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Analysis of Serum Electrolytes in Acute Exacerbations of COPD

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A B S T R A C T

Background: Acute exacerbations of Chronic Obstructive Pulmonary Disease (COPD) significantly contribute to patient morbidity and mortality. Although electrolyte imbalances may influence the course and severity of these exacerbations, they are not well characterized in clinical practice. **Objectives:** To assess the pattern and frequency of serum electrolyte abnormalities during acute exacerbations of COPD compared to the stable disease state, and to explore their association with clinical parameters and disease severity. **Methods:** A hospital-based study was conducted involving 120 COPD patients—60 experiencing acute exacerbations and 60 in a stable phase. Data collected included demographics, clinical features, pulmonary function tests, and serum sodium and potassium levels. In the exacerbation group, electrolytes were measured at both admission and discharge. **Results:** Patients with acute exacerbations were older (mean age: 65.62 vs. 63.15 years; p=0.038) and more likely to be current smokers (33.3% vs. 0%; p<0.001). Hyponatremia and hypokalemia were significantly more common in the exacerbation group (95.0% and 91.7%, respectively) compared to the stable group (both 0%; p<0.001). Mean serum sodium and potassium levels were substantially lower during exacerbation (128.95 mEq/L and 3.07 mEq/L) than in the stable phase (138.17 mEq/L and 4.01 mEq/L; p<0.001). Strong inverse correlations were found between electrolyte levels and MMRC dyspnea scores (sodium: r = –0.76; potassium: r = –0.70), GOLD stages (sodium: r = –0.85; potassium: r = –0.81), and respiratory rate, with positive correlations observed with oxygen saturation (p<0.001 for all). **Conclusion:** Electrolyte disturbances, particularly hyponatremia and hypokalemia, are highly prevalent during acute COPD exacerbations and show strong correlations with clinical markers of disease severity. Routine monitoring and timely correction of electrolyte imbalances should be integrated into the management of COPD exacerbations.

Key Words: Chronic Obstructive Pulmonary Disease (COPD); Acute Exacerbation; Electrolyte Imbalance; Hyponatremia; Hypokalemia.

INTRODUCTION-

Chronic Obstructive Pulmonary Disease (COPD) is one of the topmost causes of death worldwide. More than 3 million people died of COPD in 2012 accounting for 6% of all deaths globally. COPD is a major cause of chronic morbidity and mortality throughout the world; many people suffer from this disease for years and die prematurely from it or its complications. Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population. (1)

Chronic Obstructive Pulmonary Disease (COPD) is defined by Global Initiative for Chronic Obstructive Lung Disease (GOLD) as "a common preventable and treatable disease and is characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lung to noxious particles or gases" (1).

An exacerbation of COPD is an acute worsening of respiratory symptoms beyond normal day-to-day variations. It is a significant cause of mortality and morbidity and categorized in terms of clinical presentations or healthcare utilization. Exacerbations may cause increased dyspnea, productive cough with altered sputum, and fever.

The acute exacerbation of COPD patients, present not only with the features of acute respiratory infections, but also several metabolic disorders like hyponatremia, hypokalemia, hypomagnesemia, hyperbilirubinemia, elevated renal parameters arising either because of the disease process or because of the therapy like beta 2 agonists, steroids, diuretics.
Very often they are missed, thus overlooking the coexisting metabolic abnormalities may contribute to great morbidity and mortality. Serum electrolytes are important for nerve conduction and muscle contraction. Hyponatremia, hypokalemia, and other electrolyte disorders cause cardiac arrhythmias, convulsions, coma, renal insufficiency, hampered nerve muscle conduction and respiratory muscle paralysis and even death.

METHODOLOGY

Source of data: This study is conducted at JJM Medical College, Davangere over a period of one and half year. The study was conducted on patients admitted to the Pulmonology medicine ward at Bapuji Hospital affiliated with JJM Medical College, Davangere.

Methods of Collection of Data:
Study design: Hospital based study.
Study period: June 2023 to March 2025
Place of study: JJM Medical college Bapuji Hospital, Davangere

Inclusion Criteria:
Patient willing to give informed consent.
Patients that present with acute exacerbation of COPD.

Exclusion Criteria:
Patient not willing to give informed consent.
Pregnant women
Kidney failure patients
Liver failure patients
Congestive cardiac failure
Diabetic ketoacidosis

Methodology:
Diagnosis is made based on history, clinical examination, pulmonary function test, modified medical research council grading of dyspnea. Age and sex matched healthy controls enrolled from general population. Two samples of serum electrolytes level measured at the time of admission and at the time of discharge of the patients.

The patient's questionaries in Annexure-2 are filled out to assess the demographic of the patient and also the pulmonary history to base MMRC assessment.

Statistical Analysis:
All the data will be collected and entered MS Excel and statistical analysis will be done on the data set. Numbers and percentages are used in reporting categorical values. Mean and standard deviation are used while reporting numerical values. Independent t-test, chi-square test and other suitable tests of significance are applied at the time of statistical analysis. Statistical significance will be considered if p value was less than 0.05, confidence interval of 95%

Investigations
1. Clinical history
2. Spirometer Function Test – Take atleast 3 reading of forced expiration of breath after full inspiration. This is to calculate FEV1 and FVC and thus FEV1/FVC parameters in order to assess the severity exacerbation of COPD
3. Two Blood samples for each Patient – To assess the serum electrolyte of patients at the time of admission and time of discharge, blood samples need to be taken in the morning as diet and exercise affect the electrolyte balance.

SAMPLE SIZE OF ESTIMATION
Based on literature review, "Evaluation of Serum Electrolytes in Patients of Chronic Obstructive Pulmonary Disease" By Hitesh Kumar et al (14), sample size is determined by the statistician as follows. $n=((Z\alpha+Z\beta)2*S2*2)(d2)$;
Zα = Standard normal deviate for α of 0.05 =1.96

Zβ = Standard normal deviate for β of 0.2 = 0.842
S1 = Standard deviation of calcium in stable COPD group = 1.81mg/dl
S2 = Standard deviation of calcium in acute COPD group =1.58mg/dl
S = Common standard deviation between two groups
D = clinically meaningful difference = m1 – m2 = 0.71mg/dl
Then n = 45. 45 in each group of acute exacerbation COPD and stable COPD

RESULTS

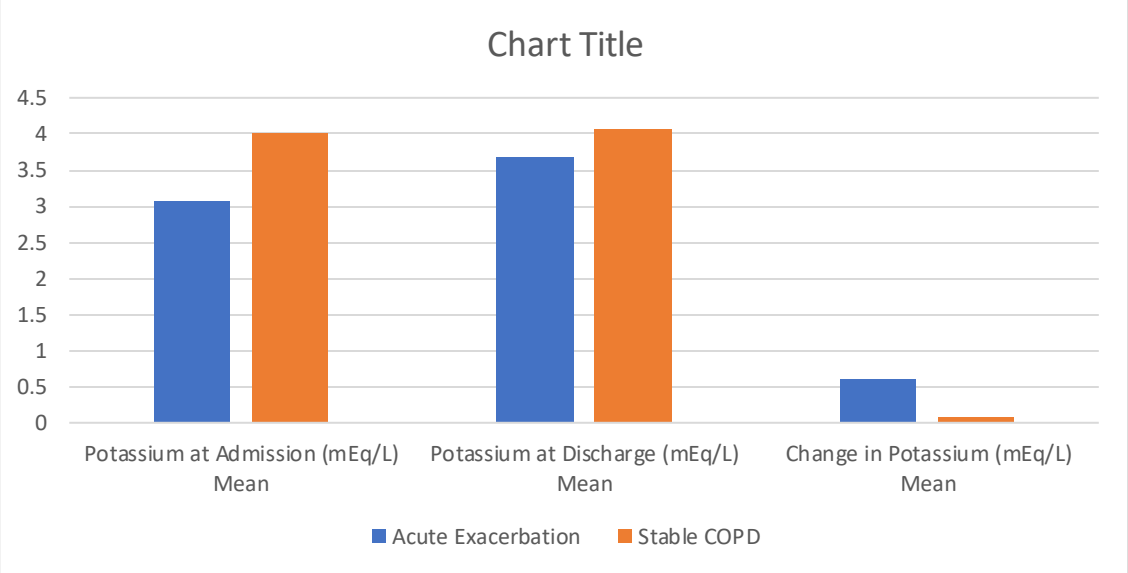
The prevalence of electrolyte abnormalities was strikingly different between the groups ($p < 0.001$). Hyponatremia (<135 mEq/L) was present in 95.0% (n=57) of acute exacerbation patients but in none of the stable COPD patients (0.0%), with $\chi^2 = 110.53$. Similarly, hypokalemia (<3.5 mEq/L) affected 91.7% (n=55) of acute exacerbation patients and none of the stable patients (0.0%), with $\chi^2 = 103.33$. No patients in either group had hypernatremia (>145 mEq/L) or hyperkalemia (>5.0 mEq/L). These findings demonstrate that electrolyte disturbances, particularly hyponatremia and hypokalemia, are almost universal in acute COPD exacerbations but absent in stable disease.

Serum Sodium Levels

Variable	Acute Exacerbation (n=60)	Stable COPD (n=60)	Statistics
Sodium at Admission (mEq/L) Mean ± SD	128.95 ± 3.83	138.17 ± 1.89	t = 16.87, p < 0.001
Sodium at Discharge (mEq/L) Mean ± SD	135.38 ± 2.32	139.13 ± 1.87	t = 9.83, p < 0.001
Change in Sodium (mEq/L) Mean ± SD	6.43 ± 1.81	0.97 ± 0.18	t = 23.52, p < 0.001

Serum Potassium Levels

Variable	Acute Exacerbation (n=60)	Stable COPD (n=60)	Statistics
Potassium at Admission (mEq/L) Mean ± SD	3.07 ± 0.26	4.01 ± 0.18	t = 22.96, p < 0.001
Potassium at Discharge (mEq/L) Mean ± SD	3.69 ± 0.19	4.08 ± 0.19	t = 11.32, p < 0.001
Change in Potassium (mEq/L) Mean ± SD	0.62 ± 0.15	0.08 ± 0.03	t = 26.97, p < 0.001



Electrolyte Disturbances at Admission

Electrolyte Disturbance	Acute Exacerbation (n=60)	Stable COPD (n=60)	Statistics
Hyponatremia (<135 mEq/L)	57 (95.0%)	0 (0.0%)	$\chi^2 = 110.53$, p < 0.001
Hypernatremia (>145 mEq/L)	0 (0.0%)	0 (0.0%)	-
Hypokalemia (<3.5 mEq/L)	55 (91.7%)	0 (0.0%)	$\chi^2 = 103.33$, p < 0.001
Hyperkalemia (>5.0 mEq/L)	0 (0.0%)	0 (0.0%)	-

DISCUSSION

This study provides a comprehensive evaluation of serum electrolyte disturbances in patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) compared to those with stable disease. Findings reveal a high prevalence of hyponatremia and hypokalemia during exacerbations, with strong correlations to clinical severity markers, highlighting their potential pathophysiological and therapeutic significance.

Demographic and Clinical Characteristics

Patients with acute exacerbations were significantly older than those with stable COPD (65.62 vs. 63.15 years, p=0.038), consistent with prior studies indicating age as an independent risk factor for exacerbations. Gender distribution was similar across groups (76.7% vs. 78.3% male, p=0.823), aligning with studies reporting no significant gender impact on exacerbation rates. However, current smoking was strongly associated with exacerbation (33.3% vs. 0%, p<0.001), corroborating evidence linking active smoking to increased exacerbation risk. Both Hoogendoorn et al.[5] and García-Sanz et al.[6] provide strong evidence that increasing age is significantly associated with a higher risk and frequency of COPD exacerbations. Hoogendoorn et al.[5] in a longitudinal study involving 738 COPD patients, reported that individuals aged over 65 experienced a significantly greater number of annual exacerbations (2.14; 95% CI: 1.87–2.43) compared to younger patients (1.67; 95% CI: 1.41–1.95), with a p-value of <0.001. Similarly, García-Sanz et al.[6] in a prospective cohort study of 543 patients, found that age was an independent predictor of exacerbation risk (OR 1.03; 95% CI: 1.01–1.06; p = 0.007), indicating that each additional year of age increased the risk of exacerbations by approximately 3%.

Clinical Severity and Pulmonary Function

Exacerbation patients exhibited significantly higher MMRC dyspnea scores (3.22 vs. 1.47, p<0.001) and worse pulmonary function parameters (FEV_1% predicted: 33.28% vs. 44.62%, p<0.001). GOLD stage distribution further confirmed disease severity, with 55% of exacerbation patients in GOLD 3–4 compared to 1.7% in the stable group (p<0.001). These findings align with established evidence linking lower FEV_1 and advanced GOLD stages with higher exacerbation risk [4]. Han et al.[7] in their analysis of the COPDGene study comprising 1,843 patients, found a significant association between reduced lung function and increased exacerbation frequency. The study reported that frequent exacerbators had a significantly lower mean FEV_1% predicted (42.3%) compared to non-exacerbators (57.7%), with the difference reaching strong statistical significance (p < 0.001). These findings underscore the role of impaired lung function as a key determinant of exacerbation risk in COPD.

Electrolyte Disturbances

Hyponatremia was observed in 95% of exacerbation cases, significantly higher than previously reported. Mean sodium levels were markedly lower in the exacerbation group at admission (128.95 mEq/L vs. 138.17 mEq/L, p<0.001)[2], improving significantly by discharge (135.38 mEq/L, p<0.001)[3]

Similarly, hypokalemia was prevalent in 91.7% of exacerbation patients, with admission potassium levels significantly reduced (3.07 vs. 4.01 mEq/L, p<0.001)[3], improving with treatment (3.69 mEq/L at discharge, p<0.001). Several studies have documented varying prevalence rates of hypokalemia during acute exacerbations of COPD. Ganapathy et al.[8] reported that 47.2% of 125 hospitalized patients with COPD exacerbation exhibited hypokalemia. In a similar context, Ravindra et al.[9] found a hypokalemia prevalence of 37.5% among 184 patients with acute exacerbations, which was significantly higher compared to control subjects (p < 0.001). These findings highlight the common occurrence of hypokalemia in the setting of COPD exacerbations.

Correlations with Disease Severity and Strong negative correlations were found between electrolyte levels and MMRC scores (sodium: r = –0.76; potassium: r = –0.70), GOLD stage (sodium: r = –0.85; potassium: r = –0.81), and respiratory rate. Positive correlations were noted with oxygen saturation. These findings suggest that electrolyte abnormalities reflect and may exacerbate clinical deterioration during acute exacerbations. Karadag et al.[10] demonstrated a significant negative correlation between serum potassium levels and the severity of dyspnea in patients experiencing acute COPD exacerbations. The study reported a correlation coefficient of r = –0.58, with a p-value < 0.001, indicating that lower potassium levels were strongly associated with more severe dyspnea symptoms.

Pathophysiological Insights-Hyponatremia may result from inappropriate antidiuretic hormone secretion due to hypoxia and inflammation, while hypokalemia may be driven by beta-agonist use, corticosteroids, and intracellular potassium shifts. These mechanisms underline the complex interplay between COPD pathophysiology and electrolyte homeostasis. Clinical Implications-Electrolyte disturbances are common and clinically relevant in acute COPD exacerbations. Their presence correlates with disease severity and may affect outcomes such as hospital stay, symptom resolution, and need for ventilatory support. Routine monitoring and correction of these abnormalities should be considered an integral part of COPD exacerbation management. Further research is warranted to determine prognostic value and guide targeted therapeutic strategies.

CONCLUSION

This comprehensive study evaluated serum electrolyte disturbances in patients with acute exacerbation of COPD compared to those with stable disease. Our findings demonstrate that electrolyte abnormalities, particularly hyponatremia and hypokalemia, are exceptionally prevalent during acute COPD exacerbations, affecting 95.0% and 91.7% of patients, respectively. These disturbances demonstrate strong correlations with established markers of disease severity, including MMRC dyspnea scores, GOLD stages, oxygen saturation, and respiratory rate.

The consistently significant associations between electrolyte levels and various clinical parameters suggest that electrolyte disturbances are not merely laboratory abnormalities but integral components of the pathophysiological processes underlying COPD exacerbations. The progressive decrease in both sodium and potassium levels with increasing GOLD stage severity further supports this relationship. While treatment resulted in significant improvements in electrolyte levels, many patients still had abnormal values at discharge, which may have implications for long-term outcomes.

Our findings have important clinical implications for the management of COPD exacerbations. First, routine monitoring of electrolyte levels should be considered standard practice in all patients presenting with acute exacerbations. Second, the presence of significant electrolyte disturbances may serve as a marker of exacerbation severity and potentially guide treatment intensity. Third, targeted correction of electrolyte abnormalities should be integrated into comprehensive management protocols for COPD exacerbations.

Future research should explore whether electrolyte disturbances precede and predict exacerbations, evaluate the impact of targeted electrolyte correction on clinical outcomes, and investigate the underlying pathophysiological mechanisms. Additionally, the potential role of electrolyte parameters as prognostic markers in COPD exacerbations deserves further exploration.

In conclusion, electrolyte disturbances represent significant and previously under appreciated aspects of COPD exacerbations that correlate strongly with disease severity. Clinicians should be vigilant for these abnormalities when managing acute exacerbations, and further research is needed to fully elucidate their clinical significance and therapeutic implications.

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