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# Effect of Phosphate Level on The Outcome of COPD Patients in The Intensive Care Unit

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## ABSTRACT

**Background:** A preventable and curable condition, chronic obstructive pulmonary disease (COPD) has certain notable extrapulmonary side effects that might increase a patient's severity. Airflow restriction that is not entirely reversible is a characteristic of its pulmonary component. The airflow restriction is often progressive and linked to an aberrant lung inflammatory response to harmful gasses or panicles.

**Objective:** To assess the impact of hypophosphatemia on cases experiencing acute exacerbations of COPD, focusing on exacerbation severity, mechanical ventilation (MV) requirements, ventilation duration, and patient outcomes.

**Patients and Methods:** This observational research was conducted on 50 cases with acute exacerbation of COPD who were hospitalized to the Intensive Care Department of Ain Shams University.

**Results:** In older males who smoked heavily and for a long time, the severity of COPD exacerbations and the necessity for ventilation rose. Ventilation was more necessary when $PaCO_2$ levels were high. The severity of a COPD exacerbation and the requirement for ventilation were both enhanced by hypophosphatemia in the absence of other electrolyte deficiencies. Additionally, our findings demonstrated that hypophosphatemia was linked to prolonged ventilation, poor outcomes, and a high mortality rate because it weakened the diaphragmatic and respiratory muscles, which resulted in weaning failure and, ultimately, death. While multiple electrolyte shortage without hypophosphatemia had no influence on the requirement for MV, length of MV, or outcome, hypophosphatemia combined with multiple electrolyte deficiency exacerbated these factors and led to a poor result.

**Conclusion:** Hypophosphatemia exacerbates the severity of COPD exacerbations, necessitates MV, prolongs MV duration, contributes to weaning failure, and therefore elevates death rates. Additionally, the demand for ventilation increased when hypophosphatemia and various electrolyte deficiencies were present.

**Keywords:** Mechanical ventilation; Phosphate; ICU; COPD.

## INTRODUCTION

The frequency of COPD in industrialized nations is gradually growing as people age. Acute exacerbations of COPD with decompensated respiratory acidosis result in several hospitalizations and significant mortality, making it the major cause of disability and morbidity[(1)].

By 2020, COPD has moved up from its present position as the 12th most frequent disease globally to the 5th, and from the 6th most common cause of mortality to the 3rd, according to WHO predictions. Since 74% of COPD cases necessitate MV support, it is typical for them to be admitted to an intensive care unit. Many patients still require traditional MV even though non-invasive MV has been used more widely recently. Blood phosphorus levels and illness severity have been linked in several studies [(2)].

Although it is unclear if COPD patients who are on pulmonary support require extended ventilation, the more severe the condition, the lower the blood phosphorus levels [(3)].

Serious side effects such tetany, convulsions, coma, rhabdomyolysis, respiratory failure, and ventricular tachycardia can result with severe hypophosphatemia. It is yet unknown how hypophosphatemia affects the functioning of the respiratory muscles in patients admitted for other reasons, despite the fact that it has only been sporadically linked to respiratory failure [(4)].

The objective of this study was to assess the impact of hypophosphatemia on patients experiencing acute exacerbations of COPD, focusing on exacerbation severity, ventilation requirements, ventilation duration, and patient outcomes.

## PATIENTS AND METHODS

This observational research was conducted on 50 cases with acute exacerbation of COPD who were hospitalized to the Intensive Care Department of Ain Shams University. Serum phosphorus was assessed at admission; hypophosphatemia is defined as a serum phosphorus level less than 2.5 mg/dl. In our research, 32 cases exhibited hypophosphatemia, whereas 18 patients maintained normal phosphorus values, out of a total of 50 cases.

COPD with an acute exacerbation leads to confusion, lethargy, tachypnea, respiratory muscles fatigue, worsening hypoxemia, or respiratory acidosis (pH is less than 7.30), as well as clinical concern for impending or active ventilatory failure and the need for mechanical ventilation.

While patients with CKD (Creatinine >2.0 mg%), patients receiving phosphorus compounds treatment or



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parenteral nutrition, hypoparathyroidism, and patients with malignancy were excluded from the study.

**Sampling Method and Tools:**

***All patients were examined for:***

**(1)** Complete history from family members or the patient, if available: History of chest symptoms (cough, expectoration, dyspnea, and wheezing), history of intubation and/or ventilator support, and history of smoking (current, ex-current, and non-current).

**(2)** Complete clinical assessment.

**(3)** Evaluation of the intensity of an exacerbation in accordance with **Pauwels *et al.*** [3]: ***Severe:*** includes the three main symptoms of purulence, increasing sputum volume, and worsening dyspnea. ***Moderate:*** includes two of them. ***Mild:*** consists of at least one of the following symptoms in addition to one main symptom: Five days of upper respiratory infection, fever without a known cause, increased wheezing and coughing, or a respiratory rate more than 25 breaths per minute.

Laboratory examinations included a complete blood count, renal function tests (urea and creatinine), liver function tests (AST and ALT), arterial blood gas, random blood sugar, PT, PTT, and INR, electrolytes (Na, K, C, Mg, and Phosphorus), and radiographic investigations. - Chest X-Ray.

**Serum phosphorus** was determined in the laboratory using one sample taken at the time of admission.

**Follow up parameters:** - Indication for MV: Severe dyspnea not responding to initial emergency treatment. Altered mental state (confusion, lethargy and coma). Persistent or worsening hypoxia ($PaO_2$ < 40 mmHg). Hypercapnia ($PaCO_2$ > 60 mmHg) and (pH < 7.25) in spite of oxygen therapy. - Mode of MV: SIMV in all patients. - Duration of ventilation in ICU. -Outcome: whether death or discharge for improvement.

**Ethical approval:**

**The study was approved by the Ethics Board of Al-Azhar University. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.**

**Statistical analysis:**

SPSS version 20.0 was utilized to analyze the recorded data. The mean± SD was used to express quantitative data. Frequencies and percents were utilized to represent the qualitative data. Separate samples two means were compared using the t-test. Proportions between qualitative indicators were compared by the $X^2$-test. A P-value < 0.05 was deemed significant.

**RESULTS**

This study included 50 patients admitted with acute exacerbation of COPD, 42 (84%) men and 8 (16%) women with mean age 70.24± 10.86 years.

Our study showed statistically significant differences between patients with hypo and normal phosphorus level regarding all demographic studies except for sex. Patients with hypophosphatemia were older, smoked for longer period of time, and had higher smoking index (Table 1).

**Table (1):** Demographic data of the studied patients regarding to phosphate level:

| **Demographic** | **Group** (A) **Normal phosphorus (n=18)** | **Group (B) Hypo-phosphatemia (n=32)** | **P value** |
|---|---|---|---|
| Age (years) | 62.14±9.88 | 75.64±7.74 | <0.001* |
| Sex<br>Males<br>Females | <br>13(72.2%)<br>5 (27.8%) | <br>29 (90.6%)<br>3 (9.4%) | <br>0.088 |
| Duration of smoking (years) | 38.17±13.62 | 52.42±8.64 | 0.006* |
| Smoking index packs (year) | 61.00±24.09 | 79.07±23.41 | 0.032* |

*: Significant

The mean phosphorus level in studied patients was 2.79±0.67 mg/dl (Table 2).

**Table (2):** Level of phosphorus among all studied patients

| | **Mean ±SD** |
|---|---|
| **Phosphorus** (mg/dl) | 2.79±0.67 |

The number of cases on MV was significantly greater in the hypophosphatemic group compared to those with normal phosphorus levels (Table 3).

**Table (3):** Ventilation need according to level of phosphorus

| **Ventilation need** | **Group (A) Normal phosphorus (n=18)** | **Group (B) Hypo-phosphatemia (n=32)** | **value** |
|---|---|---|---|
| Present<br>Absent | 8 (44.4%)<br>10 (55.6%) | 26 (81.3%)<br>6(18.7%) | **0.007*** |

*: Significant

Level of $PCO_2$ was higher in group of patients who required MV than patients who did not, also the level of pH, $SO_2$, $PO_2$ were significantly lower in the group who needed ventilation than those who did not (Table 4).

**Table (4):** Need for ventilation as regard to ABG parameters in all studied patients

| ABG | Need for MV | | P value |
|---|---|---|---|
| | Present (n=34) | Absent (n=16) | |
| pH | 7.18±0.11 | 7.05±0.11 | <0.001* |
| $PCO_2$ (mmHg) | 92.74±15.28 | 68.79±3.18 | <0.001* |
| $HCO_3$ (mmHg) | 35.67±3.79 | 33.85±3.61 | 0.115 |
| $SO_2$ | 77.55±7.13 | 87.66±2.71 | <0.001* |
| $PO_2$ | 51.45±5.48 | 58.31±3.01 | <0.001* |
| Base excess (BE) | -1.34±1.19 | -0.61±1.22 | 0.047* |

*: Significant

Table (5) shows that the electrolyte levels of ventilated and non-ventilated patients did not differ statistically significantly, with the exception of K and phosphorus.

**Table (5):** Need for ventilations as regard to electrolytes

| Serum electrolytes | Need for MV | | P value |
|---|---|---|---|
| | Present (n=34) | Absent (n=16) | |
| Phosphorus Normal level 2.5-5 (mg/dl) | 2.66±0.65 | 3.11±0.76 | **0.037*** |
| Na Normal level 135-145 (mmol/L) | 131.04±7.01 | 131.49±5.19 | 0.755 |
| K Normal level 3.5-5.5 (mmol/L) | 3.45±0.52 | 3.84±0.52 | **0.017*** |
| Ca Normal level 8.5-10.5 (mg/dL) | 8.65±0.62 | 8.83±0.47 | 0.312 |
| Mg normal level 1.4 -2 (mg/dL) | 1.96±0.18 | 1.93±0.18 | 0.607 |

*: Significant

There was a substantial statistical correlation between the fate of ventilated patients and their phosphorus levels (Table 6).

**Table (6):** Outcomes of patients on MV:

| | Ventilated cases with hypophosphatemia (N=26) | Ventilated cases with normal phosphorus (N=8) | P value |
|---|---|---|---|
| **Discharged** | 12 (46.2%) | 5 (62.5%) | **0.024*** |
| **Died** | 14 (53.8%) | 3 (37.5%) | |

*: Significant.

The length of ventilation and the phosphorus level were statistically significantly correlated. The individuals with hypophosphatemia had a longer ventilation duration than those with normal phosphorus levels (Table 7).

**Table (7):** Duration of MV:

| Duration of ventilation (days) | Mean± SD | Range | p-value |
|---|---|---|---|
| Ventilated cases with hypophosphatemia (N=26) | 13.27±6.27 | 5-21 | **0.009*** |
| Ventilated cases with normal phosphorus (N=8) | 4.25±3.21 | 2-9 | |

*: Significant

Significant differences in outcome existed between hypophosphatemic and normal phosphorus group (Table 8).

**Table (8):** Outcome of studied subjects:

| | Hypophosphatemia (n=32) | Normal phosphorus (n= 18) | value |
|---|---|---|---|
| Discharged | 18 (56.3%) | 15 (83.3%) | **0.037*** |
| Died | 14 (43.7%) | 3 (16.7%) | |

*: Significant

Table (9) shows that combined hypophosphatemia and hypokalemia increased the necessity for MV, the length of MV, and the poor outcome.

**Table (9):** Potassium levels in hypophosphatemic patients who needed MV (n=32):

| | **Hypokalemia** | **Normal K (3.5-5.5)** | **P value** |
|---|---|---|---|
| Number | 18 | 14 | **0.028*** |
| Necessity for MV | 18 | - | **0.004*** |
| Duration of MV (range) | 6-21 days | - | **0.008*** |
| Outcomes | 6 Discharged<br>12 Died | - | **0.012*** |

*: Significant

Table (10) shows that combined hypophosphatemia with hypocalcemia had significant increase in necessity for MV, but no significant differences in number of cases, duration of MV and outcomes.

**Table (10):** Calcium levels in hypophosphatemic patients who needed MV (n=32):

| | **Hypocalcemia** | **Normal Ca (8.5-10.5)** | **P value** |
|---|---|---|---|
| Number | 18 | 14 | 0.182 |
| Necessity for MV | 16 | 7 | **0.048*** |
| Duration of MV (range) | 7-19 days | 9-16 | 0.235 |
| Outcomes | 8 Discharged<br>8 Died | 3 Discharged<br>4 Died | 0.144 |

*: Significant

Combined hypophosphatemia and hyponatremia demonstrated a significant increase in the requirement for MV, the length of MV, and worse outcomes (Table 11).

**Table (11):** Sodium levels in hypophosphatemic patients who needed MV (n=32):

| | **Hyponatremia** | **Normal Na (135-145)** | **P value** |
|---|---|---|---|
| Number | 30 | 2 | 0.028* |
| Necessity for MV | 26 | 2 | 0.014* |
| Duration of MV (range) | 6-20 days | 5-9 days | 0.042* |
| Outcomes | 14 Discharged<br>12 Died | 1 Discharged<br>1 Died | 0.014* |

*: Significant

Since just one patient in our research had hypomagnesemia, we were unable to remark on the condition due to the limited number of patients.

In our study, hypophosphatemic individuals with various electrolyte deficiencies had a higher demand for ventilation and a longer time of MV with unsatisfactory outcomes (Table 12).

**Table (12):** Prognosis of multiple electrolytes deficiency in hypophosphatemic group (n=32):

| | **Number** | **Necessity for MV** | **Duration of MV** | **Outcomes** |
|---|---|---|---|---|
| Combined<br>↓Na, ↓K, ↓Ca | 17 | 17 | 6-21days | 6 Discharged<br>11 Died |

Combined multiple electrolytes deficiency in patients with normal phosphorus had no effect on the necessity for MV, only one patient required MV for one week and died (Table 13).

**Table (13):** Prognosis of multiple electrolytes deficiency in normal phosphorus patients (n=18):

| | **Number** | **Necessity for MV** | **Duration of MV** | **Outcome** |
|---|---|---|---|---|
| Combined<br>↓Na, ↓K, ↓Ca | 6 | 1 | 7 days | 1 died |

## DISCUSSION

By 2020, COPD has moved up from its position as the fourth largest cause of mortality to the third. In 2012, COPD claimed the lives of over 3 million individuals, making about 6% of all fatalities worldwide. One significant public health issue that is curable and avoidable is COPD. A vital component of all living cells, phosphorus has an important role in the structure of nucleic acids and is crucial to the synthesis of adenosine triphosphate. The performance of several systems can be impacted by low blood phosphorus levels, which can be brought on by an imbalance between the elements involved in the phosphorus cycle [(5)].

Severe hypophosphatemia, defined as a blood phosphorus value less than 1.5 mg/dl, increases the risk of cardiac dysfunction, muscular breakdown, immunological and neurological system damage, and blood cell formation damage. Additionally, respiratory muscles, particularly the diaphragm, may become weak [(6)].

Weaning failure and MV are known to be caused by diaphragm weakness, which is due to low blood phosphorus levels [(6,7)].

We measured serum phosphorus on admission; patients were diagnosed with hypophosphatemia if their phosphorus levels were less than 2.5 mg/dl. In our study, 84 % of the patients were men and 16 % were women. Our study sample was mostly males (84%), old (70.24± 10.86 years) and smokers with the mean duration of smoking was 46.72±12.89 years.

Our sample population is similar to that conducted by **Pauwels *et al.*** [(8)] in 2001 who investigated 200 individuals hospitalized with AECOPD, 120 of whom were men and 80 of whom were women, as part of a study on gender in COPD. They discovered that guys who were older and had smoked for a longer period of time also saw an increase in COPD exacerbations. However, **Mannino *et al.*** [(9)] found that women experienced more COPD exacerbations because they may be more susceptible to smoking-induced pulmonary impairment, more severe dyspnea, and worse health outcomes after exposure to the same amount of tobacco because their airways are smaller, meaning that each cigarette represents a proportionately higher exposure, with increasing trends in COPD hospitalizations and death among females.

In our present study, it was clear that the necessity for MV significantly increased among elderly men (n=34) with mean age 73.03±9.57 years with high smoking index (81.84±21.40 packs/year).
This matched the study conducted by **Ai-Ping *et al.*** [(10)] who reported that the necessity for MV increased in old heavy smokers with mean age 70.0±8.3 years and almost half of them were still actively smoking. More than 90% of cases needed MV, with a mean duration f 2.3±2.2 days.

This result also supported the findings of **Anthonisen *et al.*** [(11)] who found that smoking enhanced the severity of exacerbations of COPD and the requirement for MV because smoking has a greater incidence of respiratory symptoms and abnormalities of pulmonary functions (index 39.9±18.6 packs/year).
In our work; a relation existed between increased level of $PaCO_2$ (92.74±15.28) and decrease level of pH (7.18±0.11) and increase need for MV. Level of $PaCO_2$ was higher in group of cases that required MV compared to cases that did not require MV (p value 0.017).

Our results agreed with **Ai-Ping *et al.*** [(10)] in 2005 who reported that the increased $PaCO_2$ level had a direct relationship with severity of COPD exacerbation and necessity for MV with P $CO_2$ in survivors 40.9±3.3 and in non-survivors 45.6±6.8 with p value 0.021; in addition, the high levels of $PaCO_2$ lowered the patient's awareness level, causing respiratory discomfort.

In our investigation 32 patients exhibited hypophosphatemia, whereas 18 had normal phosphorus levels. Our results showed that the level of $PaCO_2$ significantly increased in hypophosphatemic patients (89.44±15.39) greater than in patients with normal levels of phosphorus (80.91±18.26) with p value = 0.037. This probably was due to COPD exacerbation due to hypophosphatemia which caused respiratory muscle weakness; hence the patient couldn't wash $CO_2$.

**Patil *et al.*** [(12)] discovered that hypophosphatemia worsened COPD exacerbation by raising $PaCO_2$ levels, resulting in respiratory failure.

We discovered a link between hypophosphatemia and the need for MV. Patients with hypophosphatemia required MV at a higher rate than patients with normal phosphorus levels; this was the case for 81.3 percent of hypophosphatemia patients and only 44.4% of patients with normal phosphorus levels.

Also, hypophosphatemia was associated with poor outcome; as 46.2% of patients with hypophosphatemia were discharged and 53.8% died, while among patients with normal phosphorus levels, 62.5% of patients were released while 37.5% died. Because hypophosphatemia results in respiratory muscle weakness and diaphragmatic weakness, we found that patients with hypophosphatemia had a longer ventilation duration than patients with normal phosphorus levels. This difference was caused by the failure of weaning. In hypophosphatemic group duration of ventilation ranged from 5-21 days (mean 13.27±6.27) while in normal phosphorus group ranged from 2-9 days (mean 4.25±3.21) with p value 0.009.

This outcome was consistent with research conducted by **Farah *et al.*** [(5)], who examined the connection between hypophosphatemia and the requirement for MV in patients with AECOPD who were hospitalized. They examined 255 patients and

discovered that, in contrast to 15.6% of individuals with normal phosphorus, 76.5% of patients with low phosphorus levels during hospital stays required MV. This was explained by hypophosphatemia-induced respiratory muscle weakening.

Additionally, our findings concurred with those of **Schweickert and Hall** [13] who discovered that low phosphorus levels led to respiratory muscle and diaphragmatic weakening, which in turn increased the requirement for MV and the length of ventilation. They explained why it also seems prudent to maintain the internal milieu of the patient, with attention to electrolyte disorders, including phosphate depletion as the body will otherwise cannibalize muscle for sources of energy.

This result is in concordance with **Gravelyn *et al.*** [7] they discovered that low blood phosphorus levels made it harder to cough, which led to secretion buildup in the respiratory tract and may have increased the risk of infection in ventilated patients.

Our results matched with **Zhao *et al.*** [4] who examined 67 patients with AECOPD; 29 of them had normal blood phosphate levels, and 38 of them had hypophosphatemia. Therefore, among AECOPD patients receiving MV, the morbidity rate of hypophosphatemia was 56.72%. Three instances (10.34%) failed weaning, while 26 cases (10.34%) were successful in the normophosphatemic group. In comparison, 13 instances (34.21%) failed weaning whereas 25 cases (34.21%) were successful in the hypophosphatemic group. Compared to the normophosphatemic groups, the hypophosphatemia group experienced a considerably greater rate of weaning failure ($P < 0.05$).

Our study in addition found that combined hypophosphatemia and hypokalemia significantly increased the need for ventilation, the length of ventilation, and the poor outcome. Of the 18 patients with hypophosphatemia and hypokalemia, all were ventilated for a duration ranging from 6 to 22 days, six were discharged, and twelve died.

This matched the study done by **Farah *et al.*** [5] as they discovered a relationship between the severity of the disease and the need for MV and low blood potassium levels ($P < 0.001$). Of the 48 patients who required MV, 16 (33%) had low potassium levels, while only 3% of non-ventilated patients had hypokalemia.

Also, **Boles *et al.*** [14] in 2007 found that combination between hypophosphatemia and hypokalemia may also contribute to difficulty weaning as they cause muscle weakness.

Our study showed that hypokalemia alone without hypophosphatemia had no effect on the necessity for MV, its duration or outcome with no statistically significant differences.

This study didn't match with that done by **Das *et al.*** [15] in a 2010 study of 64 COPD patients, the average blood potassium levels were 3.39 ± 0.96 meq/L. The researchers concluded that hypokalemia in COPD patients might be caused by metabolic alkalosis and respiratory acidosis. Furthermore, it was shown that among COPD patients, abrupt respiratory failure linked to hypokalemia had a significant death rate. Heart arrhythmias or impaired nerve-muscle transmission may potentially be the cause of the high mortality rate in hypokalemia. According to this study, hypokalemia may be a prevalent related finding in COPD people that has to be treated right away to prevent deadly consequences.

Again, and in contrast to our findings, **Nelson and Cox** [16] investigated the relationship between K level at admission and the necessity for MV. They discovered that hypokalemia was present in 33% of ventilated patients but only 3% of non-ventilated patients. This suggests that hypokalemia alone increased the need for MV.

Our results demonstrated that while hypocalcemia by itself had no significant impact on the patient's necessity for MV, its duration, or outcomes, the combination of hypophosphatemia and hypocalcemia significantly increased the necessity for MV without influencing on duration of MV or outcomes. Eighteen patients had hypophosphatemia and hypocalcemia, (n=16) of them required MV, (8) discharged and (8) died. On the other hand, 14 patients had hypophosphatemia and normal Ca level with (7) of them underwent MV, (3) discharged and (4) died.
This was consistent with the findings of **Rabe *et al.*** [17] who discovered that the correlation between hypophosphatemia and hypocalcemia exacerbated the severity of exacerbations of COPD and increased the requirement for MV because of the weakening of the respiratory muscles.

Against our results, **Qin *et al.*** [18] found that hypocalcemia alone might be related to the disease progression, incidence of respiratory infections and length of hospitalization among AECOPD patients. In the examined 153 patients, they found significant differences in the incidence of hypocalcemia among patients of different ages ($P = 0.002$), the respiratory infection rate ($P < 0.001$) and hospital stay ($P < 0.001$).

In our study, combined hypophosphatemia and hyponatremia demonstrated a significant increase in the requirement for MV, the length of MV, and poor outcomes. Thirty patients suffered from hypophosphatemia and hyponatremia; twenty-six of them required ventilation, fourteen were released, and twelve died. In contrast, one patient required ventilator and died despite having hypophosphatemia and a normal Na level.

Our results also showed that hyponatremia alone without hypophosphatemia had no effect on the necessity for MV, its duration and outcomes with no statistically significant differences.

This result is not matched with that reported by **Rashid** [19] when he examined acute exacerbation of COPD in 60 patients with a minimum $Na^+$ of 118 mEq/L and a maximum of 138 mEq/L was found to be associated with high mortality and morbidity. Hyponatremia can cause detrimental effects such as arrhythmia, neurological dysfunction, convulsion, altered mental status, renal insufficiency, impairment of nerve-muscle conduction, respiratory muscle weakness, and even death.

According to our study, a combination of hypophosphatemia and numerous electrolyte deficiencies led to a higher requirement for MV, longer ventilation times, and worse outcomes. On the other hand, the requirement for ventilation, the length of ventilation, and the result were unaffected by various electrolyte deficiencies without hypophosphatemia.

In contrary **Das *et al.*** [15] discovered that deficiencies in only one of the electrolytes (K, Ca, and Na) had a negative impact on the severity and prognosis of COPD because hypokalemia and hypocalcemia resulted in weakening of the respiratory muscles. Furthermore, hyponatremia may worsen the patient's state of consciousness.

Since just one patient in our research had hypomagnesemia, we were unable to remark on the condition due to the limited number of patients.

## CONCLUSION

Hypophosphatemia exacerbates the severity of COPD exacerbations, necessitates ventilation, prolongs ventilation duration, contributes to weaning failure, and therefore elevates death rates. Additionally, the demand for ventilation increased when hypophosphatemia and various electrolyte deficiencies were present.

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