchloremic, normal anion gap acidosis). In increasingly severe renal insufficiency, organic and anion other conjugates (nonvolatile acids) cannot be excreted adequately, and Anion gap increase in acidosis appears[31-33].

Acidosis due to advanced renal insufficiency called uremic acidosis. Uremic acidosis develops in a variety of ways depending on on many factors, and related to GFR. Endogenous acid production is important factor, and this depends on the adequacy of the diet. Consumption of vegetables and fruits produce alkaline-free metabolites, and therefore increased consumption these foods will tend to delay the onset of metabolic acidosis in renal failure chronic. Diuretic therapy and hypokalemia, which tend to stimulate production ammonia, can also delay the occurrence of acidosis. The etiology of kidney disease also role. In kidney disease especially tubulointerstitial, acidosis tends to develop earlier than most glomerular diseases[27-30].

In general, metabolic acidosis rarely occurs when the GFR is greater than 20-25 ml,/ min. Several complications are associated with uremic acidosis, including muscle wasting, bone disease, growth hormone disorders, and thyroid hormone secretion, impaired insulin sensitivity, and exacerbation of beta-2 microglobulin accumulation. Other complications include negative nitrogen balance, anorexia, fatigue, impaired function of the cardiovascular system, hyperkalemia, and altered gluconeogenesis and triglyceride metabolism. Treatment of uremic acidosis should aim to get the serum bicarbonate level as close to normal as possible (22-26mmol/L) [30-33].

Alkali therapy can be carried out with sodium bicarbonate orally (1 tablet three times a day). A standard 650 mg sodium bicarbonate tablet contains 7.5 mmol of alkali (ion HCO3-). In dialysis patients, treatment of acidosis depends on the intake of alkaline dialysate, either as bicarbonate in haemodialysis or as lactate in dialysis peritoneal. In CKD, metabolic acidosis occurs when the renal excretory mechanisms cannot following daily acid build-up, usually after the GFR falls below ~30 mL/day. minute. This is due to a decrease in total renal ammonia genesis as a result from a decrease in the number of functioning nephrons, even during ammonia genesis of the nephron units single increase[29-31].

Clinically, CKD is characterized by a mild metabolic acidosis, with serum bicarbonate values usually remaining above ~15mEq/L, if not present comorbid disease. Usually the anion gap remains normal until stage end of PGK. The patient's serum pH and bicarbonate may remain stable, if additional amounts occur buffering that occurs in bone. The clinical consequences of chronic metabolic acidosis in CKD include osteopenia, worsening secondary hyperparathyroidism, reduced respiratory reserve and exhaustion of the body's buffer systems, which makes the patient more sensitive to its effect smaccompanying acute illness, and reduction of Na+-K+[17,19-29].

ATPase activity in red blood cells and myocardial cells can cause decreased contractilitym myocardial infarction and congestive heart failure. Another clinical complication is related to acidosis metabolic including abnormalities in glucose homeostasis, accumulation of beta-2 microglobulin, chronic inflammation and disturbances in growth hormone and function thyroid. Observational studies also link metabolic acidosis to increased mortality in patients with ESRD and in those with CKD who are not dependent on dialysis. This relationship can be explained by a deleterious effect of the metabolic acidosis listed above, but the correlation of metabolic acidosis and Alkali therapy with mortality is still uncertain[29-31].

Role of Metabolic Acidosis in CKD Development In addition to the systemic effects discussed above, metabolic acidosis is associated with kidney damage and CKD development. Baseline serum bicarbonate levels

as large as in patients with 15-20 mEq / L experienced a more significant decrease in GFR compared to patients with serum bicarbonate > 20 mEq / L. There is a relationship significant difference between higher serum bicarbonate levels and lower incidence of ESRD [30-34].

The role of metabolic acidosis in the progression of progressive CKD is related to the induction of kidney damage through a complex mechanism and clinical symptoms (Figure 1). Increased renal ammonia production in response to metabolic acidosis leads to activation and increased tubulointerstitial damage (Figure 2), which can be reversed by administration of sodium bicarbonate. The role of endothelin in renal acidification is through activation of ET-B receptors, but it could also simultaneously activate ET-A receptors with resultant tubulo interstitial injury (Figure 2).

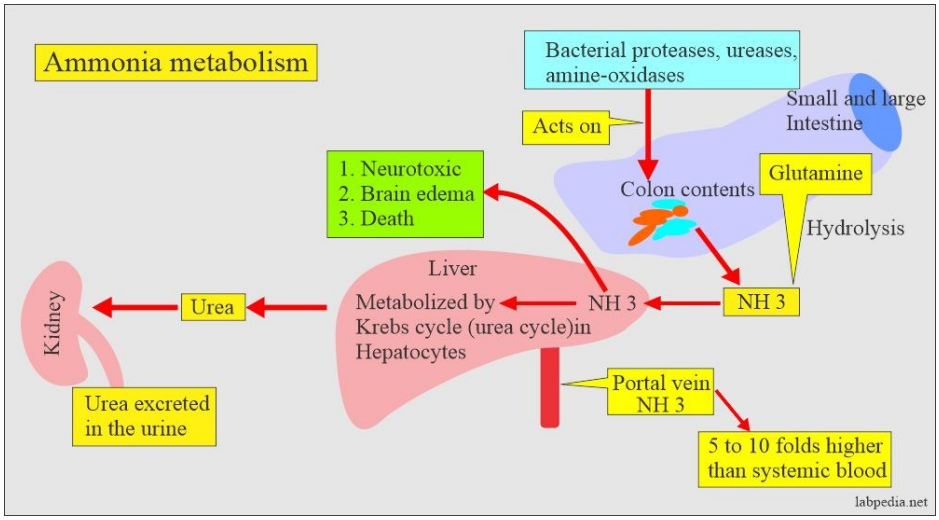

Fig. 2. Ammonia Metabolism

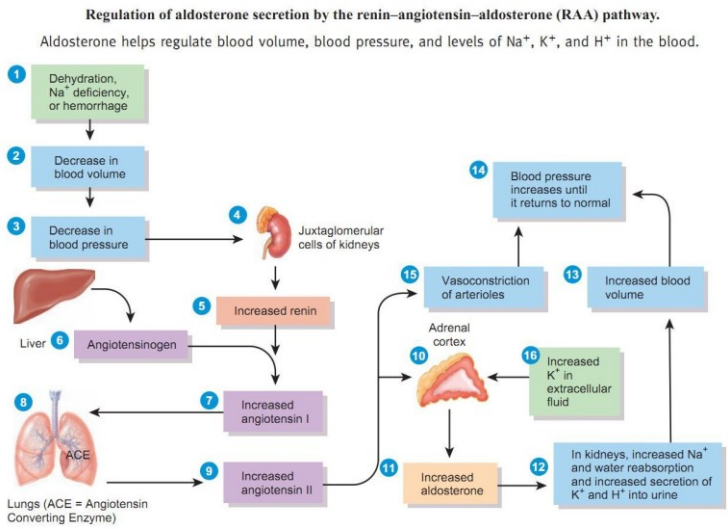

Fig. 3. Mechanisms may involve activation of the renin-angiotensin system

This effect is also overcome by the simultaneous administration of sodium bicarbonate. Interestingly, dietary alkalinization appears to be a more effective reno-protective strategy than endothelin antagonist administration, suggesting a complex mechanism of action for the nephrotoxic effects of metabolic acidosis (Figure 1 & 3). Other mechanisms may involve activation of the renin-angiotensin system, which also plays a role in acidification of the urine, and continued activation may also result in proteinuria, kidney damage and progressive CKD (Figure 3). In conclusion, metabolic acidosis activates a series of regulatory mechanisms

intended to correct the imbalance acid-base induced CKD progression, and prolonged activation which can then induce additional kidney damage and contribute to progressive CKD[7-9].

Based on the size of the anion gap, two types of metabolic acidosis have been identified as normal anion gap acidosis (hyperchloremic), and high anion gap acidosis. Early-stage CKD often exhibits normal anion gap acidosis, whereas severe anion gap acidosis develops as the disease progresses because of the buildup of nonchloride anions like phosphate, sulfate, and other organic acids [38]. Low bicarbonate levels have been linked, as previously mentioned, to the quick onset of CKD [14–18]. However, there is currently a lack of clinical knowledge regarding how high anion gap acidosis influences renal outcome, particularly in advanced stages of CKD. Early research found that uremic acids like indoxyl sulfate, p-cryl sulfate, and trimethylamine N-oxide increase renal fibrosis in response to renal damage [39–42].

The relationship between anion gap and renal outcomes was studied by Asahina et al. [47] utilizing cohort data from 1,168 Japanese CKD patients. It is well known that significant anion gap acidosis emerges in the latter stages of CKD and that the anion gap shifts as the disease progresses. In Japanese outpatients, the anion gap has frequently been measured in conjunction with the eGFR, and the eGFR has a direct impact on the anion gap. Additionally, a larger anion gap may eventually have an impact on renal function (eGFR) [45,49].

As a result, it is thought that eGFR influences the anion gap and renal outcomes in a time-dependent manner. Application of the traditional time-dependent Cox proportional hazard model alone was noted as an insufficient method for analysis because it can produce biased estimates when the association between the anion gap and renal outcomes was analyzed in the presence of a time-dependent confounder [48,49]. G-methods should be applied for analysis in these circumstances.

Based on the inverse probability of treatment weights and the inverse probability of censoring weights, Asahina et al. [47] produced time-varying inverse probability weights. They identified an assumption for the exposure effect on outcomes by examining variations between these pseudo-populations. Stage 4 CKD [47] resulted in considerably higher high anion gap acidosis, as was previously mentioned [50]. In the MSM analysis, metabolic acidosis with a high anion gap was compared to the normal anion gap with a 3.04-fold rate of KFRT and a 5.56-fold rate of all-cause mortality.

However, high anion gap acidosis was not associated with a significantly higher rate of KFRT or all-cause death compared with normal anion gap acidosis in the conventional multivariate Cox proportional hazard models, suggesting that analyses using Cox proportional hazard models may understate the association between the anion gap and renal outcome/mortality.According to a frailty model, adults in the highest tertile of the entire anion gap (19.54max imum mEq/L) had a greater chance of dying from any cause than adults in the middle tertile (15.93-19.54 mEq/L) (relative hazard, 1.20; 95% CI, 1.01-1.39).

Instead of differences in statistical techniques, the difference in participants' renal function (eGFR: 30-60 vs. 10-60 mL/min/1.73 m2, respectively) may be the cause of the lesser effect size in Banerjee et alanalyses .'s compared with those of 's analyses. According to the Asahina et al. study's re-analyses that were stratified by eGFR [47], high anion gap patients with eGFRs of less than 30 mL/min/1.73 m2 did not have a significantly higher risk of KFRT than patients with normal anion gaps within the same renal function range[49-50].

8. ANION GAP CONSTITUENTS IN CKD

When albumin and phosphate, two important components of the anion gap in CKD patients, were taken into account in the analysis of Asahina et alstudy .'s [47], the association between a high anion gap and an increased incidence of KFRT remained significant, indicating that substances other than albumin and phosphate may be involved in the development of CKD in response to a high anion gap. In fact, the formation of uremic solutes has recently been shown to be considerably influenced by human intestinal flora in a study of 3416 CKD patients by the Chronic Renal Insufficiency Cohort, patients with lower tubular production of organic acids, including kynurenic acid [56].

Renal insufficiency alters the composition of the gut flora and has a major impact on the colonic milieu, which creates an environment that is more favorable for the generation of toxic uremic retention solutes [57,58]. Several small-scale intervention trials in people with renal insufficiency were developed as a result of these discoveries on the relationship between loss of kidney function and changes in the gut flora (known as dysbiosis). Therapies that have been demonstrated to lower indoxyl sulfate or p-cresol sulfate in dialysis and predialysis patients include probiotics, prebiotics, and synbiotics [59–64]. However, little is known about how well these treatments work in reducing patients' levels of anion gap. So, more investigation will be required to understand the mechanics and clinical implications.

9. CONLUSIONS

If venous pH is measured, alkali treatment targets for CKD patients with metabolic acidosis may be lowered. As a result, it might be able to lower the number of instances where supplementing with sodium bicarbonate has negative effects. An innovative therapeutic strategy for metabolic acidosis, anion gap-reducing reagents like veverimer are superior to sodium bicarbonate and may enhance renal outcomes in CKD patients

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