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THE ROLE OF ELECTROLYTE IMBALANCE IN ASSESSING DISEASE SEVERITY AND OUTCOMES IN ACUTE EXACERBATION OF COPD: A TERTIARY CARE HOSPITAL STUDY.

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ABSTRACT

BACKGROUND: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) significantly increase morbidity and mortality. Electrolyte imbalances are common in hospitalized patients with AECOPD, but their prevalence, clinical correlations, and impact on outcomes in South Asian tertiary care settings remain underexplored. Determining the prevalence of electrolyte anomalies, such as those involving sodium, potassium, chloride, calcium, and magnesium, in AECOPD and evaluating their correlation with the severity of the disease and in-hospital outcomes are the goals of this study. **OBJECTIVE:** The study's goal is to find out how common and what kinds of electrolyte imbalances patients with AECOPD have in a Karachi tertiary care hospital, as well as how they relate to the disease's severity and in-hospital outcomes. **DESIGN:** Since this research is a prospective observational study, data will be gathered starting at the time of patient admission and continuing throughout time. Without changing the management or treatment plan, the research will record clinical data in real time. An in-depth study of how electrolyte imbalances arise and connect to the course and results of disease will be possible by tracking patients during their hospital stay. **RESEARCH LOCATION:** The study was conducted in Karachi, Pakistan, at the Jinnah Postgraduate Medical Centre (Ward 12, Chest Medicine Centre). **RESEARCH DURATION:** The research was conducted from early February 2025 to the end of July 2025. **METHODS:** A prospective observational research was carried at the Department of Chest Medicine (Ward 12), Jinnah Postgraduate Medical Centre, Karachi, from February 2025 to July 2025. Consecutive patients ≥40 years with spirometry-confirmed COPD admitted with AECOPD were enrolled. Serum sodium, potassium, calcium, magnesium, and chloride were measured within 24 hours of admission. Electrolyte disturbances were defined using standard laboratory reference ranges. Outcomes included disease severity (GOLD criteria), ICU admission, need for mechanical ventilation, hospital stay, and in-hospital mortality. Logistic regression was used to recognize predictors of severe AECOPD. **RESULTS:** The study included 150 patients with a mean age of 63.8 ± 9.7 years, 74.7% of whom were male. 82.7% of patients had electrolyte abnormalities, with the most prevalent being hyponatraemia (57.3%), hypokalaemia (42.7%), hypochloremia (27.3%), hypocalcaemia (25.3%), and hypomagnesaemia (19.3%). **CONCLUSION:** Electrolyte imbalances—particularly hyponatremia, hypokalemia, and hypochloremia—are highly prevalent in AECOPD and are strongly linked to increased disease severity, prolonged hospitalization, and mortality. Routine electrolyte monitoring, including chloride, and prompt correction should be integral to the management of hospitalized AECOPD patients to improve outcomes.

KEYWORDS: acute exacerbation of COPD, electrolyte imbalance, hyponatremia, hypokalemia, hypochloremia, hypocalcemia, hypomagnesemia.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a considerable health issue world wide, being among the primary causes of illness and death. AECOPD contribute substantially to disease burden by accelerating lung function decline, increasing hospital admissions, and raising short- and long-term mortality rates[1]. Comorbidities, metabolic abnormalities, and systemic physiological stress frequently make management during exacerbations more difficult.

Electrolyte imbalance is one such metabolic disruption that is commonly seen in AECOPD and may be the cause as well as the result of poor outcomes. High prevalence rates have been reported in studies conducted in a variety of contexts. For example, in Nepal, dyselectrolytemia was present in 57% of AECOPD patients, with hyponatraemia (51%) and hypokalaemia (40%) being the most prevalent[2]. Strong inverse relationships between electrolyte levels and GOLD staging, oxygen saturation, and peak expiratory flow rate were observed in an Indian population, which revealed even higher rates—92% hyponatraemia and 86% hypokalaemia[3]. Strong inverse relationships between sodium and potassium levels and markers of disease severity, such as respiratory rate, GOLD stage, and mMRC dyspnoea score, were verified by another recent investigation[4].

Multicenter evidence also supports the significance of these anomalies in terms of prognosis. Hyponatraemia, which was found in 10.8% of AECOPD patients in Spain, was found to be independently associated with 30-day readmission, in-hospital mortality, and extended hospital stays[5]. Smoking, pneumonia, higher anion gap, high ESR, and hypomagnesaemia were risk factors for hyponatraemia in China. These variables linked to metabolic acidosis, SIADH, and systemic infection[6]. However, not all studies agree: A Swiss emergency department cohort found electrolyte disorders more common in AECOPD than in general ED patients, but without statistically significant associations with ICU admission, ventilation requirement, or mortality.[7] Beyond acute episodes, even stable-state hyponatremia in COPD has been shown to predict shorter survival and increased exacerbation frequency.[8]

Despite these findings, there is a notable gap in data from Pakistan and other low- to middle-income countrieswhere COPD burden is high, health system resources are limited, and nutritional and comorbidity profiles may differ from those in high-income settings. Most available studies are unicenter, have small sample sizes, or focus on a limited range of electrolytes, limiting their generalizability.

Given the potential of electrolyte disturbances to act as readily measurable and modifiable prognostic markers, understanding their prevalence and clinical impact in our setting could have important implications for early risk stratification and management. This research seeks to analyze the impact of electrolyte imbalances on disease severity and short-term outcomes in AECOPD patients hospitalized at a tertiary care facility in Karachi.

OBJECTIVE

To detect the frequency and types of electrolyte abnormalities in patients admitted with AECOPD at a tertiary care hospital in Karachi, and to assess their association with disease severity and in-hospital outcomes.

MATERAIL AND METHODS

Study Setting and Research Design

The prospective observational research carried at the Department of Chest Medicine (Ward 12), Jinnah Postgraduate Medical Centre (JPMC), Karachi, a tertiary care referral hospital serving a large and diverse population from urban and rural areas of Sindh and adjoining provinces. The study was carried out over a period of 6 months, (i.e., February 2025 to July 2025). 150 patients admitted with AECOPD were consecutively recruited from the inpatient service. AECOPD was defined according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2023 guidelines as an acute worsening of respiratory symptoms (sputum production, dyspnea and severe cough) exceeding the usual daily fluctuations, leading to a change in medication or hospital admission.

Criteria for Inclusion of Patients

1. Age over 40 years.
2. Based on clinical history, a confirmed diagnosis of COPD was made, smoking/exposure history, and spirometric evidence of post-bronchodilator $FEV_1/FVC < 0.70$.
3. Admission to hospital with AECOPD, diagnosed by attending pulmonologist.
4. Availability of serum electrolyte results within 24 hours of admission.

Criteria for Exclusion of Patients

1. Coexisting acute or chronic kidney disease.
2. Congestive heart failure (NYHA class III–IV).
3. Chronic liver disease.
4. Recent use of diuretics, corticosteroids in supraphysiologic doses, or electrolyte supplementation within the past 2 weeks.
5. Concomitant illnesses known to independently cause electrolyte disturbances (e.g., adrenal insufficiency, uncontrolled diabetes mellitus with hyperglycemic crisis).
6. Patients refusing consent.

Data Collection Procedure

On admission, clinical as well as demographic data were collected, including:

- Age, gender, BMI.
- Smoking status (current, former, never) and pack-years.
- COPD duration and previous GOLD stage.
- Number of exacerbations and hospitalizations in past 12 months.
- Comorbidities (hypertension, diabetes mellitus, ischemic heart disease, etc.).

Clinical assessment included heart rate, respiratory rate, blood pressure, oxygen saturation (SpO_2 on room air), mMRC dyspnea grade, and use of accessory muscles.

Severity of exacerbation was categorized using GOLD criteria and standard clinical parameters (PaO_2, $PaCO_2$, need for non-invasive or invasive ventilation).

Laboratory Investigations

Within **24 hours of admission**, venous blood samples were obtained for:

- **Serum sodium (Na^+), potassium (K^+), chloride (Cl^-), calcium (Ca^{2+}), magnesium (Mg^{2+})** — measured using ion-selective electrode method on a fully automated biochemistry analyzer.
- **Arterial blood gases (ABG)** for PaO_2, $PaCO_2$, pH, HCO_3^-.
- Complete blood count (CBC), renal function tests, and random blood glucose.

Outcome Measures

Primary outcome measures:

- Frequency and types of electrolyte disturbances in AECOPD patients.
- Association between electrolyte disturbances and exacerbation severity.

Secondary outcome measures:

- Number of days admitted in hospital.
- Requirement of ICU admission and mechanical ventilation (non-invasive/invasive).
- In-hospital mortality.

Ethical Practices

The research protocol received approval from the Institutional Review Board/Ethics Committee at JPMC, Karachi. Before the participation, consent in writing was received from all participant patients or their attendants. Throughout the study, patient confidentiality was ensured, and all data were anonymized for analysis.

Statistical Analysis

To examine the data, IBM SPSS Statistics version 26.0 was utilised. If applicable, continuous variables are given as the median (interquartile range, or IQR) or mean ± standard deviation (SD). Frequencies and percentages are used to report categorical variables. The chi-square test or Fisher's exact test was utilised to assess correlations amid categorical variables. Depending on the data distribution, either the Mann-Whitney U test or an independent t-test was used for continuous variables. Statistical importance was established as a p-value below 0.05. Using electrolyte values as covariates, multivariate logistic regression was used to find independent predictors of severe illness and death.

RESULTS

Baseline Characteristics

During the trial period, 150 patients with acute exacerbations of COPD were included. The mean age was **63.8 ± 9.7 years** (range 42–85), with a male predominance (**n = 112, 74.7%**). The majority were current or

former smokers (**n = 126, 84%**), with a mean smoking exposure of **39.5 ± 12.1 pack-years**.

The distribution of GOLD stage prior to admission was:

- Stage II: 18 (12.0%)
- Stage III: 64 (42.7%)
- Stage IV: 68 (45.3%)

The mean number of exacerbations in the preceding 12 months was **2.4 ± 1.2**.

Frequency of Electrolyte Disturbances

Overall, **electrolyte disturbances were present in 124 patients (82.7%)**.

- **Hyponatremia:** 86 patients (57.3%)
- **Hypernatremia:** 6 patients (4.0%)
- **Hypokalemia:** 64 patients (42.7%)
- **Hyperkalemia:** 8 patients (5.3%)
- **Hypochloremia:** 41 patients (27.3%)
- **Hypocalcemia:** 38 patients (25.3%)
- **Hypomagnesemia:** 29 patients (19.3%)

Multiple electrolyte abnormalities were observed in 54 patients (36%), most commonly the combination of hyponatremia and hypokalemia, followed by hyponatremia with hypochloremia.

Mean serum electrolyte levels on admission were:

- Sodium: **132.6 ± 4.8 mmol/L**
- Potassium: **3.42 ± 0.56 mmol/L**
- Chloride: **94.8 ± 4.6 mmol/L**
- Calcium: **8.26 ± 0.54 mg/dL**
- Magnesium: **1.58 ± 0.21 mg/dL**

Association Between Electrolyte Abnormalities and Disease Severity

- **Hyponatremia** was associated with significantly higher mMRC dyspnea grades (mean 3.6 ± 0.5 vs. 2.8 ± 0.4, $p < 0.001$), higher respiratory rate (27.8 ± 4.2 vs. 24.1 ± 3.5 breaths/min, $p < 0.001$), and lower mean SpO_2 on admission (83.2 ± 5.4% vs. 88.9 ± 4.1%, $p < 0.001$).
- **Hypokalemia** was linked to higher $PaCO_2$ levels and greater frequency of acute respiratory failure ($p = 0.004$).
- **Hypochloremia** correlated with increased $PaCO_2$ ($p = 0.009$) and was more frequent in severe AECOPD.
- **Hypomagnesemia** was significantly linked to disease severity and occurred more frequently in severe exacerbations ($p = 0.049$).

According to GOLD severity classification at presentation:

- Severe AECOPD (n = 102): Electrolyte disturbance prevalence = 91.2%
- Moderate AECOPD (n = 48): Electrolyte disturbance prevalence = 64.5% (Chi-square $p < 0.001$)

Table 1: Association Between Electrolyte Abnormalities and Severity

Electrolyte Abnormality	Severe AECOPD (n, %)	Moderate AECOPD (n, %)	p-value
Hyponatremia	78 (90.7%)	8 (9.3%)	<0.001
Hypokalemia	56 (87.5%)	8 (12.5%)	0.018
Hypocalcemia	32 (84.2%)	6 (15.8%)	0.047
Hypochloremia	35 (85.4%)	6 (14.6%)	0.031
Hypomagnesemia	24 (82.8%)	5 (17.2%)	0.049

Hospital Outcomes

- The mean hospital stay was **7.9 ± 3.1 days overall**, but significantly longer in patients with any electrolyte disturbance (**8.6 ± 3.2 vs. 5.4 ± 2.3 days, p < 0.001**).
- **ICU admission** was required in **38 patients (25.3%)**, of whom **34 (89.5%)** had at least one electrolyte abnormality.
- **Mechanical ventilation** (invasive or non-invasive) was needed in **46 patients (30.7%)**, with higher rates in hyponatremic (39.5%), hypokalemic (37.5%), hypochloremic (36.6%), and hypomagnesemic (34.5%) groups ($p < 0.05$).

Mortality

In-hospital mortality occurred in **11 patients (7.3%)**. Nine of these had multiple electrolyte imbalances at admission (most commonly hyponatremia + hypokalemia, followed by hyponatremia + hypochloremia).

Mortality was significantly associated with:

- Hyponatremia (OR = 3.2, 95% CI: 1.02–10.0, $p = 0.047$)

- Hypokalemia (OR = 2.9, 95% CI: 1.01–8.41, p = 0.049)
- Hypochloremia (OR = 2.6, 95% CI: 1.03–6.71, p = 0.042)
- Hypomagnesemia (OR = 2.4, 95% CI: 1.01–5.87, p = 0.048)

Multivariate Logistic Regression

After adjusting for age, sex, smoking history, and GOLD stage, independent predictors of severe AECOPD were:

- Hyponatremia (adjusted OR = 2.84; 95% CI: 1.47–5.49; p = 0.002)
- Hypokalemia (adjusted OR = 2.15; 95% CI: 1.14–4.08; p = 0.018)
- Hypocalcemia (adjusted OR = 1.92; 95% CI: 1.01–3.68; p = 0.047)
- Hypochloremia (adjusted OR = 1.88; 95% CI: 1.05–3.38; p = 0.034)
- Hypomagnesemia (adjusted OR = 1.76; 95% CI: 1.01–3.12; p = 0.049)

DISCUSSION

Our study confirms a notably high prevalence of electrolyte disturbances—especially hyponatremia, hypokalemia, and hypochloremia—in AECOPD patients, with significant associations to worse clinical outcomes. This is consistent with an Imphal-based study in India, which reported significantly lower serum sodium and chloride in AECOPD compared with stable COPD and healthy controls (mean Na: 135.2 mEq/L; Cl: 95.9 mEq/L; both $p < 0.01$). [9] Similarly, a Patna study observed markedly reduced sodium (128.85 ± 3.17 mEq/L) and potassium (3.29 ± 0.68 mEq/L) in acute exacerbations compared to controls, reinforcing our findings.[10]

In terms of prognostic implications, Lindner et al. found electrolyte disturbances more common in AECOPD patients presenting to the emergency department, although their study did not detect statistically significant associations with ICU admission, ventilation requirement, or mortality—highlighting that population and context may influence outcome impact.[11] Meanwhile, a multicenter cross-sectional study of 586 AECOPD patients identified smoking, community-acquired pneumonia, elevated anion gap, high ESR, and hypomagnesemia as independent predictors of hyponatremia, pointing toward mechanisms of metabolic acidosis and systemic inflammation behind dysnatremia.[12]

The prognostic value of hyponatremia extends beyond acute episodes. A Hong Kong longitudinal analysis found that stable-state hyponatremia predicted shorter overall survival (adjusted HR 1.74) and increased exacerbation frequency over an 8-year follow-up.[13] From a pathophysiological standpoint, hyponatremia in COPD may be due to inappropriate ADH secretion triggered by hypoxia or hypercapnia, compounded by SIADH and fluid retention in advanced disease.[14]

Hospital-based outcomes also support our results. In a Spanish cohort, hyponatremia in AECOPD was associated with longer hospital stay, more invasive ventilation days, and higher mortality—both in-hospital and post-discharge.[15] These findings were echoed in a respiratory therapy report summarizing multicenter data, which emphasized sodium deficiency as a warning sign for adverse prognosis in COPD.[16]

The link between hypokalemia and poor respiratory function is also well documented. Hypokalemia can exacerbate muscle weakness, impair diaphragmatic function, and predispose patients to arrhythmias—mechanisms that may explain its association with more severe disease and higher ICU admission in our cohort.[17] Furthermore, hypocalcemia and hypomagnesemia, while less frequent, may worsen neuromuscular dysfunction and contribute to respiratory muscle fatigue.[18]

Hypochloremia, observed in over one-quarter of our patients, is an often-overlooked abnormality in COPD exacerbations. Chloride plays a critical role in acid-base regulation, particularly through its influence on bicarbonate balance and maintenance of serum osmolality. In the context of AECOPD, low chloride levels can be both a marker and mediator of disease severity. Mechanistically, hypochloremia in COPD may arise from chronic hypercapnia leading to compensatory metabolic alkalosis, where renal bicarbonate retention is accompanied by chloride loss [9,19], diuretic use or poor nutritional intake (though excluded in our study, prior exposure cannot be completely ruled out), and increased

inflammatory and metabolic stress during acute exacerbations.

In our cohort, hypochloremia correlated with higher $PaCO_2$, increased ICU admissions, greater mechanical ventilation requirements, and mortality—indicating that it may reflect more advanced ventilatory failure and a higher burden of acid-base disturbance. These findings align with previous critical care literature suggesting that hypochloremia can impair respiratory drive and worsen CO_2 retention [19,21].

Collectively, these findings underscore that electrolyte disturbances in AECOPD are neither incidental nor benign. They reflect systemic dysregulation and carry measurable prognostic weight. Given that electrolytes are inexpensive and rapidly measurable, routine screening and early correction represent a pragmatic and potentially life-saving intervention, particularly in resource-limited healthcare settings like ours.

Strengths of our study include adherence to GOLD diagnostic criteria, comprehensive assessment of multiple electrolytes, and robust analysis of both clinical severity and outcomes. Limitations include single-center design, lack of outpatient follow-up, and inability to fully control for prior outpatient diuretic or steroid use.

Future research should focus on multicenter trials to assess whether proactive correction of electrolyte disturbances can reduce ICU admissions, shorten hospital stays, and improve survival, as well as mechanistic studies to better understand the interplay between systemic inflammation, hormonal regulation, and electrolyte balance in COPD.

CONCLUSION

This prospective study from a tertiary care hospital in Karachi demonstrates that electrolyte imbalances—particularly hyponatremia and hypokalemia—are highly prevalent in patients admitted with AECOPD and are significantly associated with increased disease severity, prolonged hospitalization, greater ICU utilization, and in-hospital mortality. These disturbances are not incidental findings; rather, they reflect underlying pathophysiological stressors such as hypoxia, hypercapnia, systemic inflammation, and hormonal dysregulation. Given their high frequency, ease of detection, and modifiable nature, routine assessment of electrolytes at admission should be considered an essential component of AECOPD management. Early recognition and timely correction may serve as cost-effective strategies to reduce adverse outcomes, especially in resource-limited settings. Future multicenter studies having longer follow-up are warranted to determine whether proactive electrolyte management can improve both short- and long-term survival in COPD patients and to further elucidate the mechanistic pathways linking electrolyte derangements to disease progression.

ETHICS APPROVAL: The ERC gave ethical review approval. **NO F.2.81/2025GLNL/257/JPMC DATED: 08/04/2025.**

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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AUTHORS' CONTRIBUTIONS:

All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

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