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# EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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#### Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a common, preventable and treatable chronic lung disease and is the third leading cause of death worldwide, affecting both men and women. Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) patients present with many metabolic disorders, including electrolyte imbalance. The objective is to estimate and compare the levels of serum electrolytes (sodium, potassium and chloride) in COPD patients and controls. Materials and Methods: This is a cross-sectional study conducted in the Department of Biochemistry in collaboration with the Department of Respiratory Medicine, RIMS, Imphal. The study included 90 COPD patients (47 AECOPD and 43 stable COPD) and 90 controls. Serum electrolytes were estimated using Beckman Coulter DxC 700 AU autoanalyzer. Result: In this study, we found that serum sodium in cases (136.5±4.4 mEq/L) was significantly lower (P=0.001) as compared to controls (138.3±2.2 mEq/L). Furthermore, serum chloride levels in cases (97.8±4.7 mEq/L) were also significantly low (P=0.001) as compared to controls (99.8±2.7). It was also found that serum sodium (135.2 mEq/L; p=0.003) and serum chloride (95.9 mEq/L; p<0.001) were significantly lower among the patients with acute exacerbation of COPD as compared to stable COPD patients. Conclusion: This study demonstrated decreased serum sodium and chloride levels in patients with AECOPD. Therefore, serum electrolyte levels should be monitored routinely in AECOPD patients.

## **INTRODUCTION**

Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide, affecting both men and women and causing 3.23 million deaths in 2019.<sup>[1]</sup> It is defined as a disease state characterized by airflow limitation and persistent respiratory symptoms that are not fully reversible.<sup>[2]</sup> Acute exacerbations of COPD (AECOPD) are defined as acute events characterized by dyspnoea, cough and/or sputum that is beyond normal day-to-day variations warranting a change in regular medication and/or hospitalization.<sup>[3]</sup>

The cause of AECOPD is multifactorial, and the viral infection or levels of air pollutants in the environment may exacerbate the existing inflammation in the airway, which will predispose to secondary bacterial infections.<sup>[4]</sup> The economic and social burden created by AECOPD is substantial and increasing. Therefore,

it is crucial to identify factors associated with exacerbation and poor outcomes.<sup>[5]</sup> Severe exacerbations of COPD are associated with worse survival consequences.<sup>[6]</sup>

AECOPD patients present with a number of metabolic disorders hyponatremia, such as hypokalaemia, hypomagnesemia, hyperbilirubinemia, elevated transaminases, blood urea and creatinine which may be due to the disease process itself or, as a consequence of the treatment (such as beta2 agonists, steroids, diuretics etc).<sup>[7]</sup> The electrolyte imbalances impair smooth muscle and skeletal muscle contraction as well as nerve conduction, which leads to respiratory muscle weakness and cardiac arrhythmias and, in turn, will lead to poor outcomes.[8]

In hospitalized patients, hyponatremia is the most common electrolyte disorder among the elderly and women and in the presence of comorbidities that may contribute substantially to mortality and morbidity.<sup>[9-14]</sup> During acute exacerbations, chronic hypoxia and hypercapnia due to underlying pulmonary disease, heart failure or renal insufficiency, use of diuretics, syndrome of inappropriate antidiuretic hormone secretion (SIADH), malnutrition and poor intake are the factors contributing to hyponatremia.<sup>[15]</sup> Hypochloraemia is caused due to respiratory acidosis with metabolic alkalosis and chronic hypercapnia.<sup>[16,17]</sup>

Although most of these electrolyte imbalances are correctable, very often, they are overlooked or confuse the diagnosis, and it may contribute to a great deal of morbidity and mortality. Therefore, early recognition and prompt treatment of these metabolic abnormalities are crucial.

In this study, we aim to estimate and compare the levels of serum electrolytes in COPD patients and controls.

## **MATERIALS AND METHODS**

This cross-sectional study was conducted in the Department of Biochemistry and Respiratory Medicine, Regional Institute of Medical Sciences (RIMS), Imphal, Manipur, India, from March 2022 to March 2025. The study was approved by the Research Ethics Board, RIMS, Imphal.

#### **Inclusion Criteria**

Diagnosed cases of COPD patients with symptoms of acute exacerbations were identified using GOLD criteria.[18] Participants whose ages were 40 years and above and who gave written consent to participate in the study voluntarily were included. Healthy individuals were also included as controls for comparison.

#### **Exclusion Criteria**

- 1. COPD patients hospitalized for causes other than COPD exacerbation.
- 2. COPD patients requiring mechanical ventilation.
- 3. Patients with pre-existing renal, hepatic, endocrinal or cardiac illness.

### Methods of Data and Sample Collection

Before starting the study, informed written consent was obtained from all the participants. Eligible participants with AECOPD and stable COPD were recruited from the Respiratory Medicine outpatient department (OPD) and wards of RIMS, Imphal. When one patient with AECOPD or stable COPD was recruited, one eligible healthy participant was also recruited conveniently from the patient party or OPD attendees. 5ml venous blood sample was collected in a plain vial and was then centrifuged for 10 minutes at 3000 rpm in a centrifuge machine, and serum electrolytes were estimated using ion-selective electrodes method,<sup>[19]</sup> using Beckman Coulter DxC AU 700 autoanalyzer with a cut-off range of serum sodium: 136-146 mEq/L, serum potassium: 3.5-5.1 mEq/L and serum chloride: 96-107 mEq/L.

**Statistical analysis:** The collected data were analyzed using IBM: SPSS version 26.0 for Windows. Continuous data such as age, SBP, DBP,

BMI, serum sodium, serum potassium and serum chloride were expressed as mean  $\pm$  SD. Independent samples t-test was used to compare the levels of sodium, potassium and chloride in cases and controls. A p-value <0.05 was taken as statistically significant.

## RESULTS

[Table 1 and Figure 1] show that the mean age of the study participants in Group 1 was 73.3 years, and Group 2 was 71.8 years, which was comparable between the groups (p=0.197). Table 2 and Figure 2 show that 52.2% of cases with COPD were diagnosed with Acute exacerbation of COPD in our study. [Table 3 and Figure 3] show that the study participants were comparable between the groups with respect to gender (p=0.881). [Table 4] shows no significant differences in the baseline characteristics (age, systolic blood pressure [SBP], diastolic blood pressure [DPB] and body mass index [BMI]) in the two groups. [Table 5 and Figure 5] show that the mean serum sodium levels were significantly lower among the patients with COPD (Group 1) compared to those without COPD in Group 2 (136.5 mEq/L vs 138.3 mEq/L; p=0.001). [Table 6] and Figure 6 show that the mean serum potassium levels were comparable between the groups (4.5 mEq/L in Group 1 vs 4.4 mEq/L in Group 2; p=0.706). Table 7 and Figure 7 show that the mean serum chloride levels were significantly lower among the patients with COPD (Group 1) compared to those without COPD in Group 2 (97.8 mEq/L vs 99.8 mEq/L; p=0.001). Table 8 shows that serum sodium (135.2 mEq/L; p=0.003) and serum chloride (95.9 mEq/L; p<0.001) were significantly lower among patients with acute exacerbation of COPD as compared to stable COPD. With regard to serum potassium, the mean potassium levels were lower for the patients with exacerbation, but this was not found to be statistically significant (p=0.168).



Figure 1. Age distribution of study participants between the groups



Figure 2: Distribution of cases of COPD as per their diagnosis (N=90)



Figure 3. Gender distribution of study participants between the groups



Figure 5: Distribution of the patients by serum sodium levels between the groups



Figure 6: Distribution of the patients by serum potassium levels between the groups

Table 1: Distribution of the patients by age between the groups (N=180).				
Group	Age in years		p-value	
	Mean	SD		
Group 1 (n=90)	73.3	8.8	0.197	
Group 2 (n=90)	71.8	6.2		

Diagnosis	Frequency (n)	Percentage
AECOPD	47	52.2
COPD	43	47.8
Total	90	100.0

#### Table 3: Gender distribution of study participants between the groups (N=180)

Gender	Group		p-value
	Group 1 (n=90) n (%)	Group 2 (n=90) n (%)	
Males	39 (43.3)	40 (44.4)	0.881
Females	51 (56.7)	50 (55.6)	

## Table 4: Baseline characteristics of the study participants

Parameters	Cases (n=90) Mean±SD	Control (n=90) Mean±SD	p-value
SBP (mm/Hg)	117.1±10.8	117.4±10.1	0.854
DBP (mm/Hg)	80.1±10.3	80.2±9.9	0.953
BMI (Kg/m2)	22.5±2.6	22.3±2.3	0.594

Table 5: Comparison of serum sodium levels between the groups (N=180)				
Group	Serum sodium in mEq/L	p-value		
_	Mean	SD	_	
Group 1 (n=90)	136.5	4.4	0.001	
Group 2 (n=90)	138.3	2.2		

Table 6: Comparison of serum potassium levels between the groups (N=180)				
Group	Serum potassium in mEq/L		p-value	
	Mean	SD		
Group 1 (n=90)	4.5	0.8	0.706	
Group 2 (n=90)	4.4	0.4		

Table 7: Comparison of serum chloride levels between the groups (N=180)			
Group	Serum chloride in mEq/L	p-value	

	Mean	SD	
Group 1 (n=90)	97.8	4.7	0.001
Group 2 (n=90)	99.8	2.7	

Table 8: Association of acute exacerbation with the serum electrolytes among the patients with COPD (N=90)				
Acute exacerbation	Serum electrolytes in mEq/L			
	Sodium Mean (SD)	Potassium Mean (SD)	Chloride Mean (SD)	
Yes	135.2 (5.1)	4.3 (0.7)	95.9 (4.7)	
No	137.9 (2.9)	4.6 (0.8)	99.8(3.8)	
p-value	0.003	0.168	< 0.001	



Figure 7: Distribution of the patients by serum chloride levels between the groups

## DISCUSSION

COPD is known to be one of the significant causes of morbidity and mortality worldwide. Acute exacerbations are the most common cause of hospitalization among patients with COPD.<sup>[20]</sup> It has been seen that electrolyte imbalances of sodium, potassium, calcium, and chloride are often linked to COPD. These electrolytes play a vital role in maintaining cellular function, acid-base balance, and neuromuscular action. Due to abnormalities in these electrolytes, the severity of the disease is exacerbated, and the patient outcomes worsen, leading to consequences like respiratory failure, muscular weakness, and cardiac arrhythmias.[8] It is essential to understand the role of COPD and electrolyte imbalances for proper management and to improve the prognosis of the patient.

Many metabolic disturbances may be seen in AECOPD patients due to the effect of drugs used in COPD treatment (i.e., beta2 agonists and corticosteroids), which can decrease the levels of sodium and increase serum levels of bilirubin, transaminases, blood urea and creatinine. Although most of these are correctable, they are often missed or overlooked. Therefore, early recognition and prompt management of these abnormalities are very crucial.<sup>[7]</sup>

In this present study, the mean age of patients was  $73.3\pm8.8$  years, and healthy controls were  $71.8\pm6.2$ . The mean serum sodium and chloride levels were lower in COPD patients than in the control group, and this was found to be statistically significant (p=0.001). Serum sodium and chloride levels in AECOPD patients were  $135.2\pm5.1$ mEq/L and  $95.9\pm4.7$  mEq/L, respectively, and in stable COPD patients, were  $137.9\pm2.9$  mEq/L and  $99.8\pm3.8$  mEq/L respectively. Hence, serum sodium and chloride levels were found to be significantly lower in AECOPD patients than in stable COPD patients, and similar findings were found in a study conducted by Rathore HK et al.<sup>[15]</sup>

In concordance with our findings, Saxena R et al,<sup>[21]</sup> found significantly abnormal levels of serum electrolytes (sodium, chloride, ionized calcium and magnesium) levels in AECOPD patients compared to healthy controls. Similar observations were found in the study done by Ahmed SU et al,<sup>[22]</sup> and Asati AK et al.<sup>[23]</sup>

Rathi N3 found that mean serum sodium, potassium, chloride and magnesium levels were significantly lower in AECOPD patients. Decreased levels of serum sodium can occur secondary to water retention in the presence of other comorbidities such as heart or renal failure, and it may also result from different drug therapies or the syndrome of inappropriate antidiuretic hormone secretion.<sup>[24]</sup>

In AECOPD patients, hypochloraemia is mainly due to respiratory acidosis with metabolic alkalosis (due to renal compensation) and chronic hypercapnia.<sup>[7]</sup> Das P et al.<sup>[25]</sup> found significantly lower levels of serum sodium and potassium in COPD patients mEq/L and 3.39±0.96 (133±6.86 mEa/L respectively) than in normal controls (142.0±2.28 mEq/L and  $4.52\pm0.02$  mEq/L respectively, p< 0.05). Acharya CP et al,<sup>[26]</sup> and Harshavardhan L et al,<sup>[27]</sup> also found that hyponatremia and hypokalaemia are prevalent in patients suffering from AECOPD. Aashish R et al,<sup>[17]</sup> concluded that AECOPD patients frequently have abnormal serum electrolyte levels. Since serum electrolytes and AECOPD are significantly correlated, they should be corrected as soon as possible to hasten remission and shorten hospital stays. Vashanthakumar V et al.<sup>[28]</sup> and Ogan N et al,<sup>[29]</sup> found that in acute exacerbation of COPD, the levels of serum electrolytes and uric acid were significant predictors of mortality, and these parameters should be monitored and corrected to decrease mortality.

However, in this study, the two groups had no significant differences in potassium levels, which indicates that homeostatic mechanisms might be involved in maintaining potassium balance even in chronic disease.<sup>[30]</sup> On the other hand, drug use, disease severity, and individual patient variability

may influence serum potassium changes, necessitating further research.

The limitation of the present study is that the sample size is small, and there may be a correlation between serum electrolyte levels and disease severity. The cross-sectional nature of the study itself has its own limitations, as temporal association cannot be ascertained.

## CONCLUSION

In this present study, serum sodium and serum chloride were significantly lower in acute exacerbation of COPD patients; however, they were not significant for serum potassium. These findings indicate that monitoring the levels of serum electrolytes in COPD patients could be beneficial in managing COPD. Future studies with larger cohorts and systematic analyses are needed to support the metabolic disturbances in the progression of COPD.

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