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Serum Electrolyte Alterations in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Hospital-Based Case-Control Study.

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Abstract

Background: Electrolyte imbalances frequently occur during acute exacerbations of chronic obstructive pulmonary disease (AECOPD) and can lead to clinical complications. However, comparative data on electrolyte abnormalities between AECOPD and stable chronic obstructive pulmonary disease (COPD) are scarce. This study investigated the characteristics and incidence of dyselectrolytemia in AECOPD and compared serum electrolyte levels with those of stable COPD patients. ***Methods:*** A hospital-based case-control study was conducted in the Departments of General Medicine and Pulmonology at a tertiary care hospital in Rajasthan, India, from September 2022 to September 2023. A total of 120 participants were enrolled, including 60 patients with AECOPD and 60 age- and sex-matched patients with stable COPD. Serum sodium, potassium, chloride, calcium, magnesium, and phosphorus levels were measured. Continuous variables were compared using the independent-samples t-test, while categorical variables were analyzed using the Pearson chi-square or Fisher's exact test. ***Results:*** Hypokalemia and hypochloremia were the most prevalent abnormalities, occurring in 100% of AECOPD patients. Hyponatremia and hypocalcemia were observed in 98.3%, followed by hypomagnesemia in 85.0%. Overall, 81.7% had abnormalities involving all five assessed electrolytes. AECOPD patients had significantly lower serum sodium, potassium, chloride, calcium, and magnesium levels than stable COPD patients ($p<0.0001$ for all). Phosphorus levels did not differ significantly between groups (3.54 ± 0.46 vs. 3.57 ± 0.30 mg/dL; $p=0.6726$). ***Conclusion:*** Dyselectrolytemia is highly prevalent in AECOPD, with concurrent abnormalities in multiple electrolytes being common. The routine assessment and timely correction of electrolyte disturbances warrant consideration as a critical aspect of AECOPD management.

Keywords: Acute Exacerbation; Chronic Obstructive Pulmonary Disease; Dyselectrolytemia; Electrolytes.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD), one of the most common diseases causing mortality, accounts for about 3.4 million deaths worldwide [1]. The crude prevalence of COPD in India has been estimated at 7.4% with biomass fuel smoke, tobacco smoking and occupational and ambient air pollution contributing to the high burden of the disease in the country [2]. COPD is defined as chronic bronchitis and emphysema with persistent symptoms of the respiratory system and airflow limitation that cannot be fully reversed, due to chronic exposure to noxious particles or gases [3]. The natural course of COPD is punctuated by acute exacerbations (AECOPD), defined as an acute worsening of respiratory symptoms, including increased dyspnea, cough, and sputum volume or purulence, necessitating additional therapy. Exacerbations worsen lung function, decrease the quality of life, and contribute to hospitalisation, health-care expenditure and death in COPD [4,5].

During an exacerbation, hypoxemia, hypercapnia, and acidosis of the respiratory system cause a disruption of renal and neurohormonal homeostasis with electrolyte disturbance often being the initial clinical manifestation [6]. Hypoxia and hypercapnia induce non-osmotic stimulation of production of arginine vasopressin and activation of the renin-angiotensin-

aldosterone system, which in turn affects water and solute handling of the kidney [7]. At the same time, there is much evidence that the pharmacological treatment of AECOPD, such as systemic corticosteroids and high dose nebulized SABA, leads to hypokalemia via intracellular potassium shift and renal kaliuresis [8,9]. Sodium, potassium and magnesium electrolyte disturbances are direct causes of impairment of neuromuscular conduction and respiratory muscle strength, and if not recognised can progress to cardiac arrhythmia, seizures, coma and death [10,11].

Even though there is a well-established pathophysiological relation, it is not common practice to routinely screen for COPD patients with dyselectrolytemia because clinical focus is on correcting hypoxemia and bronchospasm [12]. Hyponatremia, hypokalemia, hypochloremia and hypomagnesemia are common in AECOPD, as documented by multiple studies from India and other countries, but the incidence and severity of these disorders differ significantly between the studies and are dependent on the severity of the disease, nutritional status, and therapeutic practice. The severity of these derangements relative to clinically stable COPD patients, not healthy controls, is still relatively sparse. Therefore, the present study was undertaken to characterize the nature and frequency of dyselectrolytemia among patients with AECOPD and to compare their serum electrolyte levels with those of patients with stable COPD.

MATERIALS AND METHODS

Study Design and Setting: This hospital-based case-control study was conducted in the Department of General Medicine, in association with the Department of Pulmonology, at a tertiary care hospital in Rajasthan, India, from September 2022 to September 2023.

Participants: Patients were screened for those aged 40 years and older, who have clinical and spirometric diagnosis of COPD, according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD). The case group included those who were admitted to the emergency or ward with acute exacerbation of COPD. The patients in the control group were age- and sex-matched patients with stable COPD who had not had any COPD exacerbation or change in maintenance therapy in the previous 4 weeks.

Patients who were excluded included those who did not give informed consent in writing and those with a primary diagnosis of other chronic respiratory disease (bronchial asthma, active pulmonary tuberculosis, bronchiectasis or interstitial lung disease), pre-existing severe organ dysfunction likely to independently affect electrolyte balance (end-stage renal disease, decompensated chronic liver disease, or decompensated congestive heart failure), and those who did not want to receive routine COPD medication.

Sample Size: A total of 120 participants, comprising 60 patients with acute exacerbation of chronic obstructive pulmonary disease and 60 patients with stable chronic obstructive pulmonary disease, were enrolled in the study.

Data Collection: After obtaining written informed consent, a structured proforma used to record age, sex, dyspnea grading (modified Medical Research Council, mMRC) scale, duration of disease, smoking history (pack-years) and exposure to occupational dust and biomass fuel smoke (chulha exposure). General physical examination included vital signs, oxygen saturation and respiratory distress. Spirometric parameters (FEV1, FVC, FEV1/FVC) were extracted from recent records or carried out while clinically stable to ensure the base line grading for GOLD.

Laboratory Analysis: In cases, a random venous blood sample was drawn at the time of admission, prior to institution of corrective electrolyte therapy. Samples in the controls were collected during the outpatient visit. All the samples were analyzed within the institution central lab. Serum sodium and potassium was measured by ion-selective electrode (ISE) method, while serum chloride, calcium, magnesium and phosphorus were measured by standardised automated spectrophotometric procedure.

Statistical Analysis: Statistical Package for the Social Sciences (SPSS) version 27.0 was used to analyse the data collected in Microsoft Excel. The continuous variables were presented as mean ± SD and compared between groups by using the independent-samples Student t-test. The frequencies and percentages of categorical variables were compared with the Pearson chi-square test (or Fisher exact test if applicable). The p-values were taken as significant at a value < 0.05 (two-tailed).

Ethical Considerations: This study was done after receiving approval from the Human Research Ethics Committee (HREC), Geetanjali University, which considered and approved the research protocol. Informed consent was taken in written form from all participants before recruitment into the study, and this study has been performed following the Declaration of Helsinki (Ref. GU/HREC/EC/2022/2058).

RESULTS

Baseline Characteristics of Study Participants

The baseline characteristics of both the AECOPD and stable COPD group were similar with respect to age group, sex and chulha exposure with no statistically significant differences (p=0.086, 0.409 and 0.191, respectively). There was a significantly higher smoking prevalence among AECOPD patients compared to stable COPD patients (76.7% vs. 43.3%, p<0.001) and a significantly higher prevalence of occupational exposure (86.7% vs. 66.7%, p=0.010) (Table 1).

Nature and Frequency of Dyselectrolytemia in AECOPD

Hypokalemia and hypochloremia were the most common types of dyselectrolytemias in AECOPD populations, with 100% of patients having hypokalemia and hypochloremia. Multiple electrolyte abnormalities were present in patients with AECOPD, with hyponatremia being present in 59 patients (98.3%) and hypocalcemia in 51 patients (85.0%) and hypomagnesemia in 50 (85.3%) (Table 2).

Pattern of Dyselectrolytemia According to the Number of Abnormalities

Multiple electrolyte abnormalities were predominant among AECOPD patients, with 49 patients (81.7%) exhibiting abnormalities in all five assessed electrolytes and the remaining 11 patients (18.3%) having abnormalities in four electrolytes. No patients had only two or three electrolyte abnormalities, indicating a high burden of concurrent dyselectrolytemia in the study population (Table 3).

Comparison of Serum Electrolyte Levels Between AECOPD and Stable COPD

The levels of serum electrolytes were significantly lower in the AECOPD group than in stable COPD group for sodium (131.23 ± 2.09 vs. 138.58 ± 4.62), potassium (3.23 ± 0.05 vs. 4.42 ± 0.17), chloride (89.74 ± 4.04 vs. 99.78 ± 1.45), calcium (7.50 ± 0.37 vs. 7.96 ± 0.46), and magnesium (1.26 ± 0.03 vs. 1.94 ± 0.02 mg/dL), with all differences being statistically significant (p<0.0001). Conversely, there was no statistically significant difference between the levels of phosphorus among the two groups (3.54 ± 0.46 vs. 3.57 ± 0.30 mg/dL, p=0.6726) (Table 4).

Table 1. Baseline Characteristics of Study Participants According to Study Group

Variable	Category	AECOPD (n=60)	Stable COPD (n=60)	χ^2 value	P-value
Age group	<40 years	2 (3.3%)	4 (6.7%)	6.582	0.086
	41–50 years	5 (8.3%)	6 (10.0%)		
	51–60 years	44 (73.3%)	31 (51.7%)		
	>60 years	9 (15.0%)	19 (31.7%)		
Sex	Female	14 (23.3%)	18 (30.0%)	0.682	0.409
	Male	46 (76.7%)	42 (70.0%)		
Smoking	No	14 (23.3%)	34 (56.7%)	13.889	**<0.001**
	Yes	46 (76.7%)	26 (43.3%)		
Occupational exposure	No	8 (13.3%)	20 (33.3%)	6.708	**0.010**
	Yes	52 (86.7%)	40 (66.7%)		
Chulha exposure	No	49 (81.7%)	54 (90.0%)	1.713	0.191
	Yes	11 (18.3%)	6 (10.0%)		

Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; COPD, chronic obstructive pulmonary disease; χ^2, chi-square; n, number of participants.

Table 2. Nature and Frequency of Dyselectrolytemia in Patients with Acute Exacerbation of COPD

Serum Electrolyte	Nature of Abnormality	Frequency (n)	Percentage (%)
Sodium	Hyponatremia	59	98.3
	Normal	1	1.7
Potassium	Hypokalemia	60	100.0
Chloride	Hypochloremia	60	100.0
Calcium	Hypocalcemia	59	98.3
	Normal	1	1.7
Magnesium	Hypomagnesemia	51	85.0
	Normal	9	15.0

Abbreviations: COPD, chronic obstructive pulmonary disease; n, number of patients.

Table 3. Pattern of Dyselectrolytemia According to the Number of Electrolyte Abnormalities Among Patients with Acute Exacerbation of COPD

Number of abnormalities	Frequency (n)	Percentage (%)
2 abnormalities	0	0.0
3 abnormalities	0	0.0
4 abnormalities	11	18.3
5 abnormalities	49	81.7

Abbreviations: COPD, chronic obstructive pulmonary disease; n, number of patients.

Table 4. Comparison of Serum Electrolyte Levels Between Acute Exacerbation of COPD and Stable COPD

Electrolytes	Acute Exacerbation (n=60)	Controls (n=60)	Mean Difference	P-value
Serum Sodium	131.23 ± 2.09	138.58 ± 4.62	7.35	**<0.0001**
Serum Potassium	3.23 ± 0.05	4.42 ± 0.17	1.19	**<0.0001**
Serum Chloride	89.74 ± 4.04	99.78 ± 1.45	10.04	**<0.0001**
Serum Calcium	7.50 ± 0.37	7.96 ± 0.46	0.46	**<0.0001**
Serum Magnesium	1.26 ± 0.03	1.94 ± 0.02	0.68	**<0.0001**
Serum Phosphorus	3.54 ± 0.46	3.57 ± 0.30	0.03	0.6726

Abbreviations: COPD, chronic obstructive pulmonary disease; n, number of patients.

DISCUSSION

The mean serum sodium in our AECOPD cohort (131.23 ± 2.09 mEq/L) was significantly lower than in stable controls (138.58 ± 4.62 mEq/L, p<0.0001), a finding that closely mirrors previously published data. Maklad and Basiony reported nearly identical values of 131 ± 4.45 mEq/L in cases versus 138 ± 2.28 mEq/L in controls [13]. Harshvardhan et al reported a mean sodium of 131.7 ± 4.07 mEq/L in AECOPD compared with 138.66 ± 3.83 mEq/L in stable patients [14]. Similarly, Goli et al observed a mean sodium of 132 ± 5.65 mEq/L in COPD patients against 140 ± 2.28 mEq/L in controls,7 and Das et al reported comparable figures of 133 ± 6.86 mEq/L versus 142 ± 2.28 mEq/L [12,15]. Rashid similarly documented a mean sodium of 131.55 ± 5.66 mEq/L in AECOPD, with hyponatremia present in 70% of patients [16]. The consistency of these findings across geographically diverse Indian and Egyptian cohorts supports a shared underlying mechanism. Hypoxemia and hypercapnia during exacerbation trigger a non-osmotic surge in arginine vasopressin release and activation of the renin-angiotensin-aldosterone system, promoting free-water retention in the renal collecting ducts and consequent dilutional hyponatremia [17].

Hypokalemia was universal in our AECOPD cohort (mean 3.23 ± 0.05 mEq/L) compared with controls (4.42 ± 0.17 mEq/L, p<0.0001). This finding is consistent with several prior reports: Goli et al documented a mean potassium of 3.29 ± 0.96 mEq/L,7 Das et al reported 3.39 ± 0.96 mEq/L,10 and Rashid found 3.20 ± 0.44 mEq/L with hypokalemia present in 76.6% of patients [12,15,16]. Rathore et al similarly reported serum potassium below 3.5 mmol/L in 52% of acute exacerbation patients compared with only 20% of stable patients [18].

Serum chloride was significantly reduced in the AECOPD group (89.74 ± 4.04 mEq/L) relative to controls (99.78 ± 1.45 mEq/L, p<0.0001), with hypochloremia present in all cases. This finding parallels the hydro-electrolyte pattern described by Terzano et al in patients hospitalized for hypercapnic COPD exacerbation, in whom combined hyponatremia and hypochloremia were common and correlated with the severity of the underlying acid-base disturbance and the need for non-invasive ventilation [19]. Rathore et al similarly reported chloride below 98 mmol/L in 58% of acute exacerbation patients versus 36% of stable patients [18].

Mean serum calcium was significantly lower in cases (7.50 ± 0.37 mg/dL) than controls (7.96 ± 0.46 mg/dL, p<0.0001), with hypocalcemia present in 98.3% of AECOPD patients. Bhansali et al reported comparable values of 7.53 ± 0.53 mg/dL in exacerbation patients, and Rathore et al found calcium below 8.7 mg/dL in 80% of acute exacerbation patients compared with 68% of stable patients [18,20].

Hypomagnesemia showed one of the largest relative differences in our cohort, with a mean magnesium of 1.26 ± 0.03 mg/dL in cases against 1.94 ± 0.02 mg/dL in controls (p<0.0001), affecting 85.0% of AECOPD patients. Bhansali et al reported a very similar magnitude of reduction (1.18 ± 0.22 mg/dL),13 and Rathore et al documented magnesium below 1.30 mmol/L in 72% of acute exacerbation patients compared with only 12% of stable patients [18,20]. Maklad and Basiony reported a comparatively milder reduction (1.85 ± 0.17 mg/dL in cases versus 2.2 ± 0.14 mg/dL in controls), suggesting that the severity of magnesium depletion may vary with exacerbation severity and background nutritional status [13].

Unlike the other electrolytes studied, serum phosphorus did not differ significantly between the groups in our cohort, with a mean level of 3.54 ± 0.46 mg/dL in AECOPD patients compared with 3.57 ± 0.30 mg/dL in stable COPD controls (p=0.6726). A closely comparable finding was reported by Deep et al, who observed serum phosphate levels of 3.554 ± 1.0726 mg/dL in AECOPD patients and 3.565 ± 0.7702 mg/dL in stable COPD patients, with no significant difference between the groups (p=0.960) [21].

CONCLUSION

Dyselectrolytemia was frequently observed in patients experiencing acute exacerbations of COPD, with several concurrent electrolyte imbalances being common. Compared to patients with stable COPD, those with acute exacerbations exhibited significantly reduced serum concentrations of sodium, potassium, chloride, calcium, and magnesium. In contrast, serum phosphorus levels did not differ between the two groups. These observations underscore the necessity of regular electrolyte monitoring and prompt correction of detected abnormalities during acute exacerbations. Further studies with larger cohorts and extended follow-up periods are recommended to corroborate these results and ascertain the prognostic impact of specific electrolyte disturbances on clinical endpoints.

Ethical Considerations

The study was approved by the Human Research Ethics Committee, Geetanjali University (Ref. No. GU/HREC/EC/2022/2058). Written informed consent was obtained from all participants, and the study was conducted in accordance with the Declaration of Helsinki.

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None.

Author Contributions

All authors contributed to the conception and design of the study, data collection, analysis and interpretation of data, and drafting and critical revision of the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

Conflict of Interest

The authors declare that they have no conflict of interest.

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