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Prevalence and Diagnostic Markers of Metabolic Acidosis in Chronic Kidn Disease: A Cross-Sectional Study

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ABSTRACT

Introduction: Metabolic acidosis (MA) is the most common complication of chronic kidney disease (CKD), exacerbating the progression of disease and adverse outcomes. This study aims to determine the prevalence of MA and its predicting factors among CKD patients in the southern governorates of Iraq. **Methods**: A cross-sectional study of adult CKD patients ($eGFR < 60\,mL/min/1.73\,m^2$) was performed in Basra, Thi-Qar, and Missan. Demographic, clinical, and laboratory data were collected, including blood gas analysis and electrolytes assessed using the epoc® Blood Analysis System. Serum bicarbonate levels determined the classification into MA and non-MA groups. Statistical analyses included t-tests, Pearson correlations, and logistic regression. **Results**: Compared with patients without MA, those with MA had significantly lower pH and bicarbonate levels and higher BUN and creatinine levels ($p < 0.001$). Lower GFR was independently related to MA ($OR = 0.929,\ p < 0.001$). Males were more affected by MA (67.3%) than were females (55.6%). **Conclusion**: MA is common among CKD patients in southern Iraq and strongly correlated with renal function deterioration. Early detection and treatment of MA is vital, especially in patients with reduced GFR.

1. INTRODUCTION

Chronic kidney disease (CKD) is a worldwide health problem, ultimately leading to progressive loss of renal function with time. Metabolic acidosis (MA) is one of the most prevalent and clinically relevant metabolic complications in patients with CKD [1]. The inability of the kidneys to excrete acid and maintain acid-base homeostasis worsens with declining kidney function, resulting in the accumulation of acid in the body [2]. This retention of acid results in a reduction of serum bicarbonate (HCO3), the hallmark of metabolic acidosis in patients with CKD [3]. The prevalence of metabolic acidosis appears to increase with progression of CKD, with estimates of 15% at stage 3 CKD and 35% at stage 4 CKD [4]. In advanced stages of CKD (stage 5), the prevalence may be more than 70% [5]. Differences in the definition of metabolic acidosis, study populations, and measurement methods [6]. could explain why previous studies had different prevalence estimates. Metabolic acidosis due to CKD is usually defined as serum bicarbonate <22 mmol/L [7]. However, new data indicate that even low-normal serum bicarbonate concentrations ($22 - 24\,mmol/L$) may have adverse consequences related to subclinical acid retention [8]. This has resulted in greater attention to recognizing and treating metabolic acidosis earlier in the course of CKD. MA is common in patients with CKD, and it has substantial clinical implications; however, little data is available regarding the factors contributing to MA in CKD patients in specific geographic regions. This study aims to fill this gap by determining the frequency of MA and its association with blood gas variables, electrolytes, and markers of renal functions in CKD patients residing in the southern governorates of Iraq. We hope to determine the key predictors of this population for the development of targeted interventions to improve patient outcomes. This study adds to the broader understanding of the MA in CKD and can provide local implications and insights for clinicians and researchers working in similar environments while also emphasizing the significant regional variability that may exist in the presentation of and the responses to this condition).

2. MATERIALS AND METHODS

Study Design and Population

Data were collected using a cross-sectional study design. Inclusion criteria adult patients ($\geq 18\ years$) with a diagnosis of chronic kidney disease (CKD) (eGFR < 60 mL/min/1.73 m2 for at least three months). We excluded patients with acute kidney injury or other non-CKD causes of metabolic acidosis and patients with incomplete laboratory data. Statistical significance was ensured by recruiting 100 CKD patients from nephrology clinics.

LABORATORY ASSESSMENTS

Laboratory Evaluations were performed using the epoc® Blood Analysis System. This point-of-care device is also portable and uses a combination of electrochemical measurement techniques to analyze blood samples [9] Potentiometry is used for pH, pCO2, sodium, potassium, and ionized calcium. Selected techniques are also described: methods based on immunometric, potentiometry (e.g., pO2), and amperometry methods (e.g., glucose, lactate). Hematocrit is measured using conductometry [10]. The epoc® system uses a biosensor for each analyte on a single-use test card. As blood flows across these sensors when a sample is introduced, multiple parameters can be measured simultaneously. The electrical signals from the sensors are captured and analyzed by the epoc® Reader, and the epoc® Host mobile computer processes and displays the results [11]. This allows for rapid analysis, with results for a complete panel of tests available in less than 1 minute after sample introduction [12]. The epoc® Blood Analysis System measures a comprehensive list of critical blood parameters (blood gases, electrolytes, metabolites, and hematocrit) with only 92 µL of whole blood [13].

DATA ANALYSIS

Statistical analyses were conducted using SPSS version 26 (IBM Corp., Armonk, NY, USA). The characteristics of the cohort population were summarized descriptively by means, standard deviations, and frequencies. The patients were classified into two groups based on the presence or absence of metabolic acidosis (MA), which was defined as a serum bicarbonate level below 22 mmol/L. Continuous variables, including pH, bicarbonate (HCO3-), blood urea nitrogen (BUN), creatinine, and glomerular filtration rate (GFR), were compared between the two MA and non-MA groups using independent samples t-tests. Pearson correlation coefficients (r) were calculated to determine the relationships between blood gas variables (pCO2, HCO3-) and the electrolytes (sodium, potassium, calcium, chloride) in the MA and non-MA groups. The maximum correlation between fields was interpreted as follows: $|r| < 0.3$ indicates a weak correlation, $0.3 \leq |r| < 0.5$ indicates a moderate correlation, and $|r| \geq 0.5$ indicates a strong correlation. $p < 0.05$ was considered statistically significant. Univariable binary logistic regression analysis was performed to identify independent predictors of metabolic acidosis. GFR was added as a predictor variable in the model. Results were reported as odds ratios (OR) with 95% confidence intervals (CI). The Hosmer-Lemeshow test was used to assess the model fit, and the classification table was used to determine the model's overall accuracy.

ETHICAL APPROVAL

The Research Ethics Board of Al-Zahrawi University College (REBZ) approved the study on February 10, 2025 (REBZ Rec No. 14/2025). The study was executed in alignment with the ethical standards and institutional guidelines of the institutions involved, with all participants providing written informed consent and all outcomes maintained confidentially.

3. RESULTS

Clinical and Laboratory Parameters Comparison

Table 1 compares clinical and laboratory parameters between patients with and without metabolic acidosis (MA). The overall mean pH level among patients with MA (7.237 ± 0.164) was significantly lower than among patients without MA (7.382 ± 0.054) ($P < 0.001$). Moreover, we found that the bicarbonate (HCO3−) levels were significantly lower in the MA group ($14.8 \pm 5.5 mmol/L$) than in the non-MA group ($27.2 \pm 3.5 mmol/L$), with a p-value of <0.001. Blood urea nitrogen (BUN) levels were greater in the MA group ($75 \pm 35 mg/dL$) versus the non-MA group ($42 \pm 20 mg/dL, p < 0.001$). Additionally, the MA group had higher creatinine levels than their non-MA counterparts ($5.74 \pm 3.38\ mg/dL\ vs.\ 4.38 \pm 5.30\ mg/dL 4.38 \pm 5.30 mg/dL$, p value 0.024. Patients with MA had lower GFR than those without MA ($p < 0.001$).

Gender Distribution

Table 2 shows the gender distributions of patients with MA and without MA. MA was more common in males (67.3%) compared to females (55.6%).

Correlation Between Blood Gas Variables and Electrolytes

Table 3 shows a correlation analysis of blood gas variables and electrolytes. For the Non-MA group, pCO2 was shown to be strongly correlated with potassium ($r = 0.555, p < 0.01$) and calcium ($r = 0.341, p < 0.05$). In the Non-MA group, HCO3− was negatively correlated with the chloride ($r = -0.426, p < 0.01$). These correlations are shown visually in Figures 1, 2, and 3, illustrating the relationship between pCO2 and potassium, pCO2 and calcium, and HCO3− and chloride in the non-MA group, respectively. Conversely, different patterns were observed in the metabolic acidosis (MA) group. There was a positive correlation between pCO2 and calcium ($r = 0.364, p <$

0.05); however, no significant correlation was identified with sodium, potassium, or chloride. Figure 4 also shows the relationship between pCO2 and calcium in the MA group.

Logistic Regression Analysis

Table 4 presents a logistic regression model with GFR as a predictor for MA. The multivariable model showed that lower GFR was significantly associated with higher odds of metabolic acidosis (odds ratio $0.929, p < 0.001$). The model classified 79% of cases correctly overall (88.7% for MA, 63.2% for non-MA).

Table 1. Comparison of Clinical and Laboratory Parameters Between Group with and Without Metabolic Acidosis

Variable	Non-MA (Mean ± SD)	MA (Mean ± SD)	P-Value
Age (years)	65 ± 12	61 ± 17	0.122
pH	7.382 ± 0.054	7.237 ± 0.164	<0.001
pCO_2 (mmHg)	45.8 ± 7.1	32.8 ± 8.7	0.082
HCO_3^- (mmol/L)	27.2 ± 3.5	14.8 ± 5.5	<0.001
Sodium (Na^+) (mmol/L)	137 ± 9	138 ± 9	0.74
Potassium (K^+) (mmol/L)	4.3 ± 0.8	4.5 ± 1.0	0.592
Chloride (Cl^-) (mmol/L)	100 ± 10	110 ± 9	0.468
Calcium (Ca^{2+}) (mmol/L)	1.23 ± 0.26	1.05 ± 0.18	0.984
BUN (mg/dL)	42 ± 20	75 ± 35	<0.001
Creatinine (mg/dL)	4.38 ± 5.30	5.74 ± 3.38	0.024
GFR (mL/min/1.73m²)	30.38 ± 19.05	13.55 ± 9.72	<0.001
AG Gap (mmol/L)	9.40 ± 1.79	12.77 ± 5.24	0.109

Notes: 1. P-values were calculated using the independent t-test
2. Metabolic Status Abbreviations:
a. Non-MA: Non-Metabolic Acidosis.
b. MA: Metabolic Acidosis

Table 2. Comparison of Gender Among Patients with and Without Metabolic Acidosis

Gender	Non-MA (Count, Row %)	MA (Count, Row %)
Males (M)	18 (32.7%)	37 (67.3%)
Females (F)	20 (44.4%)	25 (55.6%)

Table 3. Correlations Between Blood Gas Variables and Electrolytes in Various Metabolic States

Variable	Sodium (Na^+) (mmol/L)	Potassium (K^+) (mmol/L)	Chloride (Cl^-) (mmol/L)	Calcium (Ca^{2+}) (mmol/L)	Metabolic Status
pCO_2 (mmHg)	-0.065	0.555**	-0.151	0.341*	Non-MA
HCO_3^- (mmol/L)	-0.16	0.009	-0.426**	Nan	Non-MA
pCO_2 (mmHg)	0.209	-0.125	0.048	0.364*	MA
HCO_3^- (mmol/L)	0.158	0.014	-0.163	0.119	MA

1. Significance Levels:
   Correlation is significant at the 0.05 level (2-tailed).
   Correlation is significant at the 0.01 level (2-tailed).
2. Metabolic Status Abbreviations:
   Non-MA: Non-Metabolic Acidosis.
   MA: Metabolic Acidosis.

Table 4. Logistic Regression for Prediction of Metabolic Acidosis (MA) by GFR

Observed Metabolic Status	Predicted Metabolic Status		Percentage Correct
	Non-MA	MA	
Non-MA	24	14	63.2
MA	7	55	88.7
Overall Percentage			79.0

Cut value: 0.500

Table 5. Results of binary logistic regression analysis assessing the effect of GFR (mL/min/1.73 m²) on the studied outcome.

Variable	B	S.E.	Wald	df	Sig.	Exp(B)
GFR (mL/min/1.73 m²)	-0.074	0.016	20.465	1	<0.001	0.929
Constant	2.024	0.411	24.258	1	<0.001	7.567

a. The classification table shows that the logistic regression model correctly classified 79% of cases overall, with better performance for

predicting MA (88.7% *accuracy*) compared to non-MA (63.2% accuracy).

b. The negative coefficient for GFR indicates that lower GFR is associated with higher odds of metabolic acidosis, as reflected by the odds ratio (Exp(B) = 0.929).
c. Statistical significance is confirmed for GFR and the constant ($p < 0.001$).

FIGURES

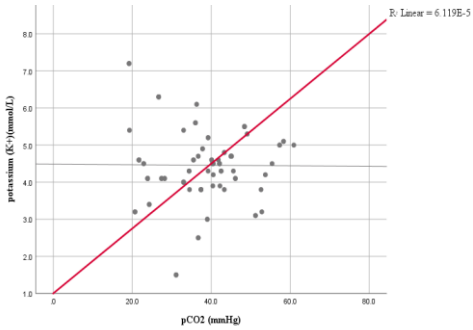

Figure 1. Relationship Between pCO_2 and Potassium Levels in Non-MA Group

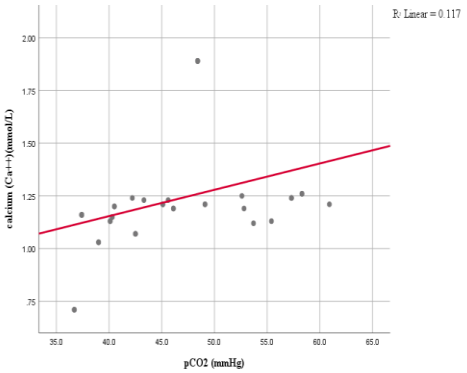

Figure 2. Relationship Between pCO_2 and Calcium Levels in Non-MA Group

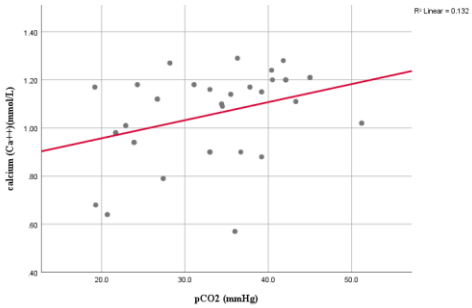

Figure 3. Relationship Between HCO_3^- and Chloride Levels in Non-MA Group

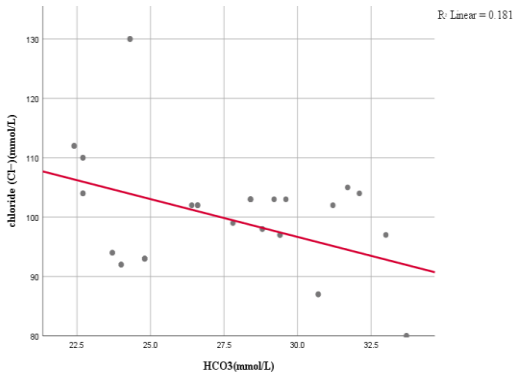

FIGURE 4: RELATIONSHIP BETWEEN pCO_2 AND CALCIUM LEVELS IN MA GROUP

4. DISCUSSION

Our results provide insight into the intricate relationship between metabolic acidosis, electrolyte abnormalities, and renal physiology. However, metabolic acidosis was not only associated with changes in multiple parameters of blood gas and electrolyte levels, but these changes also tended to be significantly higher in patients with CKD. The findings align with recent studies that show that metabolic acidosis is a frequently present complication of CKD, as determined by lower levels of serum bicarbonate and its association with accelerated decline in kidney function and greater risk of AKI [1,14,15]. Our study shows that patients with metabolic acidosis have lower GFR than those without it. This correlates with findings demonstrating that metabolic acidosis hastens the decline in glomerular filtration rate in patients with chronic kidney disease (CKD) by stimulating inflammatory and fibrotic pathways by angiotensin II, aldosterone, and endothelin-1(1). In a recent study by Adamczak M and Surma S. this is even better established in which metabolic acidosis promotes CKD progression and many of its complications leading to worse prognosis in such patients [16]. Regarding the gender distribution of patients with or without metabolic acidosis, our results showed that males were more representative among MA patients than females (67.3% and 55.6%, respectively). However, unlike some published studies, our results suggest a higher prevalence in females. A 2022 study noted gender differences in CKD, where metabolic acidosis was more associated with the female gender [17]. Such differences could be due to disparities in study populations or methodologies. Therefore, the impact of gender and sex on kidney disease must also be viewed in the context of biological and sociocultural factors that influence the complex interplay between gender, sex, and kidney disease. Blood gas variables and electrolytes were correlated; this analysis showed significant correlations in the non-metabolic acidosis group. For example, potassium and calcium were highly correlated with pCO2. These results are consistent with those reporting the involvement of electrolyte disturbances in metabolic acidosis, with altered handling of potassium and calcium likely contributing to acid-base imbalances [18]. Using logistic

regression, we found a significant association between lower GFR and higher odds of having metabolic acidosis (OR 0.929, p <0.001). This means that decreasing GFR increases the risk of metabolic acidosis. This finding is consistent with studies that show decreased renal function impairs the kidney's ability to excrete acid and leads to metabolic acidosis. For instance, one recent study (Chan JYM A et al. found an inverse association between eGFR and metabolic acidosis, observing that for each 1 mL/min/1.73 m² increase in eGFR, the odds of metabolic acidosis decreased 4% [19]. Metabolic acidosis has been documented in approximately 20% of patients with CKD, according to a study published in 2021, with the frequency of metabolic acidosis increasing as GFR declines, especially below 40 mL/min/1.73 m² (16). These findings have important implications for the management of CKD patients with metabolic acidosis, as early recognition and treatment of metabolic acidosis may be needed to ameliorate renal injury and reduce the progression of CKD. Studies that would provide more long-term data of the effects of alkali therapy among those patients with a more advanced stage of subclinical metabolic acidosis could be ideal, and need novel therapeutic pathways that would address the complicated pathophysiology present in metabolic acidosis in CKD.

5. STUDY LIMITATIONS

There are some limitations that need to be considered with this study. First, due to the cross-sectional study design, we are unable to determine the causal relationships of metabolic acidosis with the associated factors identified. Since only cross-sectional data are available to support these associations, longitudinal studies are necessary to confirm temporal order and psychosocial interventions to determine their efficacy toward progression of metabolic acidosis in this population. Second, the population studied was limited to the southern governorates of Iraq which may limit the generalizability of the information of such studies for other populations with different genetic or environmental exposures, or access to healthcare. Further studies must consider other geographic areas to confirm these findings in a variety of populations. Third, laboratory assessments in our study were based on a single point-of-care device (epoc® Blood Analysis System), which, although allowing for rapid results might have introduced potential measurement bias compared to a standard laboratory method. The epoc® system has shown acceptable analytical performance, yet it is recommended to validate against a reference laboratory.

6. CONCLUSIONS

This study would be a new insight to clarify metabolic acidosis and its predictors in CKD patients in the southern governorates of Iraq. Nevertheless, metabolic acidosis is strongly correlated with renal insufficiency, electrolysis, and partial blood gas disorder. The independent association of lower GFR with metabolic acidosis underscores the necessity of detecting and managing declining renal function as early as possible to avoid acid-base disturbances.

RECOMMENDATIONS

The following recommendations can be made based on the findings of this study:

1. Early Screening and Monitoring: Implement regular screening for metabolic acidosis in all patients with CKD, especially if GFR is declining. Timely recognition and management require regular monitoring of serum bicarbonate, blood gas indices, and electrolytes.
2. Guided Interventions: Guide interventions for modifiable risk factors for metabolic acidosis, e.g., optimizing GFR via medical management and diet
3. Future Directions: Perform longitudinal studies to examine the causal role of the metabolic acidosis-CKD relationship. What is alkali therapy, and how it might slow the decline of renal function and improve clinical outcomes?
4. Education and Awareness: Work towards increasing awareness amongst healthcare providers and patients about the significance of early detection and management of metabolic acidosis in CKD. Advise on lifestyle changes and dietary practices to prevent acid-base disorders.

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AUTHORS' DECLARATION:

We confirm that all the Figures and Tables in the manuscript belong to the current study.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this study.

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