Assessment of serum electrolytes (sodium, potassium, and ionized calcium) during chronic obstructive pulmonary disease exacerbation
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Background
Chronic obstructive pulmonary disease (COPD) is the third leading universal cause of mortality. Although chronic obstructive pulmonary disorder is primarily a chronic disease, a great number of patients complain of exacerbations. Severe exacerbations are associated with worse survival consequences. This study aimed to detect changes in serum sodium, potassium, and ionized calcium (Na, K, and ionized Ca) during COPD exacerbation.

Patients and methods
A total of 45 patients with exacerbation of COPD and 15 apparently healthy participants were included. Serum electrolytes (Na, K, and ionized Ca) were obtained from patients and controls. Full clinical history, complete blood count, renal and liver function, serum electrolytes (Na, K, and ionized Ca), and oxygen saturation measurement were done for patients.

Results
Serum Na, K, and ionized Ca were decreased in patients than controls (with statistically significant difference). These electrolytes levels were lowest in life-threatening exacerbation than other grades of exacerbations (with statistically significant difference).

Conclusion
COPD exacerbation is associated with low levels of Na, K, and ionized Ca.

Keywords:
chronic obstructive pulmonary disease, exacerbation, serum electrolytes

Introduction
Chronic obstructive pulmonary disease (COPD) is the third leading cause of mortality worldwide [1]. Although COPD is mainly a chronic disease, great numbers of patient complain of exacerbations, which is known as change in the ordinary pathway of the disease with change in the usual shortness of breath, cough, and/or expectoration and beyond normal daily variations, which is sudden and may warrant a change in regular medication in a patient with underlying COPD. Exacerbations are a principal medical and health care issue. Severe exacerbations of COPD are associated with worse survival consequence [2].

Patients and methods
This cross-sectional study included 60 patients: 45 patients with COPD exacerbation and 15 age-matched and sex-matched apparently healthy participants as controls. Consents were taken from sharing subjects and patients with Ethical Committee approval. Patients were admitted to Chest Department of Benha University Hospital from June 2017 to May 2018.

Severity of COPD exacerbation included in the present work involved moderate, severe, very severe, and life threatening. Rang of exacerbation severity includes mild: managed with antibiotics without need for steroids; moderate: need treatment with parenteral steroids with or without an antibiotic; severe: hypoxemia without CO2 retention or acidosis, with PaO2 < 60 mmHg; very severe: hypoxia, CO2 retention but no acidosis, with PaO2 <60 mmHg, PaCO2 >45 mmHg, and pH more than 7.35; and life-threatening: acidosis and CO2 retention, with PaCO2 >45 mmHg and pH<7.35 [3].

Patients admitted for reasons other than exacerbation; those with pre-existing renal, hepatic, endocrinal (e.g. adrenal insufficiency) or cardiac illness; those with diabetic ketoacidosis; and those with cerebral causes of salt wasting were excluded. Serum electrolytes (Na, K, and ionized Ca) were measured for all participants using ST-200 plus Electrolyte Analyzer (Sensa Core, Sensa...
Core Medical Instrumentation Pvt. Ltd., Export Promotion Industrial park, Pashamylaram, Medak, Hyderabad, Telangana, India). Normal level of sodium (Na) was 135–145 mEq/l, potassium (K) 3.5–5.5 mEq/l, and ionized Ca 4.4–5.4 mg/dl [4]. Pulmonary function tests done for patients by spirometry using JAEGER carefusion (234 GmbHlebnizsr, Hoechberg, Germany). Complete blood count and renal and liver function tests were done, oxygen saturation was measured by pulse oximetry, and those with SaO2 less than 92% underwent arterial blood gas analysis.

Statistical analysis [5]
The collected data were tabulated and analyzed using SPSS, version 16 software (SPSS Inc., Chicago, Illinois, USA) and Medcalc software, version 16.1 (1993–2016, Medcalc Software bvba). Data were presented using χ² test to analyze them. Quantitative data were presented as a mean±SD. Shapiro–Wilks tests were used to assess normality of data. Assuming normality at P value more than 0.05, Student t test and analysis of variance for normally distributed variables were used. P value less than 0.05 is significant, P value more than 0.05 is nonsignificant, and P value less than or equal to 0.001 is highly significant.

Results
The present study included 60 patients of which 45 were cases and 15 were apparently healthy controls. Cases included 41 (91.1%) males and four (8.9%) females and controls included 12 (80%) males and three (20%) females. There was a nonsignificant difference in mean age of cases (60.4±8.6) and controls (59.2±8.1). Na, K, and ionized Ca levels were lower in patients (134.34±4.6, 3.4±0.4, and 4.4 ±0.3, respectively) than in controls (143.9±1.2, 3.5±0.2, 5.4±0.2, respectively), with statistically significant difference (Table 1). Hyponatremia, hypokalemia, and hypocalcemia constituted 55.5% (25), 48.9% (22), and 53.3% (24), respectively, among the patients (Table 2). Mean serum Na, K, and ionized Ca were lowest in life-threatening COPD exacerbation (127.5±5.3, 2.9±0.3, and 4.1±0.2, respectively) versus very severe ones (131±4.4, 3.2±0.2, and 4.4±0.3, respectively), severe exacerbation (134±4.1, 3.4±0.4, and 4.4±0.4, respectively), and finally moderate ones (136±3.2, 3.7±0.3, and 4.6±0.12, respectively), with statistically significant difference (Table 3).

Discussion
COPD is one of the main cause of morbidity and mortality all over the world. With increasing industrialization and smoking, the prevalence of COPD is increasing. Exacerbations are the most common cause of admission into hospital among patients with COPD [6]. There may be a number of metabolic disturbances arising owing to effect of drugs used in COPD treatment (i.e., beta2 agonists and corticosteroids) which can decrease levels of Na and K and increase levels of hyperbilirubinemia, transaminases, blood urea, and serum creatinine. Although most of these features are correctable, very often they are missed or confuse the diagnosis. Presence of coexisting metabolic disorder may cause severe health abnormalities and even death. Thus, early diagnosis and prompt management of these abnormalities are critical [7].

<table>
<thead>
<tr>
<th>Table 2 Percentage of hyponatremia, hypokalemia, and hypocalcemia among patients with chronic obstructive pulmonary disease exacerbation</th>
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</thead>
<tbody>
<tr>
<td>Electrolyte disturbance</td>
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<tr>
<td>-------------------------</td>
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<tr>
<td>Hyponatremia (&lt;135 mEq/l)</td>
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<tr>
<td>Hypokalemia (&lt;3.5 mEq/l)</td>
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<td>Hypocalcemia (&lt;4.4 mg/dl)</td>
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Table 1 Age, sex, serum sodium, potassium, and ionized calcium in cases and controls

<table>
<thead>
<tr>
<th>Groups</th>
<th>Case (45)</th>
<th>Control (15)</th>
<th>P value</th>
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<tbody>
<tr>
<td>Sex [n (%)]</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Male (53)</td>
<td>41 (91.1)</td>
<td>12 (80.0)</td>
<td>&gt;0.05 (Fisher’s exact test)</td>
</tr>
<tr>
<td>Female (7)</td>
<td>4 (8.9)</td>
<td>3 (20.0)</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>60.4±8.6</td>
<td>59.2±8.1</td>
<td>&gt;0.05#</td>
</tr>
<tr>
<td>Na level</td>
<td>134.3±4.6</td>
<td>143.9±1.2</td>
<td>0.000*#</td>
</tr>
<tr>
<td>K level</td>
<td>3.4±0.4</td>
<td>5.3±0.2</td>
<td>0.000*#</td>
</tr>
<tr>
<td>Ionized Ca</td>
<td>4.4±0.3</td>
<td>5.4±0.2</td>
<td>0.000*#</td>
</tr>
</tbody>
</table>

*Significant results. #Independent t test.
The present work showed that mean age of patients was 60.4±8.6 years and healthy controls was 59.2±8.1 years, with nonsignificant difference. Males constituted 88.4% (53) of them, with 41 among cases and 12 among controls, and females were seven (11.7%), with four among cases and three among controls. In a study done by Harshavardhan and Chikkahonnaiah [8] on 100 patients with COPD and 100 healthy control, they found that patients’ mean age was 57.92±12.91 years and that of controls was 53.73±8.98 years.

In the present study, mean Na, K, and ionized Ca measured in patients with COPD during exacerbation were 134.34±4.6, 3.4±0.4, and 4.4±0.3, respectively, and these levels were lower than controls (143.9±1.2, 5.3±0.2, and 5.4±0.2, respectively), with statistically significant difference. Of them, 25 (55.5%) patients had hyponatremia, 22 (48.9%) patients had hypokalemia, and 24 (53.4%) patients had hypocalcemia. Goli et al. [9] found that mean serum Na and K in patients with exacerbation were 132±5.65 and 3.29±0.96 mEq/l, respectively. Decreased Na level can occur in patients secondary to water retention in presence of other comorbidities such as heart or renal failure. Moreover, hyponatremia can occur as a result of different drug therapy, or syndrome of inappropriate antidiuretic hormone secretion [10]. Das et al. [11] reported a significant decrease in serum Na and K in patients with COPD (133±6±86, 3.39±0.96 mEq/l, respectively) than in healthy participants (142±2.28, 4.52±0.02 mEq/l, respectively, P<0.05).

Terzano et al. [12] found that among 67 patients hospitalized for type 2 respiratory failure, decreased Na level occurred in 11 patients, decreased levels of Na, chloride, and K occurred in 10 patients, and decreased chloride level occurred in seven patients. Cerci Neto and colleagues evaluated the relative frequency of decreased magnesium and other electrolyte disorders in patients with COPD receiving inhaled beta2 agonist and corticosteroids. Decreased magnesium was noticed in 27% of patients, whereas decreased calcium (Ca), K, and Na were present in 52, 42, and 2.8% of patients, respectively [13]. Harshavardhan and Chikkahonnaiah in a study on 100 patients with COPD found that levels of Na and K in patients were 131.7±5.07 and 3.3081±3.3126 mEq/l, respectively, whereas in healthy participants were 138.66±3.82 and 3.8740±3.6003 mEq/l, respectively. They concluded that the patients with acute exacerbation of COPD showed seriously decreased Na and K levels [8].

Parenteral aminophylline causes decreased magnesium, Ca, and Na in vulnerable individuals by expanding renal excretion of them [14].

Decreased Na level might be an indicator of bad outcome of COPD [15]. It might cause central nervous system abnormalities, abnormalities of cardiac conduction, secondary renal dysfunction, and even can cause mortality. Accordingly, it is better to investigate Na level carefully in every patient with COPD exacerbation and manage any abnormalities at an early stage [16].

On the contrary, decreased K level might be an additional defect in COPD. It might occur with hyponatremia either separately or simultaneously. Hypokalemia in patients with COPD may be attributed to long-standing steroid therapy and subsequent metabolic alkalosis [17]. In addition, inhaled beta 2 agonists might add to hypokalemia [18]. Acute respiratory failure accompanied with decreased K level leads to increased death in patients with COPD. This may be owing to arrhythmias or delayed cardiac conduction. So, it is obvious that decreased K level may be frequent in patients with COPD, which could be managed promptly to prevent serious consequences [19].

Vitamin D plays an important role in Ca and bone metabolism. Many factors might cause vitamin D deficiency in COPD and resulting hypocalcemia, including decreased...
dietary intake, decreased ability of aging skin for vitamin D synthesis, decreased outdoor activity and sun exposure, elevated metabolism by steroids, decreased activation owing to kidney dysfunction, and decreased storage in muscles or fat resulting from wasting. Many steps of the vitamin D pathway (intake, synthesis, storage, and metabolism) can potentially be disturbed in patients with COPD [20].

Goli and colleagues compared patients with COPD with electrolyte disorders and those without any electrolyte imbalance on admission and found that there was a significant decrease in pH, PaO₂, and oxygen saturation in patients with electrolyte disorders, whereas there was a significant increase in PaCO₂. This means that patients with electrolyte disorders experience further deterioration in arterial blood gases than the other group without any electrolyte imbalance [9]. This agrees with the results of the present study which showed that mean serum Na, K, and ionized Ca were lowest in life-threatening COPD exacerbation (127.5±5.3, 2.9±0.3, and 4.1±0.2, respectively) versus severe exacerbation (134±4.1, 3.4±0.4, and 4.4±0.4, respectively), severe exacerbation (134±4.1, 3.4±0.4, and 4.4±0.4, respectively), and finally moderate ones (136±3.2, 3.7±0.3, and 4.6±0.12, respectively), with statistically significant difference, which means that the more the electrolytes disturbance, the more the severity of COPD exacerbation and the worse the outcome.

Conclusion
Screening for serum electrolytes in COPD exacerbation is essential to decrease its severity. Correction of these electrolyte imbalance could improve outcome of exacerbation.

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Nil.

Conflicts of interest
There are no conflicts of interest.

References
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