Disorder of Acid-Base Balance in ESRD and its Relationship with Some Biochemical Variables

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Abstract

High blood acidity begins in the kidneys when they lose their ability to filter and excrete acidic substances (hydrogen ions) or when they get rid of alkaline substances (bicarbonates) that equal excessive blood acidity [1]. Metabolic acidosis (MA) is a common disorder in patients who suffer from Chronic Kidney Disease (CKD) In the fifth stage of CKD (63%) of patients suffer from acidosis and in the fourth stage (44%) compared patients with CKD in the first stage (10%) [2]. Causes of metabolic acidosis include impaired secretion of ammonia, decreased reabsorption of bicarbonate in the tubules, insufficient production of bicarbonate, and the amount of acid synthesized in the body that is ingested with food [3]. The loss of more than (80%) of the nephron impedes the regeneration of the base through the process of ammonia formation. Metabolic acidosis usually develops when the glomerular filtration rate drops to (20-30) ml/min [4].

Keywords: metabolic acidosis, acid-base balance, pH

1. Introduction

The pH is usually used to measure the acidity or alkalinity of blood and other fluids. The acidity of the blood is normal when the pH value ranges between (7.35-7.45), while the normal pH in urine is approximately [4-6].High blood acidity, also known as metabolic acidosis, is defined as a lower pH value than normal, as well as an imbalance in energy production and metabolism, caused by an increase in hydrogen ions and the accumulation of acids in the blood, or a decrease in the number of bicarbonate ions (an acid-base disturbance) [7, 8]. Metabolic acidosis is clinically defined by a serum bicarbonate concentration of less than 22 mmol/L and, in the second occurrence, a drop in partial arterial pressure of carbon dioxide (PaCO2)) [9]. There are four basic categories of illnesses that affect the human body:

1- Metabolic acidosis (MAc) 2- Metabolic alkalosis (MAlk
3- Respiratory acidosis (RAc) 4- Respiratory Alkalosis (RAlk)

The main organs that control the body's acid-base balance are the lungs and kidneys. Respiratory acidosis and alkalosis result from substantial variations in carbon dioxide exhalation due to respiratory problems, whereas metabolic acidosis and alkalosis result from an imbalance in the generation of acids or bases and their excretion by the kidneys. To put it another way, acidosis and alkalosis are classed according to their primary causes, which are either metabolic or respiratory.

The body usually maintains a pH close to (7.35-7.45) with an average of (7.40) because the pH at this level is ideal for many biological processes, the most important of which is blood oxygenation, in addition to that many of the intermediate compounds for biochemical reactions in the body ionize at a neutral pH In general, the respiratory system compensates for metabolic disorders, while the metabolic mechanisms compensate for respiratory disorders. If one of these cases occurs, the human body must create a balance in the form of an opposite case [10, 11].Increased muscle protein breakdown and wasting, which contribute to accelerated loss of muscle mass and uremic sarcopenia, promotion of inflammation, poor albumin production, atherosclerosis, hypotension, and bone disease are all key consequences of metabolic acidosis in CKD. In CKD, metabolic acidosis contributes to the progression of the inflammatory process [3, 4, 9] And disorders of the heart, leading to cardiovascular disease, shock to the circulatory system, coma, or death. Acid-base changes in patients with renal failure and dialysis treatment (HD) contribute to intra-arterial hypercarbon dioxide and hypoxia [12].Serum bicarbonate concentration [HCO3-] positively correlates with bone mineral density (BMD) and negatively correlates with serum levels of parathyroid hormone (which promotes bone resorption). In withdrawing alkaline nutrients from anywhere in the body, it begins with the hair and skin, followed by the nails until it reaches the bones, which over time leads to osteoporosis [13].Metabolic acidosis modifies gene expression at the level of osteoblasts, specifically by causing a decrease in the expression of genes responsible for the formation of collagen fibrils type I in osteoblasts. The production of prostaglandins, which are important regulators of bone metabolism, increases as a result of metabolic acidosis. Increased calcium influx from bone is caused by prostaglandin E2 [14].

Metabolic acidosis in CKD stimulates the production of hormones within the liver such as angiotensin II, aldosterone, and endothelin-1 that increase renal acid secretion,these hormones enhance the transport of hydrogen ions into the proximal tubules and proton-induced ATPase (H+ATPase) which leads to a rapid decrease in residual renal function The hormones released in the kidneys cause direct damage to the renal parenchyma and lead to local inflammation, fibrosis and atrophy tubular, Hormones whose levels pathologically altered in acidosis include aldosterone, endothelin (increased), cortisone, and IGF-1 (decreased) [15].

2. Methods

In this study, (275) samples (148) males (127) females with end-stage renal disease who were on regular dialysis (twice a

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week or three times a week) and whose ages ranged from (10-90) years were included. We obtained detailed information from each patient, including medical history, etc., in addition to (40) healthy adults as a control group. Blood was drawn from the arteriovenous fistula () [23], pH and bicarbonate were found with the ABL800 FLEX PLUS Blood gas analyzer, biochemical tests (intravenous sample) were performed using the Architect C4000 Clinical Chemistry Analyzer, and the vitamin level was measured D and PTH with cobas e 411 analyzers.

2.1 Statistical Analysis

The program (IBM: SPSS Statistics 25) was used, where the arithmetic mean and standard deviation of the variables included in the study were found using independent-samples T-Test and the comparison between the means through the statistical hypothesis test at the level of significance (P-value < 0.05, α =5%) and some variables were correlated with each other in the form of a linear correlation coefficient. The correlation coefficient was measured by Pearson's moment correlation coefficient.

3. Results and Discussion

3.1 Results of parameters of biochemical tests

The results of the parameters of the biochemical tests are presented in Table 1 for patients with renal failure compared with the control group. The statistical results indicated that there was a very high significant increase in the mean values of urea concentration, creatinine concentration, and a significant increase in glucose concentration and lactate concentration [4, 9] and a significant decrease in the mean values of albumin concentration, as for the total hemoglobin concentration, the results showed To a very high decrease in the average values of hemoglobin concentration.

Table1. Results of biochemical parameters

Parameters	Patients Group Mean±Std.Deviation	Control Group Mean±Std.Deviation	p-value
Number	275	40	-----
Urea(mmol/L)	21.213±4.2874	4.9217±3.99258	p<0.001***
Cre(μmol/L)	955.912±322.8261	64.243±17.2522	p<0.001***
Alb(g/dL)	37.136±4.9518	39.055±2.5083	p<0.001***
Glu(mg/dL)	130.661±66.0390	108.38±22.214	p<0.001***
Lac(mmol/L)	1.040±0.4628	1.560±0.5773	p<0.001***
ctHb (g/dL)	9.183±1.8625	13.110±1.3487	p<0.001***

***= Very high significant statistical difference p≤0.001

3.2 Results of acid-base balance parameters

The statistical results shown in Table 2 showed a very high significant decrease in the values of (pH) and the concentration of bicarbonate for patients with renal failure compared with the control group, which amounted to (.0603010 ± 7.34530) (.0405320 ± 7.39910) and (4.6424 ± 18.647) (2.5589 ± 24.120). respectively, where it was (p<0.001), and this indicates the presence of the component of metabolic acidosis, and this agrees with the researcher (Angéloco) [10]. And there was a significant decrease in (pCO2) values, and the results were (4.9067±33.996) (6.3992±39.335), respectively, and the value was (p-value =0.002).

Table 2. Results of acid-base balance coefficients

Parameters	Patients Group Mean±Std.Deviation	Control Group Mean±Std.Deviation	p-value
Number	275	40	-----
Ph	7.34530±0.060301	7.39910±0.040532	p<0.001***
cHCO-3(mmol/L)	18.647±4.6424	24.120±2.5589	p<0.001***
pCO2(mmHg)	33.996±4.9067	39.335±6.3992	.022*0

***= Very high significant statistical difference p≤0.001

3.3 acid-base balance disorders in patients with ESRD

If the patient has metabolic acidosis, the body will cause respiratory alkalosis, but rarely makes our pH return to normal at 7.4 to maintain acid-base balance, activity of the alkaloids and lungs is rapid but short and limited Although kidney function is slow but more effective and long-term [4]. The amount of PCO2 decreased with the stage of renal failure and carbon dioxide is excreted through the respiratory system, so the compensatory mechanism resulting from the bicarbonate buffer and the lungs reduces the stability of blood acidity and limits the decrease in pH due to renal failure. Kussmaul respirations, which is a deep breathing pattern, can be seen. When the body tries to compensate for metabolic acidosis [4]. Therefore, if the patient suffers from acute renal dysfunction, the pH drops dramatically and decreases gradually according to the severity of the chronic renal failure and the level of PCO2 determines respiratory activity.Given the reversible reaction between CO2 and H2O which produces H2CO3, the respiratory system can adjust the pH level indirectly. pH as well as low level (PCO2). Under normal conditions, the kidneys excrete acid (H+) to regenerate and reabsorption (-HCO3), during renal failure, both acid secretion and bicarbonate reabsorption decrease [16]. If the patient has metabolic acidosis, the body will cause respiratory alkalosis, but rarely makes our pH return to normal at 7.4 to maintain acid-base balance, the activity of the alkaloids and lungs is rapid but short and limited. Although the kidney function is slow, it is more effective and long-lasting [17]. Table 3 shows the types of acid-base balance disorders of the study samples.

Table3. Types of acid-base balance disorders and percentages of patients with renal failure for the study samples

Blood gas check	Types of acid-base balance disorders	number of Patients (N)	percentage%
pH= Normal cHCO-3= Normal pCO2= Normal	Normal	30	10.90%
pH= ↓ cHCO-3= ↓pCO2= Normal	Metabolic acidosis	77	28%
pH=↓ cHCO-3= NormalpCO2=↑	Respiratory acidosis	4	1.46%
pH= ↑ cHCO-3=↑pCO2= Normal	Metabolic alkalosis	0	0%
pH=↑ cHCO-3= NormalpCO2=↓	Respiratory alkalosis	2	0.73%
pH= ↓ cHCO-3=↓pCO2=↓	Metabolic acidosis with partial respiratory compensation	158	57.46%
pH=↑ cHCO-3=↑ pCO2=↑	Metabolic alkalosis with partial respiratory compensation	1	0.36%
pH=↓ cHCO-3=↑ pCO2=↑	Respiratory acidosis with partial Metabolic compensation	0	0%
pH= ↑ cHCO-3=↓ pCO2=↓	Respiratory alkalosis with partial Metabolic compensation	3	1.09%
Total	-------	275	100%

3.4 Results Levels of Vitamin D and PTH.

The statistical results of the current study shown in Table 4 indicate a very high significant decrease in the mean values of vitamin D concentrations for patients with renal failure compared with the control group, which amounted to (13.89677 ± 19.1386) (22.5253 ± 43.947) respectively, and (p<0.001) these results are consistent with researcher (Behairy) [18] that showed vitamin D deficiency that sometimes reaches more than 80% in patients with chronic kidney disease (CKD).The statistical results indicated that there was a significant increase in the mean values of (PTH) concentrations for patients with renal failure compared with the control group, as its levels reached (601.6911 ± 671.159) (22.9550 ± 48.4225), respectively. The results agree with the researcher (Nazzal) and his colleagues [19].

Table 4. Vitamin D and PTH concentrations and their comparison with the control group

Parameters	Patients Group Mean±Std.Deviation	Control Group Mean±Std.Deviation	p-value
Vitamin D (25 OH) (pg/mL)	19.1386±13.89677	43.947±22.5253	p<0.001***
PTH (pg/mL)	671.159±601.6911	48.4225±22.9550	p<0.001***

3.5 Electrolyte Concentrations Results

The statistical results of the study shown in Table 5 showed a significant increase in the mean values of phosphate, potassium, chloride and anion gap for patients with renal failure compared with the control group [20], and a significant decrease in the mean values of sodium and ionic calcium concentrations [20, 21].

Table 5. Electrolyte concentrations of patients with renal failure compared with the control group

Parameters	Patients Group Mean±Std.Deviation	Control Group Mean±Std.Deviation	p-value
Number	275	40	-----
PO4-3 (mmol/L)	1.7047±0.43063	1.1218±0.16214	p<0.001***
K+(mmol/L)	4.930±0.9495	3.898±0.3977	p<0.001***
Na+(mmol/L)	138.6582±3.70040	139.9000±2.02295	0.002**
Ionized Ca+2(mmol/L)	0.9922±0.16783	1.1103±0.09294	p<0.001***
CL-1(mmol/L)	107.1055±7.23635	104.5000±2.90004	0.025*
Anion Gap(mmol/L)	13.720±6.58796	7.4167±2.71817	p<0.001***

***= Very high significant statistical difference p≤0.001**= High statistical difference p≤0. 01*= There is a statistically significant difference p≤0.05

4. The relationship between pH and biochemical variables

4.1 The relationship between pH with vitamin D and (PTH) for patients with renal failure

When drawing the correlation between (pH) and vitamin D in patients with renal failure, we notice a positive correlation (r = 0.313). This direct relationship confirms that vitamin D deficiency is related to low pH and acidosis formation, while the relationship between (pH) and (PTH)) in patients with renal failure, it was a negative correlation (r = -0.246), which is shown in Table 6.

Table 6. Correlation coefficient and type of relationship between (pH) with (vitamin D and (PTH)

pH Relationship with	r=Pearson Correlation	p-value	Relationship Type
Vitamin D (25 OH) (pg/mL)	0.313*	0.012	Positive
PTH (pg/mL)	-0.246	0.052	Negative

4.2 Relationship between pH and electrolytes

When drawing the correlation relationship between (pH) with calcium ion and sodium ion and bicarbonate in patients with renal failure, we notice a positive (direct) correlation, as for the correlation relationship (pH) with each of the chloride ion, potassium ion, phosphorous and with the anion gap was a relationship Negative (inverse) correlation The values of the correlation coefficient (r) and the value of the probability (p) are shown in Table 7.

Table 7. Correlation coefficient and type of relationship between (pH) with some electrolytes

pH Relationship with	r=Pearson Correlation	p-value	Relationship Type
cHCO-3(mmol/L)	0.507**	<0.001	Positive
PO4-3 (mmol/L)	-0.147*	0.015	Negative
K+(mmol/L)	-0.187**	0.002	Negative
Na+(mmol/L)	0.042	0.493	Positive
Ionized Ca+2(mmol/L)	0.018	0.771	Positive
CL-1(mmol/L)	-0.187**	0.002	Negative
Anion Gap(mmol/L)	-0.045	0.468	Negative
** Correlation is significant at the 0.01 level.* Correlation is significant at the 0.05 level			

4.3 TheRelation between pH and renal biochemical parameters

The correlation between (pH) and each of Creatine, urea, albumin and lactate was a negative (inverse) relationship, while the relationship between (pH) with glucose was (positive), which is shown in Table 8.

Table 8. Correlation coefficient and type of relationship between pH and some variables

pH Relationship with	r=Pearson Correlation	p-value	Relationship Type
Urea(mmol/L)	-0.383**	<0.001	Negative
Cre(µmol/L)	-0.159**	0.008	Negative
Alb(g/dL)	-0.127*	0.036	Negative
Glu(mg/dL)	0.015	0.806	Positive
Lac(mmol/L)	-0.077	0.201	Negative
** Correlation is significant at the 0.01 level.* Correlation is significant at the 0.05 level.			

4. Conclusions

Metabolic acidosis is prevalent in ESRD patients and the pH correlation is direct with calcium and vitamin D and inverse with phosphorous and (PTH). Metabolic acidosis negatively affects calcium and phosphate metabolism in patients with CKD by decreasing sensitivity of calcium receptors. As a result of the decrease in intracellular pH and by stimulating the parathyroid glands to secrete parathyroid hormone, it also contributes to the movement of bone bases, stimulates osteoclasts and inhibits the activity of osteoblasts. In addition, metabolic acidosis stimulates bone turnover and thus increases the risk of osteoporosis.

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