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Original Research Article

Predictive Role of Sodium, Potassium, and Chloride Disturbances in NIV Failure among Patients with COPD Exacerbations

Bhimani Meera Rameshbhai[1], Kishan Kumar GovindBhai Jadav[2], Yasir Salim Vaja[3]

[1]MBBS, GMERS Medical College, Junagadh, Gujarat, India
[2]Intern, Ananya College of Medicine and Research, Gandhinagar, Gujarat, India
[3]MBBS, Petre Shotadze Tbilisi Academy, Tbilisi, Georgia

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Corresponding Author: Yasir Salim Vaja
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Abstract:

Background: Electrolyte disturbances are common in hypercapnic acute exacerbations of COPD (AECOPD) and may influence clinical outcomes, particularly the response to noninvasive ventilation (NIV). Identifying early predictors of NIV failure is crucial to guide timely escalation of care. This study evaluated the association between serum electrolytes (Na^+, K^+, Cl^-) and NIV outcomes in hypercapnic AECOPD.

Methods: This retrospective study included 178 patients with hypercapnic AECOPD admitted over one year in a tertiary care hospital. Clinical parameters, ABG profiles, and serum electrolytes at admission were recorded. Patients were categorized into acid–base subgroups, and NIV was initiated based on persistent respiratory acidosis and clinical distress. Electrolytes were compared between NIV success and NIV failure groups using the Student's t-test ($p < 0.05$).

Results: NIV failure was associated with significantly lower pH, higher $PaCO_2$, reduced PaO_2/FiO_2 ratio, and elevated lactate levels. Electrolyte abnormalities were notable, with higher serum potassium and lower chloride in the NIV failure group, while sodium levels were similar. Patients with respiratory plus metabolic acidosis had the highest NIV failure rate (95%), whereas respiratory acidosis with metabolic alkalosis showed the best outcomes. Diuretic use was common and may have contributed to metabolic patterns across groups.

Conclusion: Serum potassium and chloride disturbances are important early predictors of NIV failure in hypercapnic AECOPD and should be closely monitored.

Keywords: COPD, Hypercapnia, Electrolytes, Noninvasive Ventilation, NIV Failure, Potassium, Chloride.

Introduction

Hypercapnic respiratory failure in chronic obstructive pulmonary disease (COPD) exacerbations is a complex clinical condition characterized not only by elevated $PaCO_2$ and acidosis but also by disturbances in both acid–base and hydro-electrolyte balances. Acid–base derangements arise from alveolar hypoventilation, leading to respiratory acidosis, and are frequently compounded by associated metabolic abnormalities due to comorbidities and multi-drug therapy in affected patients. Mixed acid–base disorders and hydro-electrolyte imbalances, including hyponatremia, hypokalemia and hypochloremia, have been observed in COPD patients with hypercapnic respiratory failure and are associated with more severe physiologic disturbances and prolonged need for noninvasive ventilation (NIV) support [1,2]. In one study of hypercapnic COPD exacerbations, lower serum sodium and chloride levels were correlated with longer durations of NIV and more complex acid–base profiles, suggesting that electrolyte disturbances may reflect greater severity of respiratory failure and metabolic dysregulation [1].

Electrolyte imbalances have been shown to influence outcomes in patients with respiratory failure more broadly, with sodium abnormalities exhibiting a U-shaped relationship with mortality risk and potassium derangements linked to adverse prognosis [3]. Although previous work has focused on mortality and general outcomes in heterogeneous respiratory failure populations, specific evaluation of sodium, potassium and chloride as predictors of NIV failure in COPD remains underexplored [4-6]. The interplay between acid–base compensation, renal electrolyte handling and ventilatory support efficacy suggests that derangements in Na^+, K^+ and Cl^- could serve as important biomarkers for identifying patients at heightened risk of failing NIV and requiring escalation to invasive support. Therefore, this study aims to investigate the prognostic value of serum electrolyte levels in

predicting NIV failure among COPD patients presenting with hypercapnic exacerbations.

Materials and Methods

Study Design and Setting: This retrospective observational study was conducted in a tertiary care hospital over a period of one year. All patients admitted with hypercapnic acute exacerbation of chronic obstructive pulmonary disease (AECOPD) during the study period were screened. COPD and AECOPD were defined according to GOLD guidelines, and hypercapnia was identified as a $PaCO_2$ level >45 mmHg [7,8].

Patient Selection and Sample Size: A total of 178 patients with hypercapnic AECOPD were included. Patients were excluded if they were receiving home-based NIV, had radiological evidence of pneumonia, had acute respiratory distress syndrome, or presented with severe respiratory failure requiring immediate invasive ventilation in the ICU (pH < 7.1, hypercapnic coma, or hemodynamic instability). After applying these criteria, the final analytic cohort consisted of patients suitable for evaluation of electrolyte abnormalities and NIV response.

Clinical Evaluation and Laboratory Measurements: All eligible patients underwent a standardized clinical assessment at admission that included anthropometric parameters, vital signs, neurological evaluation using the Glasgow Coma Scale, complete blood count, biochemical profile, and arterial blood gas (ABG) analysis. Serum electrolyte concentrations (Na^+, K^+, Cl^-) measured at admission were recorded as primary variables of interest. Based on ABG interpretation, patients were categorized into three acid–base profiles: compensated respiratory acidosis, respiratory acidosis with metabolic alkalosis, and respiratory acidosis with metabolic acidosis. All patients received guideline-based treatment for AECOPD, including controlled oxygen therapy, nebulized bronchodilators, systemic corticosteroids, antibiotics, and management of comorbidities.

Noninvasive Ventilation Protocol and Definition of NIV Failure: NIV was initiated when optimal pharmacological management and oxygen supplementation failed to produce clinical improvement, and patients continued to exhibit persistent respiratory acidosis (pH < 7.35 and/or $PaCO_2$ >45 mmHg), significant dyspnea, and increased work of breathing [9]. NIV was delivered using an oronasal mask connected to a pressure-support ventilator. Inspiratory pressure, PEEP, and trigger sensitivity were adjusted to achieve tidal volumes of 6–8 mL/kg, improved oxygenation, and reduced respiratory rate. NIV was discontinued when the patient achieved clinical stability, defined by normalized pH, adequate oxygenation, and reduced respiratory distress.
NIV failure was defined as the need for escalation to invasive ventilation due to worsening respiratory acidosis, increasing $PaCO_2$, altered mental status, or cardiovascular instability.

Electrolyte Analysis and Outcome Measures: Serum sodium, potassium, and chloride levels at admission were analyzed to determine their predictive value for NIV failure. The primary outcome measure was the occurrence of NIV failure, and electrolyte abnormalities were compared between successful vs failed NIV groups.

Statistical Analysis: Data were expressed as mean ± standard deviation. Differences in electrolyte levels between NIV success and NIV failure groups were analyzed using the Student's t-test. A p-value < 0.05 was considered statistically significant.

Results

In this study, NIV failure was associated with significantly worse metabolic and respiratory parameters compared to NIV success. Patients who failed NIV had lower serum albumin, higher CRP, higher heart rate, and markedly poorer gas exchange, reflected by lower pH, higher $PaCO_2$, lower PaO_2/FiO_2 ratio, and elevated lactate levels. Electrolyte disturbances were also notable, with NIV failure patients showing higher serum potassium and lower chloride levels, while sodium remained comparable between groups (Table 1).

Table 1: Clinical, Respiratory, and Metabolic Characteristics of the Study Population (N = 178)

Variables	NIV Success (N = 89)	NIV Failure (N = 89)	p-value
Age (years)	77.5 ± 8.8	77.6 ± 10.7	0.94
Gender (M/F)	47/42	45/44	0.85
Glucose (mg/dL)	142.3 ± 48.9	156.2 ± 76.5	0.26
Serum Uric Acid (mg/dL)	6.3 ± 2.0	6.6 ± 2.6	0.60
Serum Albumin (g/dL)	3.3 ± 0.5	2.9 ± 0.5	**<0.001**
C-Reactive Protein (mg/L)	76.9 ± 75.7	27.4 ± 34.4	**0.039**
Serum Creatinine (mg/dL)	1.08 ± 0.58	1.29 ± 0.88	0.14
GFR (ml/min/1.73 m², MDRD)	71.8 ± 32.0	72.7 ± 49.3	0.91
Heart Rate (bpm)	83.8 ± 12.7	93.6 ± 13.6	**<0.001**
SBP (mmHg)	124.1 ± 17.0	120.0 ± 17.9	0.21
DBP (mmHg)	74.2 ± 9.9	72.5 ± 10.2	0.38
PaO_2 (mmHg)	58.4 ± 13.5	60.2 ± 16.2	0.54
PaO_2/FiO_2	255.9 ± 38.6	200.2 ± 57.6	**<0.001**
pH	7.42 ± 0.05	7.29 ± 0.11	**<0.001**
$PaCO_2$ (mmHg)	50.5 ± 5.5	75.5 ± 19.8	**<0.001**
Lactate (mmol/L)	1.38 ± 0.68	2.01 ± 1.76	**0.017**
Serum HCO_3^- (mmol/L)	32.6 ± 5.5	36.0 ± 10.1	**0.036**
Serum Na^+ (mmol/L)	138.6 ± 3.9	139.1 ± 6.9	0.63
Serum K^+ (mmol/L)	4.4 ± 0.6	4.7 ± 0.8	**0.037**
Serum Cl^- (mmol/L)	99.4 ± 3.9	96.6 ± 8.1	**0.030**

Values are presented as mean ± SD.

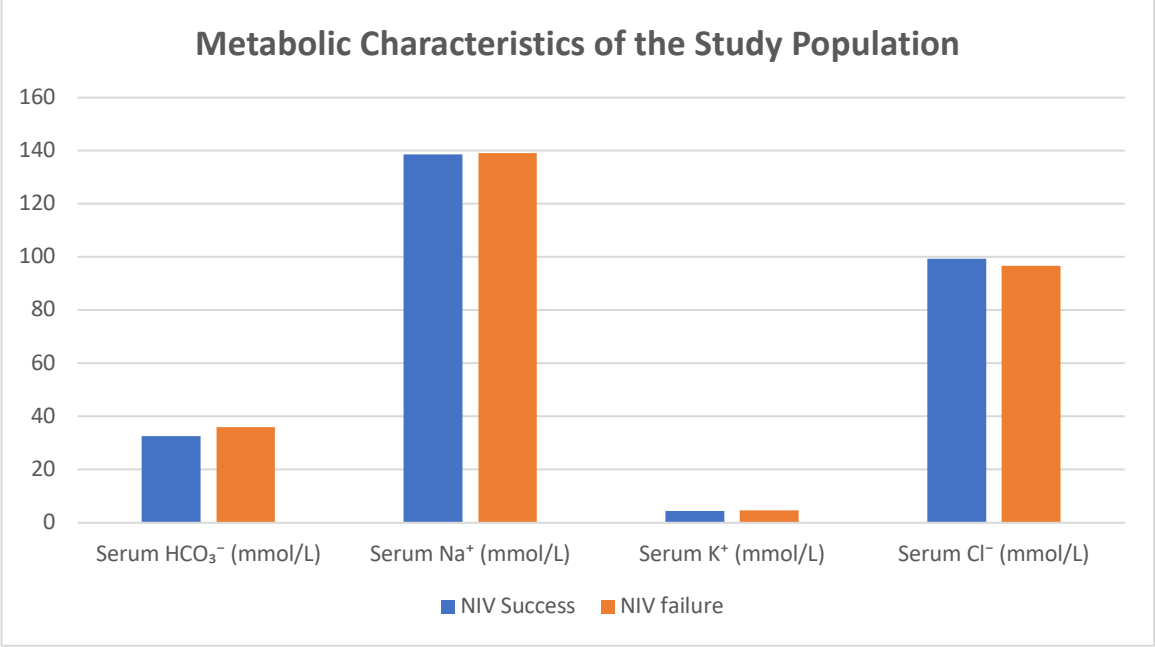

Figure 1: Metabolic Characteristics of the Study Population

Analysis of acid–base patterns showed that patients with respiratory acidosis plus metabolic alkalosis had the highest NIV success rate, whereas those with combined respiratory and metabolic acidosis had a very high NIV failure rate. Compensated respiratory acidosis demonstrated an intermediate risk, highlighting a clear gradient of NIV outcomes based on acid–base status (Table 2).

Table 2: NIV Outcomes According to Acid–Base Classification (N = 178)

Acid–Base Pattern	Total (N)	NIV Success n (%)	NIV Failure n (%)
Respiratory acidosis + metabolic alkalosis	58	44 (76%)	14 (24%)
Compensated respiratory acidosis	82	43 (52%)	39 (48%)
Respiratory + metabolic acidosis	38	2 (5%)	36 (95%)

$\chi^2 < 0.001$

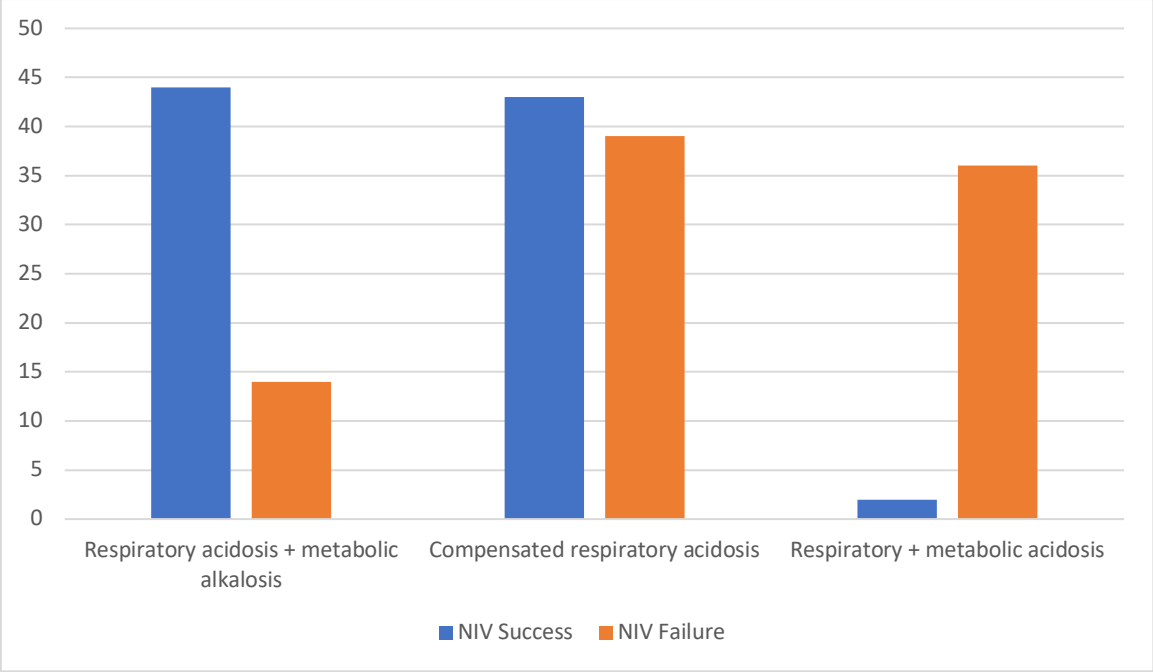

Figure 2: NIV Outcomes According to Acid–Base Classification

Medication profiling revealed that diuretic use was extremely common across all acid–base categories, particularly in patients with metabolic alkalosis. ACE inhibitors, ARBs, calcium channel blockers, and beta-blockers showed variable distribution across groups, indicating heterogeneous cardiovascular drug exposure that may influence metabolic patterns but not necessarily NIV outcomes (Table 3).

Table 3: Cardiovascular Drug Use by Acid–Base Category and in the Overall Cohort (N = 178)

Medication	Metabolic Alkalosis Group (N = 58)	Compensated Respiratory Acidosis Group (N = 82)	Metabolic Acidosis Group (N = 38)	Total Cohort (N = 178)
Diuretics	53/58	62/82	35/38	150/178
ACE inhibitors	15/58	20/82	6/38	41/178
ARBs	19/58	24/82	8/38	51/178
Calcium channel blockers	8/58	24/82	5/38	37/178
Beta-blockers	5/58	6/82	1/38	12/178
Nitroglycerin	8/58	5/82	2/38	15/178
Potassium-sparing diuretics	6/58	5/82	2/38	13/178

Discussion

Hypercapnic AECOPD is a critical clinical event requiring careful evaluation, as multiple determinants—age, comorbidities, disease severity, hemodynamic stability, respiratory acidosis, and underlying acid–base (AB) and hydro-electrolytic (HE) imbalances—affect the likelihood of recovery and the need for ventilatory support [10]. In our 178-patient cohort, we observed that NIV failure was strongly associated with more severe respiratory acidosis, markedly lower pH, higher $PaCO_2$, elevated lactate, and significant electrolyte abnormalities, particularly increased serum potassium and reduced chloride levels. These physiological disturbances reflect the acute metabolic burden experienced by patients presenting with sudden decompensation, often driven by renal impairment, poor diabetes control, or fluid loss, all of which can rapidly destabilize AB and HE equilibrium.

Patients classified with combined respiratory and metabolic acidosis exhibited the poorest prognosis, showing a 95% NIV failure rate and the highest need for escalation of care, consistent with earlier findings that inadequate metabolic compensation and renal dysfunction worsen outcomes in hypercapnic AECOPD [11]. In contrast, patients with respiratory acidosis accompanied by metabolic alkalosis demonstrated a substantially lower NIV requirement, mirroring situations where diuretic- or steroid-induced alkalosis, hypovolemia, or chloride depletion can be rapidly corrected. Similar to

previous evidence showing improved ventilation after withdrawal of loop diuretics in COPD patients with edema [13], many of these patients in our cohort recovered stabilizing acid–base status once volume and chloride levels were restored, highlighting the importance of targeted correction of metabolic alkalosis in preventing NIV failure.

Lactate levels were significantly higher in the NIV failure group, supporting prior observations that elevated lactate serves as a marker of tissue hypoxia, respiratory muscle fatigue, and more severe COPD exacerbations [1]. However, the clinical interpretation of lactate varied depending on the acid–base category. In metabolic alkalosis, moderate lactate elevation may reflect an adaptive metabolic response ("good lactate"), whereas in combined respiratory and metabolic acidosis, elevated lactate likely indicates impaired perfusion and more severe physiological compromise ("bad lactate") [13,14]. This distinction was evident in our patients, where the highest lactate levels and highest NIV failure rates co-occurred in those with mixed acidosis, underscoring lactate's role as a clinically meaningful predictor of adverse outcomes.

The observed associations between $PaCO_2$ and electrolyte changes align with established physiological responses described in classical hypercapnia studies. As $PaCO_2$ increased, bicarbonate rose due to renal compensation, while serum chloride decreased proportionately—an expected pattern that maintains electroneutrality and reflects the renal adjustments described by Brackett et al. [15] and in chronic hypercapnia research [16]. Interpreted through Stewart's Strong Ion Difference framework, this relative hypochloremia increases SID and drives metabolic alkalosis through shifts in the H^+/HCO_3^- equilibrium [17]. In our cohort, the inverse correlation between $PaCO_2$ and chloride was consistent across all acid–base groups, reinforcing the significance of chloride as an indicator of metabolic compensation and as a potential contributor to NIV failure risk in hypercapnic AECOPD.

Conclusion

Serum electrolyte abnormalities, particularly elevated potassium and reduced chloride levels, were strongly associated with NIV failure in patients with hypercapnic AECOPD. These disturbances reflect underlying acid–base derangements that impair physiological compensation and worsen ventilatory status. Given their routine availability, electrolytes can serve as simple, early predictors of NIV outcome, enabling clinicians to identify high-risk patients and initiate timely escalation of care, ultimately improving clinical decision-making in acute COPD management.

References

1. Terzano C, Di Stefano F, Conti V, Di Nicola M, Paone G, Petroianni A, Ricci A. Mixed acid-base disorders, hydroelectrolyte imbalance and lactate production in hypercapnic respiratory failure: the role of noninvasive ventilation. PLoS One. 2012;7(4):e35245. doi: 10.1371/journal.pone.0035245. Epub 2012 Apr 23. PMID: 22539963; PMCID: PMC3335154.
2. Öztürk Şahin B, Gürsel G. Combined Acid-Base Abnormalities During Noninvasive Ventilation and Place of Acetazolamide. In Pharmacology in Noninvasive Ventilation 2024 Feb 3 (pp. 83-91). Cham: Springer International Publishing.
3. Menteş O, Çelik D, Yildiz M, Kahraman A, Cirik MÖ, Eraslan Doğanay G, Ensarioğlu K, Babayiğit M, Kizilgöz D. Electrolyte Imbalance and Its Prognostic Impact on All-Cause Mortality in ICU Patients with Respiratory Failure. Medicina (Kaunas). 2025 Apr 1;61(4):642. doi: 10.3390/medicina61040642. PMID: 40282932; PMCID: PMC12028514.
4. Miller PE, Van Diepen S, Metkus TS, Alviar CL, Rayner-Hartley E, Rathwell S, Katz JN, Ezekowitz J, Desai NR, Ahmad T. Association between respiratory failure and clinical outcomes in patients with acute heart failure: analysis of 5 pooled clinical trials. Journal of cardiac failure. 2021 May 1;27(5):602-6.
5. Fimognari FL, De Vincentis A, Arone A, Baffa Bellucci F, Ricchio R, Antonelli Incalzi R. Clinical outcomes and phenotypes of respiratory failure in older subjects admitted to an acute care geriatric hospital ward. Internal and Emergency Medicine. 2024 Aug;19(5):1359-67.
6. Shankar-Hari M, Santhakumaran S, Prevost AT, Prevost A, Ward JK, Ward J, Marshall T, Bradley C, Calfee CS, Calfee C, Delucchi KL. Defining phenotypes and treatment effect heterogeneity to inform acute respiratory distress syndrome and sepsis trials: secondary analyses of three RCTs. Health Technology Assessment. 2021 Aug 3;8(10):1-04.
7. Zhang X, Miao X, Ding K, Wang J, Hu B, Hu X, Shen J, Liu C, Xu Y, Zhao X, Bao L. The relationship of partial pressure of carbon dioxide (PaCO2) with disease severity indicators such as BODE and GOLD in hospitalized COPD patients. International Journal of Clinical Practice. 2022;2022(1):4205079.
8. Tyagi D, Govindagoudar MB, Jakka S, Chandra S, Chaudhry D. Correlation of PaCO2 and ETCO2 in COPD patients with exacerbation on mechanical ventilation. Indian journal of critical care medicine: peer-reviewed, official publication of Indian Society of Critical Care Medicine. 2021 Mar;25(3):305.

9. Rezoagli E, Nova A, Carteaux G, Giani M, Grieco DL, Pettenuzzo T, Lucchini A, Navalesi P, Antonelli M, Foti G, Bellani G. A clinical guide to non-invasive respiratory support in acute respiratory failure: ventilation settings, technical optimization and clinical indications. Critical Care. 2025 Nov 18;29(1):496.
10. Plant PK, Owen JL, Elliott MW. Early use of non-invasive ventilation for acute exacerbations of chronic obstructive pulmonary disease on general respiratory wards: a multicentre randomised controlled trial. Lancet. 2000; 355:1931–5.
11. Ucgun I, Oztuna F, Dagli CE, Yildirim H, Bal C. Relationship of metabolic alkalosis, azotemia and morbidity in patients with chronic obstructive pulmonary disease and hypercapnia. Respiration. 2008; 76:270–4.
12. Brijker F, Heijdra YF, van den Elshout FJ, Folgering HT. Discontinuation of furosemide decreases $PaCO_2$ in patients with COPD. Chest. 2002; 121:377–82.
13. Brackett NC Jr, Cohen JJ, Schwartz WB. Carbon dioxide titration curve of normal man: effect of increasing degrees of acute hypercapnia on acid–base equilibrium. N Engl J Med. 1965; 272:6–12.
14. Mizock BA. The hepatosplanchnic area and hyperlactatemia: a tale of two lactates. Crit Care Med. 2001; 29:447–9.
15. Schiraldi F, Guiotto G. Equilibrio acido-base. Ossigeno. Fluidi & elettroliti. 2012. p. 45–53.
16. Brackett NC, Wingo CF, Muren O, Solano JT. Acid–base response to chronic hypercapnia in man. N Engl J Med. 1969; 280:124–30.
17. Alfaro V, Torras R, Ibáñez J, Palacios L. A physical-chemical analysis of the acid–base response to chronic obstructive pulmonary disease. Can J Physiol Pharmacol. 1996; 74:1229–35.