The effect of hypophosphatemia on critically ill patient with acute exacerbation of chronic obstructive pulmonary disease (COPD)

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Abstract: Background: Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable disease with some significant extra-pulmonary effects that may contribute to the severity in individual patients. **Aim of the Work:** evaluate the effect of hypophosphatemia on patients with acute exacerbation of COPD. **Patients and Methods:** This study was performed on 50 patients with AECOPD admitted at chest department and respiratory ICU in Tanta university hospital in the period between July 2018 and January 2019., serum of phosphorus was measured on admission, hypophosphatemia is considered if serum phosphorus is below 2.5mg/dl. **Results:** Combination between hyponatremia and hypophosphatemia significantly increased the need for ventilation, duration of ventilation and associated with poor outcome (p value < 0.01), while hyponatremia alone not significantly affect the need for ventilation, duration of ventilation and outcome (p value > 0.05). **Conclusion:** Hypophosphatemia may increase the severity of COPD exacerbation, need for ventilation, duration of ventilation, weaning failure and so increases the rate of mortality. Combination between hypophosphatemia and hypokalemia or hyponatremia increased the need for ventilation, duration of ventilation and affected outcome badly.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable disease with some significant extrapulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an abnormal inflammatory response of the lung to noxious particles or gases. The chronic airflow limitation 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 [(1)].

An exacerbation of COPD 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 [(2)].

Exacerbations affect the quality of life and prognosis of patients with COPD. Hospital mortality of patients admitted for a hypercarbic COPD exacerbation is approximately 10%, and the long-term outcome is poor. Mortality reaches 40% at 1 year in those needing mechanical support, and all-cause mortality is even higher (up to 49%) 3 years after hospitalization for a COPD exacerbation. Older age, decreased lung function, lower health status, diabetes, and pre-ICU admission quality of life are important risk factors for mortality in COPD patients hospitalized for acute exacerbation. In addition, exacerbations of COPD have serious negative impacts on patient's quality of life, lung function, and socioeconomic costs. Thus, prevention, early detection, and prompt treatment of exacerbations may impact their clinical progression by ameliorating the effects on quality of life and minimizing the risk of hospitalization [(1)].

Phosphorus is an essential element in all living cells, it is extremely important in the process of production of adenosine triphosphate, main element in the structure of nucleic acids, low levels of phosphorus in blood is rare, however it may be caused by unbalance between components participating in phosphorus cycle and affect performances of several systems. A low level of phosphorus in blood increases the exacerbation and severity of chronic obstructive pulmonary disease (COPD) and requires prolonged ventilation process [(3)].

Early detection and correction of hypophosphatemia can significantly improve performance of respiratory muscles in patients with low phosphorus levels, it also improves the ability to cough and prevents the accumulation of secretions in respiratory tract which might otherwise increase the risk of infections in ventilated patients [(4)].

Aim of the work

This study evaluates the effect of low blood phosphorus levels on patients admitted with acute exacerbation of COPD regarding severity of COPD exacerbation, need for ventilation, duration of ventilation and outcome.

2. Patients and Methods

This study was performed on 50 patients with acute exacerbation of COPD admitted in chest department and respiratory ICU at Tanta university hospital in the period between July 2018 and January 2019.

Inclusion criteria:

The study included patients with age >40 years old, smoking patient with chronic obstructive pulmonary disease, increase shortness of breath, significant increase in sputum production or new expectoration of purulent sputum and severe respiratory acidosis Ph <7.25 and PCO2 > 60mmHg.

Patients with ages < 40 years old, chronic renal failure, hepatic patient, acute cerebrovascular disease and malignancy were excluded from the study.

Patients are classified into 2 groups (e.g. group I 30 pts vs group II 20pts) according to phosphate level and another 2 groups (group A 36 pts vs group B 14pts) according to need for mechanical ventilation.

Methods of studying

All patients were scheduled for:

Full medical history from the patient (if possible) or his relatives: History of smoking (current, Ex. and non-smoking), history of chest symptoms (cough, expectoration, dyspnea and wheeze), history of previous intubation and / or ventilator support., Full clinical examination., Assessment of exacerbation severity according to **GOLD** [(1)]**., Severe:** Has all the three major symptoms including worsening of dyspnea, increased sputum volume and sputum purulence., **Moderate:** Has two of them., **Mild:** Has one major symptom plus at least one of the followings:, Upper respiratory infection in the past 5 days., Fever without another apparent cause., Increased wheezing., Increased cough., Increased respiratory rate > 25 breaths/minute., Laboratory investigations:, Complete blood picture., Kidney function tests: urea, creatinine., Liver function tests: AST, ALT., Arterial blood gases., Random blood sugar., PT, PTT and INR., Serum electrolytes (Na, K, Ca, Mg and Phosphorus).

Laboratory determination of serum phosphorus:

One sample of phosphorus at time of admission.

Calculation of phosphorus concentration:

Phosphorus (mg/dl)=$10\times(\Delta A_{sample} \div \Delta A_{STD})$

Data management

The clinical data were recorded on a report form. These data were tabulated and analyzed using the computer program SPSS (Statistical package for social science) version 16 to obtain:

Descriptive data

Descriptive statistics were calculated for the data in the form of:

1. Mean and standard deviation $(\pm SD)$. for quantitative data.
2. Frequency and distribution for qualitative data.

Analytical statistics

Appropriate Statistical programs and tests were used to compare between the different groups.

3. Results

Table (1): Level of electrolytes among studied patients

Na	126.12±6.26 mg/dl	118-140
K	3.42±0.52 mg/dl	2.5-4.5
Ca	8.37±0.56 mg/dl	6.9-9.2
Mg	1.87±0.17 mg/dl	1.5-2.2

Table (2): Need for ventilation as regard to electrolytes

Need for MV / Serum electrolytes	Present (36) Mean± SD	Absent (14) Mean± SD	St t test	P value
Phosohorus Normal value 2.5-5 mg/dl	2.56±0.78	2.99±0.73	1.78	**0.041****
Na Normal value 135 -145	126.0±6.74	126.43±4.99	0.215	0.83
K Normal value 3.5-5.5	3.32±0.498	3.69±0.499	2.35	**0.023****
Ca Normal value 8.5-10.5	8.32±0.6	8.49±0.45	0.959	0.343
Mg Normal value 1.4 -2	1.88±0.17	1.86±0.174	0.434	0.667

N.B: The previous data are presented according to Mean & SD and number of patients also P value

N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study

Table (1) shows the level of electrolytes among studied patients, the mean of each electrolyte is below normal except the mean of Mg was in the normal range.

Table (2) shows no statistically significant differences regarding to electrolytes between ventilated and non-ventilated patients except for K (p value=0.023) and Phosphorus (p value =0.04).

Table (3): Level of phosphorus among studied patients

	Mean ±SD	Range
Phosphorus	2.68±0.78 mg/dl	1.6-4.3

N.B: The previous data are presented according to Mean & SD The mean of phosphorus among studied patients was 2.68±0.78 mg/dl.

Table (4) shows no statistically significant differences as regard to level of electrolytes (Na, K, Ca, Mg) in patients with hypo and normal phosphorus level with p value 0.111,0.109,0.09,0.33 respectively.

In patients with hypophosphatemia mean of (Na=123.57±4.73, K=3.32±0.53, Ca=8.22±0.60, Mg=1.89±0.18mg/dl) while in patients with normal phosphorus mean of (Na=129.95±6.4, K=3.57±0.48, Ca=8.6±0.44, Mg=1.85±0.15mg/dl).

Table (4): Comparing level of electrolytes with level of phosphorus in studied patients:

Phosphorus / Electrolytes		Hypophosphatemia (30)	Normal (20) phosphorus	Test	P value
Na mg/dl	Mean± SD	123.57±4.73	129.95±6.4	4.05	0.111
K mg/dl	Mean± SD	3.32±0.53	3.57±0.48	1.63	0.109
Ca mg/dl	Mean± SD	8.22±0.60	8.6±0.44	2.41	0.09
Mg mg/dl	Mean± SD	1.89±0.18	1.85±0.15	0.985	0.33

N.B: The previous data are presented according to Mean & SD and number of patients
N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study

Table (5) shows statistically significant differences regarding to need of ventilation in patients with hypo and normal phosphorus level (p value=0.032).

In patients with hypophosphatemia (30), 25(83.3%) patients were ventilated and 5(16.7%) not ventilated, While in patients with normal phosphorus (20),11(55%) patients were ventilated and 9(45%) not ventilated. Number of ventilated patients was higher in hypophosphatemic group more than normal phosphorus group with highly statistically significant differences and p value 0.032.

Table (5): Ventilation need according to level of phosphorus

Phosphorus / Ventilation need		Hypophosphatemia (30)	Normal (20) phosphorus	test	P value
Present Absent	No (%)	25(83.3) 5(16.7)	11(55.0) 9(45.0)	3.48	0.032

N.B: The previous data are presented according to Mean & SD and number of patients & percentage also p value
N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study

Table (6) shows that there was significant statistical relation in ventilated patients outcome and level of phosphorus with p value 0.021, in ventilated patients with hypophosphatemia 12 patients (48%) discharged and 13 patients (52%) died, while in ventilated patients with normal phosphorus 6 patients (54.54%) discharged and 5 patients (45.45%) died with p value 0.021.

Table (6): Outcome of ventilated subjects.

	Ventilated patients with hypophosphatemia No=25 pts	Ventilated patients with normal phosphorus No=11 pts	P value
Discharged	12(48%)	6(54.54%)	0.021
Died	13(52%)	5(45.45%)	

N.B: The previous data are collected according to number of patients & percentage also P value
N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study

Table (7) shows that there was significant statistical differences in outcome between hypophosphatemic and normal phosphorus group with p value 0.032. In hypophosphatemic group 17 patients (56.6%) discharged and 13 patients (43.4%) died, while in normal phosphorus group 15 patients (75%) discharged and 5 patients (25%) died with p value 0.032.

Table (7): Outcome of studied subjects

	Hypophosphatemic group No=30 pts	normal phosphorus group No=20 pts	P value
Discharged	17(56.6%)	15(75%)	0.032
Died	13(43.4%)	5(25%)	

N.B: The previous data are collected according to number of patients and percentage also P value.
N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study.

Table (8) shows that there was statistically significant relation between duration of ventilation and level of phosphorus with p value 0.022 (In hypophos-phatemic group duration of ventilation ranged from 5-20 days while in normal phosphorus group ranged from 1-8 days. Duration of ventilation increased in patients with hypophosphatemia more than patients with normal phosphorus level with p value 0.022.

Table (8): Duration of ventilation in ventilated patients

Duration of ventilation	mean± SD	range	P value
Hypophosphatemia (25)	12.76±6.03	5-20 days	0.022
Normal phosphorus (11)	4.09±3.09	1-8 days	

N.B: The previous data are presented according to Mean & SD and number of patients also P value
N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study

Study the level of each electrolyte in hypophosphatemic group:

Table (9) shows that combined hypophosphatemia with hypokalemia has highly statistically significant increase in need for ventilation, duration of ventilation and poor outcome with p value 0.007,0.001,0.002,0.003 respectively, (16) patients had hypophosphatemia and hypokalemia all of them were ventilated with duration of ventilation ranged from 5-20 days, (5) discharged and (11) died. In comparison (14) patients had hypophosphatemia and normal K level but no one needed ventilation.

Table (9): Level of K in hypophosphatemic group (30) (comparing number, need for ventilation, duration of ventilation and outcome).

	Hypokalemia	Normal K (3.5-5.5)	P value
Number	16	14	0.007
Need for ventilation	16	-	0.001
Duration of ventilation (range)	5-20 days	-	0.002
Outcome of ventilated patients	5 discharged 11 died	-	0.003

N.B: The previous data are presented according to number of patients, their need for mechanical ventilation, duration of mechanical ventilation and outcome
N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study

In our study combined hypophosphatemia with hypocalcemia shows statistically significant increase in need for ventilation (p value 0.02), but no significant differences regarding to number, duration of ventilation and outcome.

Eighteen patients had hypophosphatemia and hypocalcemia, (17) of them needed ventilation, (8) discharged and (9) died. In comparison (12) patients had hypophosphatemia and normal Ca level (6) of them were ventilated, (3) discharged and (3) died.

Table (10): Level of Ca in hypophosphatemic group (30) (comparing number, need for ventilation, duration of ventilation and outcome of ventilated patients).

	Hypocalcemia	Normal Ca (8.5-10.5)	P value
Number	18	12	0.076
Need for ventilation	17	6	0.02
Duration of ventilation (range)	5-18 days	6-14	0.098
Outcome of ventilated patients	8 discharged 9 died	3 discharged 3 died	0.06

N.B: The previous data are presented according to number of patients, their need for mechanical ventilation, duration of mechanical ventilation and outcome.
N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study.

Combined hypophosphatemia with hyponatremia in our study shows statistically significant increase in need for ventilation, duration of ventilation and poor outcome with p value 0.01, 0.03, 0.01 respectively. Twenty nine patients had hypophosphatemia and hyponatremia, (24) of them needed ventilation, (13) discharged and (11) died. In comparison one patient had hypophosphatemia and normal Na level, this patient needed ventilation and died.

We couldn't comment on hypomagnesemia due to small number of patients as only one patient had hypomagnesemia in our study.

Table (11): Level of Na in hypophosphatemic group (30) (comparing number, need for ventilation, duration of ventilation and outcome).

	Hyponatremia	Normal Na (135-145)	P value
Number	29	1	0.02
Need for ventilation	24	1	0.01
Duration of ventilation (range)	6-20 days	5 days	0.03
Outcome of ventilated patients	13 discharged 11 died	died	0.01

N.B: The previous data are presented according to number of patients, their need for mechanical ventilation, duration of mechanical ventilation and outcome.
N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study.

In our study combined multiple electrolytes deficiency in hypophosphatemic patients increased need for ventilation, duration of ventilation with poor outcome.

There were 15 patients had ↓Na, ↓K, ↓Ca, ↓Phosphorus, all of them were ventilated with duration of ventilation from 5-20 days, (5) patients discharged and (10) died.

Table (12): Prognosis of multiple electrolytes deficiency in hypophosphatemic patients (30)

	number	Need for ventilation	Duration of ventilation	Outcome of ventilated patients
Combined ↓Na,↓K,↓Ca	15	15	5-20days	5discharged 10 died

N.B: The previous data are presented according to number of patients, their need for mechanical ventilation, duration of mechanical ventilation and outcome

Combined multiple electrolytes deficiency in normal phosphorus group (20) didn't affect need for ventilation as (5) patients had ↓Na, ↓K, ↓Ca, only one patient needed ventilation for 7 days and died.

Table (13): Prognosis of multiple electrolytes deficiency in normal phosphorus group (20)

	Number	Need for ventilation	Duration of ventilation	Outcome of ventilated patients
Combined ↓Na,↓K,↓Ca	5	1	7 days	Died

N.B: The previous data are presented according to number of patients, their need for mechanical ventilation, duration of mechanical ventilation and outcome

Combined multiple electrolytes deficiency in hypophosphatemic group associated with increased need for ventilation, duration of ventilation and poor outcome more than multiple electrolytes deficiency in normal phosphorus group with highly statistically significance and p value 0.003,0.001,0.004 respectively.

Fifteen patients had Combined ↓Na, ↓K, ↓Ca in hypophosphatemic group all of them were ventilated and duration of ventilation ranged from 5-20 days,5 discharged and 10 died. In comparison 5 patients had Combined ↓Na, ↓K, ↓Ca in normal phosphorus group, one patient was ventilated for 7 days and died.

Table (14): Prognosis of multiple electrolytes deficiency in hypophosphatemic and normal phosphorus groups.

Combined ↓Na,↓K,↓Ca	Hypophosphatemic group	Normal phosphorus group	P value
Number	15	5	0.001
Need for ventilation	15	1	0.003
Duration of ventilation	5-20 days	7 days	0.001
Outcome	5 discharged 10 died	died	0.004

N.B: The previous data are presented according to number of patients, their need for mechanical ventilation, duration of mechanical ventilation and outcome

N.B:P value > 0.05 was considered statistically significant (S), while < 0.05 statistically insignificant **P value** and > 0.01 was considered highly significant (HS) in the previous study

4. Discussion

It's well known that COPD is a leading cause of death and disability. It's expected to move from it's status in 2000 as the 4th and 12th most frequent cause of mortality and morbidity, respectively, to be the 3rd and the 5th leading of mortality and morbidity, respectively, in 2020. Morever, about 10% of all hospitalizations are directly or indirectly attributable to COPD exacerbation [(5)].

Low blood phosphorus levels decrease the ability to cough, causing accumulation of secretions in respiratory tract which might overwise increase the risk of infection in ventilated patients [(6)].

Severe hypophosphatemia with blood phosohorus level less than 1.5 mg/dl, carry the risk of muscle breakdown, damage to blood cells production, myocardial dysfunction, damage to nervous and immune system. In addition, weakness of respiratory muscles especially diaphragm might develop [(7)].

Weakness of the diaphragm which is secondary to low blood phosphorus levels is a well known cause of mechanical ventilation and weaning failure [(6)].

Our study was carried out to evaluate the prognostic value of hypophosphatemia on patients with AECOPD, this study included 50 patients with COPD exacerbation admitted at chest department and respiratory ICU in Tanta university hospital in the period between July 2018 and January 2019.

In our study serum phosphorus was measured on admission, hypophosphatemia is considered if serum phosphorus is below 2.5mg/dl. In our work 90% of patients were males and 10% females, COPD exacerbation increased in males with old age and heavy smokers who had long duration of smoking, the mean age of studied subjects was 67 years. This was found also in the study done by **Pauwels et al**. [(8)] who studied the gender in Chronic Obstructive pulmonary disease and examined 200 patients admitted with AECOPD, 120 were males and 80 were females they found that COPD exacerbations increased also in males with old age and with long duration of smoking. In contrary, **Mannino et al**. [(9)] found that COPD exacerbation increased in women as women may be at greater risk of smoking induced lung function impairment, more severe dyspnea and poorer health status for the same level of tobacco exposure as airways of women are smaller and thus each cigarette represents a proportionately greater

exposure. Studies from developed countries [10] showed that the prevalence of disease was almost equal in men and women, which probably reflects changing in tobacco smoking habits.

In the present study the need for mechanical ventilation significantly increased in elderly males with high smoking index (p value < 0.01). This matched with the study done by Ai-Ping C in 2005 who found that the need for mechanical ventilation increased in heavy smokers with old age and long duration of smoking. This result also in agreement with the study **Anthonisen et al** [11] who reported that smoking increased the severity of COPD exacerbation and increased the need for mechanical ventilation as smoking has a higher prevalence of respiratory symptoms and lung function abnormalities. Also **Postma et al.** [12] found that smoking increased the severity of COPD exacerbation due to affection of tracheobronchial tree.

In the current study the increased level of PCO_2 increased need for mechanical ventilation which in agreement with the study done by **Ai-Ping** [13] who found that the increasing level of PCO_2 which is directly related to severity of COPD exacerbation increased the need for mechanical ventilation, In addition high levels of PCO_2 decrease the conscious level of the patient and cause respiratory effort and the study done by **Hnizdo et al** [14] considered PCO_2 an important predictor for mortality as it increased the need for mechanical ventilation and so might increase mortality.

In our study 30 patients had hypophosphatemia and 20 patients had normal phosphorus levels. Our results showed that the level of PCO_2 significantly increased in hypophosphatemic patients more than in patients with normal phosphorus level (p value<0.05), which increased the severity of COPD exacerbation as hypophosphatemia caused respiratory muscle weakness so patient couldn't wash PCO_2 which inturn caused accumulation of PCO_2. That is in agreement with the study of **Alsumrain et al.** [6] who found that low blood phosphorus level decreased the ability to cough causing accumulation of secretion in respiratory tract which might overwise increased risk of infection in ventilated patients. **Patil et al** [5] found that hypophosphatemia increased the severity of COPD exacerbation as it caused respiratory failure by increasing levels of PCO_2 We found a correlation between hypophosphatemia and necessity of mechanical ventilation, as the need for mechanical ventilation increased in patients with hypophosphatemia more than in patients with normal phosphorus level, (83%) of patients with hypophosphatemia were ventilated in comparison to only (11%) of patients with normal phosphorus level. Also hypophosphatemia is associated with poor outcome, in patients with hypophosphatemia (56.6%) of patients discharged and (43.4%) of patients died, while in patients with normal phosphorus levels (75%) of patients discharged while (25%) of patients died.

We observed a difference in duration of ventilation between patients with hypophosphatemia and patients with normal phosphorus level, as duration of ventilation increased in patients with hypophosphatemia due to failure of weaning as hypophosphatemia causes respiratory muscle weakness and diaphragmatic weakness.

This result matched with the study done by **Farah et al** [3] who studied the relation between hypophosphatemia and the need for mechanical ventilation in patients admitted with AECOPD, they studied 255 patients and they found that 76.5 % of patients who had low phosphorus levels during hospitalizations needed MV compared to 15.6% of patients with normal phosphorus, this explained by respiratory muscle weakness caused by hypophosphatemia. This result also agreed with **Schweickert and Hall** [15] who found that low phosphorus levels increased the need for mechanical ventilation and duration of ventilation due to respiratory muscle weakness and diaphragmatic weakness. Also **Papi et al.** [16] found that hypophosphatemia led to weaning failure so associated with poor outcome and increased mortality. While **Hogg et al** [17] found that hypophosphatemia increased need for ventilation without affection on duration of ventilation or outcome.

This study in addition demonstrated that combination between hypophosphatemia and hypokalemia significantly increased the need for mechanical ventilation, duration of ventilation and affected outcome badly (p value < 0.01). On the other hand hypokalemia alone didn't significantly affect the need for mechanical ventilation, duration of ventilation and outcome (p value> 0.05). In the study done by **Berkelhammer and Bear** [18] association between hypokalemia and hypophosphatemia increased the severity of COPD exacerbation and increased the need for mechanical ventilation due to respiratory muscle weakness. Also, in 2009 **Mair et al.** [19] found that combination between hypophosphatemia and hypokalemia, increased the need for ventilation and duration of ventilation. Again, **Fishman et al** [20] found that combination between hypophosphatemia and hypokalemia led to poor outcome and increased mortality due to prolonged ventilation and weaning failure.

This study is not matched with that done by **Schweickert et al** [15] who found that hypokalemia

alone without hypophosphatemia increased severity of COPD exacerbation and might increase mortality due to cardiac arrhythmia and muscle paralysis. Again and contrary to this result **Nelson and Cox** [21] studied the relation between level of potassium (k) on admission and the need for ventilation, they found that (33%) of ventilated patients had hypokalemia; however of non –ventilated patients, only (3%) had hypokalemia so hypokalemia alone increased the need for mechanical ventilation and due to respiratory muscle weakness and diaphragmatic weakness.

Our results showed that combination between hypophosphatemia and hypocalcemia significantly increased the need for mechanical ventilation without affection on duration of ventilation or outcome (p value <0.01), while hypocalcemia alone didn't significantly affect the need of the patient for mechanical ventilation, duration of ventilation and outcome (p value> 0.05).

This agreed with **Rabe et al** [22] who found that association between hypocalcemia and hypophosphatemia increased the severity of COPD exacerbation and increased the need for mechanical ventilation due to respiratory muscle weakness. **Fishman et al** [20] reported that combination between hypophosphatemia and hypocalcemia led to poor outcome and increased mortality due to prolonged ventilation and weaning failure. In contrast with the study, **Schweickert et al** [15] found that hypocalcemia alone without hypophosphatemia increased the severity of COPD exacerbation and might increase mortality as decreased levels of Ca caused respiratory muscle and diaphragmatic weakness. Also against to this result **Currie and Legge** [23] found that hypocalcemia alone associated with increased duration of ventilation and poor outcome due to diaphragmatic weakness.

In our study combination between hyponatremia and hypophosphatemia significantly increased the need for mechanical ventilation, duration of ventilation and associated with poor outcome (p value<0.01), while hyponatremia alone didn't significantly affect. The need of the patient for mechanical ventilation, duration of ventilation and outcome (p value > 0.05). This agreed with **Schaefer et al** [24] who found that hyponatremia alone didn't affect the need for mechanical ventilation, duration of ventilation and outcome. This result is not consistent with that reported by **Stockley et al** [25] who found that hyponatremia alone increased the need for mechanical ventilation and weaning failure as severe hyponatremia had a bad effect on the conscious level of the patient.

This study found that that combined hypophosphatemia with multiple electrolytes deficiency increased the need for mechanical ventilation, duration of ventilation and poor outcome. On other hand multiple electrolytes deficiency without hypophosphatemia had no effect on the need for ventilation, duration of ventilation and outcome.

In contrary, **Amanzadeh and Reilly** [26] found that deficiency of each electrolyte alone (K, Ca, Na) had a bad effect on severity and prognosis of COPD as hypokalemia and hypocalcemia caused respiratory muscle weakness. In addition hyponatremia may deteriorate conscious level of the patient.

We couldn't comment on hypomagnesemia due to the small number of patients as only one patient had hypomagnesemia in our study.

Finally, we found that hypophosphatemia increased severity of COPD exacerbation, need for ventilation and duration of ventilation, also hypophosphatemia was associated with poor outcome and high rate of mortality.

Conclusion

- Hypophosphatemia may increase the severity of COPD exacerbation, need for ventilation, duration of ventilation, weaning failure and so increases the rate of mortality.
- Combination between hypophosphatemia and hypokalemia or hyponatremia increased the need for ventilation, duration of ventilation and affected outcome badly.
- Combination between hypophosphatemia and hypocalcemia increased the need for ventilation without affection on duration of ventilation and outcome.

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