

## Original Article

# Electrolyte Disturbances in Acute Exacerbation of COPD

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### Abstract

**Background:** Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality worldwide. Acute exacerbation is an acute and sustained worsening of a patient's condition from a stable state and it is associated with significant electrolyte disturbances. **Objectives:** The main objective of this study was to determine the prevalence of electrolyte disturbances in patients with acute exacerbation of COPD and to determine possible effects of these electrolyte disorders. **Materials and Methods:** This observational prospective study was carried out in the Department of Pulmonology, Enam Medical College & Hospital from 1<sup>st</sup> January to 31<sup>st</sup> December 2017. Sixty patients with acute exacerbation of COPD were included. Serum electrolytes and arterial blood gases were measured. **Results:** Low level of serum sodium ( $131 \pm 5.66$  mEq/L) and potassium ( $3.20 \pm 0.44$  mEq/L) were found in subjects with acute exacerbation of COPD. In patients with respiratory failure  $\text{Na}^+$  and  $\text{K}^+$  levels were even lower. **Conclusion:** Serum electrolytes in acute exacerbation of COPD patients should be monitored routinely and should be corrected early to avoid poor outcomes.

**Key words:** COPD; Acute exacerbation; Sodium; Potassium; ABG;  $\text{PaO}_2$ ;  $\text{PaCO}_2$

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## Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide.<sup>1</sup> COPD is the fourth leading cause of death in the world, and further increases in its prevalence and mortality in the coming decade can be predicted.<sup>2</sup> According to Global Initiative for Chronic Obstructive Lung Disease (GOLD), COPD is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation which is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

The chronic airflow limitation which is a characteristic of COPD is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person. Airflow limitation is best measured by spirometry as this is the most widely available, reproducible test of lung function.

COPD can be classified into 4 stages on the basis of post-bronchodilator FEV<sub>1</sub>.

- Stage I: Mild – FEV<sub>1</sub>/FVC <0.70, FEV<sub>1</sub> ≥80% predicted
- Stage II: Moderate – FEV<sub>1</sub>/FVC <0.70, 50% ≤FEV<sub>1</sub> <80% predicted
- Stage III: Severe – FEV<sub>1</sub>/FVC <0.70, 30% ≤FEV<sub>1</sub> <50% predicted
- Stage IV: Very Severe – FEV<sub>1</sub>/FVC <0.70, FEV<sub>1</sub> <30% predicted or FEV<sub>1</sub> <50% predicted plus chronic respiratory failure

COPD is an economic and social burden that is both substantial and increasing.<sup>2,3</sup> A systematic review and meta-analysis of studies carried out in 28 countries between 1990 and 2004<sup>3</sup> and an additional study from Japan<sup>4</sup> provide evidence that the prevalence of COPD is appreciably higher in smokers and ex-smokers than in nonsmokers, in those over 40 years than those under 40, and in men than in women.

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An exacerbation of COPD (AECOPD) is defined as an event in the natural course of the disease characterized by a change in the patient's baseline dyspnea, cough, and/or sputum that is beyond normal day-to-day variations, is acute in onset, and may warrant a change in regular medication in a patient with underlying COPD.<sup>5,6</sup>

The severity of AECOPD without respiratory failure can be classified traditionally according to Winnipeg criteria. The three-stage system is based on three principal symptoms:

1. Increase in sputum volume,
2. Increase in sputum purulence and
3. Increase in shortness of breath.

The Winnipeg criteria<sup>7</sup>

Types of exacerbation	Criteria
Type 1	All the 3 symptoms above
Type 2	Any 2 of above symptoms
Type 3	Any 1 of the above plus at least 1 of the following features: upper respiratory tract infection lasting $\geq 5$ days, fever, increase in wheezes, increase in cough, and increase in heart rate by 20%

The AECOPD patients present not only with the features of acute respiratory infections (productive cough, dyspnea etc) but also a number of metabolic disorders like hyponatremia, hypokalemia, hypomagnesemia, hyperbilirubinemia, elevated transaminases, elevated blood urea and elevated serum creatinine arising out of the disease process or as a consequence of the therapy (such as beta<sub>2</sub> agonists, steroids, diuretics etc). Very often they are missed or confuse the diagnosis, thus simple overlooking of the coexisting metabolic abnormalities may contribute to a great deal of mortality and morbidity in the COPD patients.<sup>8</sup> Water retention and hyponatremia are typically observed in the final stages of COPD and the onset of edema is a poor prognostic factor. In these patients the gas exchange impairment induces several hormonal abnormalities: renin (Rn), angiotensin II (AnII), aldosterone (Ald), atrial natriuretic peptide

(ANP), vasopressin (ADH) and endothelial factors are some of the factors involved. The systemic response to hypercapnia has the effect of reducing the renal blood flow and, as a result, increasing water and sodium retention with the final effect of edema and hyponatremia.<sup>9</sup> Irrespective of the underlying mechanism of development, hyponatremia itself may be a predictor of poor outcome in patients of COPD. It may lead to central nervous system dysfunction, confusion, convulsions, coma, reversible cardiac conduction defect, secondary renal insufficiency and even death.<sup>10,11</sup>

Along with hyponatremia, hypokalemia may be another morbid accompaniment in the subjects with COPD. Hypokalemia may be present independently or concomitantly with hyponatremia. Hypokalemia in COPD may be attributed to respiratory acidosis and metabolic alkalosis or long standing steroid therapy.<sup>12</sup> Use of  $\beta_2$  agonists like fenoterol or salbutamol may also contribute to hypokalemia in COPD patients.<sup>13</sup> Moreover, acute respiratory failure associated with hypokalemia was found to have a high mortality rate among the COPD patients.<sup>14</sup> High mortality in hypokalemia may be attributed to cardiac arrhythmias or impaired nerve-muscle conduction.

With this background, in our study we attempted to measure the concentration of major serum electrolytes (sodium, potassium) in COPD patients with acute exacerbation and compare these with that of arterial blood gas (ABG) findings of the same group of patients.

## Materials and Methods

This prospective observational study was conducted in the Department of Pulmonology, Enam Medical College & Hospital (EMCH), over a period from January 2017 to December 2017. The study included a total of 60 (sixty) patients. All cases of acute exacerbation of COPD, presenting to outpatient department (OPD) or emergency of EMCH were included. COPD patients admitted for causes other than COPD exacerbation and patients with pre-existing renal, hepatic, endocrine or cardiac illness were excluded.

Criteria for diagnosis of COPD are:

- History of symptoms or risk factors (taken from relatives), previous admission for the same reason with a discharge sheet revealing the diagnosis.
- Previous spirometry report revealing the diagnosis of COPD.
- Clinical examination confirming the diagnosis.

All patients were investigated as follows:

1. Laboratory investigations including i) complete blood picture (CBC), ii) blood sugar to exclude DM and iii) liver and kidney function tests to exclude patients with liver or renal diseases that affect serum electrolytes.
2. Chest radiography to confirm the diagnosis and to exclude other chest diseases and to follow up for signs of complications.
3. Arterial blood gases (ABG) analysis including pH, PaO<sub>2</sub>, PaCO<sub>2</sub>, HCO<sub>3</sub><sup>-</sup>.
4. Echocardiography for detection and exclusion of patients with cardiomyopathy and left sided heart failure.
5. Measurement of serum electrolytes including K<sup>+</sup>, Na<sup>+</sup> on the 1<sup>st</sup> day of admission.

**Results**

Table I shows serum electrolytes among 60 AECOPD patients. The level of Na<sup>+</sup> was 131.55 ± 5.66 mEq/L and K<sup>+</sup> was 3.20 ± 0.44 mEq/L. Minimum Na<sup>+</sup> was 118 mEq/L and maximum was 138 mEq/L and for K<sup>+</sup> minimum was 2.1 mEq/L and maximum was 3.7 mEq/L. Table II shows ABG parameters among AECOPD patients. The mean pH, PaCO<sub>2</sub> and PaO<sub>2</sub> are 7.35 ± 0.067, 47.5 ± 10.49 mm Hg and 58.4 ± 8.20 mm Hg.

Table III shows serum electrolytes among patients with and without respiratory failure. There was statistically significant difference (p=0.000) in mean ± SD of Na<sup>+</sup> between patients with and without respiratory failure. In patients with respiratory failure it was 127 ± 6.51 mEq/L compared to 134 ± 2.11 mEq/L among patients without respiratory failure. There was also statistically significant difference (p=0.000) in mean ± SD of K<sup>+</sup> between patients with and without respiratory failure. In patients with respiratory failure it was 2.88 ± 0.46 mEq/L compared to 3.41 ± 0.28 mEq/L among patients without respiratory failure.

Table 1: Serum electrolytes in AECOPD patients (N=60)

Parameters	Mean ± SD	Range
Na <sup>+</sup> (mEq/L)	131.55 ± 5.66	118–138
K <sup>+</sup> (mEq/L)	3.20 ± 0.44	2.1–3.7

Table II: ABG parameters among AECOPD patients (N=60)

Parameters	Mean ± SD
pH	7.35 ± 0.067
PaCO <sub>2</sub> (mm Hg)	47.5 ± 10.49
PaO <sub>2</sub> (mm Hg)	58.4 ± 8.20

Table III: Serum electrolytes among patients with and without respiratory failure (N=60)

Electrolytes	With respiratory failure	Without respiratory failure	p values
Na <sup>+</sup> (mEq/L)	127 ± 6.51	134 ± 2.11	0.000
K <sup>+</sup> (mEq/L)	2.88 ± 0.46	3.41 ± 0.28	0.000

**Discussion**

COPD is a progressive chronic disease which is characterized by an inexorable decline in respiratory function, exercise capacity, and health status.<sup>15</sup> This underlying state is interrupted by exacerbations of symptoms which vary in severity and frequency among patients and during the course of one patient’s illness. These exacerbations are important, not only because of their impact on an individual’s life but also because of their long term effects on health status, morbidity, and mortality.<sup>16</sup> In fact, exacerbation frequency is one of the most important determinants of health-related quality of life.<sup>17</sup> Exacerbations are a significant cause of hospital admission and readmission, and the burden placed on health resources is immense.<sup>18</sup>

The economic and social burden created by acute exacerbations of COPD is extremely high. Thus, it is important to identify factors associated with exacerbation and poor outcome. Common causes of deranged serum sodium levels include hyperglycemia, use of thiazides or nonsteroidal anti-inflammatory drugs, congestive cardiac failure, chronic renal failure, and low dietary salt intake.<sup>19</sup> Common causes of hypokalemia include diarrhea, laxative abuse, vomiting, certain diuretics, drugs like insulin, β<sub>2</sub>

agonists, and theophylline.<sup>20</sup> Thus, COPD patients per se are predisposed to electrolyte imbalance. In turn electrolyte imbalance can cause respiratory muscle weakness, cardiac arrhythmia, low cardiac output, etc.<sup>21</sup> Thus the presence of electrolyte imbalance leads to significantly poor outcome among COPD patients.

In our study serum electrolyte level was done before giving any type of treatment in AECOPD patients. There was a significant decrease in  $K^+$  and  $Na^+$  in COPD patients. Among COPD patients, hypokalemia was reported in 34 (76.6%) patients, hyponatremia in 42 (70%) patients, and combined electrolyte disorders were present in 34 (56%) patients. The mean  $Na^+$  level was  $131.55 \pm 5.66$  mEq/L and mean  $K^+$  level was  $3.20 \pm 0.44$  mEq/L. These are consistent with the findings of the study done by Das et al<sup>22</sup> who reported a significant decrease in serum  $Na^+$  and  $K^+$  in COPD patients ( $133 \pm 6.86$  mEq/L and  $3.39 \pm 0.96$  mEq/L respectively) than in normal controls ( $142 \pm 2.28$  mEq/L and  $4.52 \pm 0.02$  mEq/L respectively,  $p < 0.05$ ). Similar observations were found in the study done by Gnaneshwar et al.<sup>23</sup> In the study of Teranzo et al<sup>24</sup> it was found that among 67 consecutive patients who were hospitalized for hypercapnic COPD exacerbation, hyponatremia was present in 11 patients, hyponatremia with hypochloremia and hypokalemia in 10 and hypochloremia in 7 patients.  $\beta_2$  agonists whether inhaled like formoterol and salbutamol or oral salbutamol or bumbuterol in addition to oral sustained released theophylline are the main stay treatment in stable COPD. Unfortunately all these treatments have been proved to cause some electrolyte disorders in patients with bronchial asthma and COPD.<sup>13</sup>

There was decrease in both pH ( $7.35 \pm 0.067$ ) and  $PaO_2$  ( $58.44 \pm 8.20$  mm Hg) and increase in  $PaCO_2$  ( $47.52 \pm 10.49$  mm Hg) in patients with AECOPD. Comparing AECOPD patients with electrolyte disorders and those without electrolyte disorders it was found that there was a significant decrease in pH,  $PaO_2$  and a significant increase in  $PaCO_2$  in patients with electrolyte disorders. This means that patients with electrolyte disorders may have further deterioration in arterial blood gases than the patients without any electrolyte disorders.

Respiratory acidosis with metabolic alkalosis

(due to renal compensation) in AECOPD patients with chronic hypercapnia is the usual cause of hypochloremia in these patients.<sup>23</sup> So patients with severe COPD exacerbation have factors that influence serum electrolytes levels like hypoxia, respiratory acidosis and hypervolemia, even before starting any type of treatment that may further induce electrolyte imbalance.

The effect of steroids, diuretics, and inhaled  $\beta_2$  agonists on serum electrolyte level has been proved in many studies in both COPD and asthma patients.<sup>25,13</sup> Intravenous aminophylline therapy has been recorded to cause hypomagnesemia, hypocalcemia and hyponatremia in susceptible individuals by increasing the urinary secretion of these electrolytes. These electrolyte imbalances in turn cause increased pulmonary irritability and consequently increased risk of exacerbation.<sup>26</sup>

High mortality and morbidity in patients with hyponatremia and hypokalemia and other electrolyte disorders may be attributed to its harmful effects like cardiac arrhythmias, central nervous system dysfunction, confusion, convulsions, coma, secondary renal insufficiency, hampered nerve-muscle conduction and respiratory muscle affection even death.<sup>16</sup> So it appears from our study that electrolyte disorders are a common associated finding in the subjects with severe COPD exacerbation that should be corrected promptly to avoid fatal outcomes.

Patients with acute severe exacerbation of COPD are at a higher risk of decreased serum levels of  $K^+$  and  $Na^+$ . Imbalance of serum electrolytes and wasting time for its correction increase mortality and morbidity. So, electrolyte levels should be monitored routinely in those patients and should be corrected as early as possible to avoid poor outcomes.

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