**Study of serum electrolytes in COPD with or without CVD**

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**Abstract**---Background: Chronic obstructive pulmonary disease is a respiratory disease. COPD patients present not only with the features of respiratory tract infections (cough, dyspnea, etc.) but also with other comorbidities. Cardiovascular disease is one of them. COPD and CVD cause various metabolic disturbances like dyselectrolytemia. Aim: Study of serum electrolytes in patients suffering from COPD with or without CVD. Method: in a hospital-based study that included 109 confirmed COPD patients. In our study, first we diagnosed the COPD using spirometry, then we assessed the serum electrolyte level with an echocardiograph in all the confirmed COPD patients. Results: Normal serum sodium levels were found in 69 patients (69/109; 63.30%) with or without CVD, the majority of patients (40/69; 70.18%) in the without CVD group. 32 patients (32/109; 29.36%) were found to have hyponatremia, of which 13 patients (13/32; 40.63%) were included in the without CVD group and 19 patients (19/32; 59.38%) were included in the with CVD group. There were 43 patients (43/109; 39.45%) with or without CVD who had normal serum potassium levels, with the majority of patients (28/43; 65.12%) in the without CVD group. 66 patients (66 /109; 60.55%) were found to have hypokalemia, of whom 37 patients (37/66; 56.06%) had COPD with CVD and 29 patients (29/66; 43.94%) had COPD without CVD. No one of the COPD patients, with or without CVD, was found with...
hyperkalemia. Conclusion: Our study indicates that among COPD patients, with or without CVD, serum electrolyte levels get altered. COPD patients with or without CVD do not have hyperkalemia. COPD with CVD patients have a higher chance of hypokalemia than COPD without CVD patients. There was high incidence of normal serum sodium level in COPD without CVD than the COPD with CVD.

**Keywords**—COPD, CVD, hyponatremia, hypernatremia, hypokalemia, hyperkalemia.

**Introduction:**

Chronic Obstructive Pulmonary Disease (COPD) is a group of progressive diseases of the lungs.\(^1\) Cardiovascular disease is the first, and COPD is the third leading cause of death worldwide.\(^2\) These are the major causes of morbidity and mortality worldwide. Further, increases in COPD prevalence and mortality in the coming decades can be predicted. In a published report in economic times, death due to COPD is high in comparison to AIDS, TB, diabetes mellitus, and malaria cumulatively. Despite this, only 1% of the population is aware of or has heard of COPD.\(^3\) COPD prevalence varies by country, age, and gender.\(^4\) More than 3 million people died of COPD in 2012, accounting for 6% of all deaths globally.\(^5\) Based on BOLD and other large-scale epidemiological studies, it is estimated that the number of COPD cases was 384 million in 2010.\(^6\) With the increasing prevalence of smoking in developing countries and aging populations in high-income countries, the prevalence of COPD is expected to rise over the next 40 years, and by 2060 there may be over 5.4 million deaths annually from COPD and related conditions.\(^7,8\) COPD is an economic and social burden that is both substantial and increasing.\(^9,10\) According to the 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 narrowing and loss of small airways. Due to airflow obstruction, oxygen is not fully released before the next breath is drawn in, resulting in shortness of breath. COPD makes it difficult for a person to breathe.\(^11\) Initially, symptoms can be mild, but as the disease progresses, these symptoms can become severe and frequent. Often, it is not diagnosed until the condition reaches an advanced stage. Significant exposure to noxious particles or gases is the most common cause of COPD.

People who consume tobacco smoke (in the form of cigarette/bidi/cigar/marijuana and even pipe smokers) are at a higher risk of developing COPD. Even people who are exposed to second-hand smoke can develop COPD. As well, workplace exposure to chemicals and dust can inflame the lungs and may contribute to the development of COPD. Females who are exposed to biomass fuel are at a higher risk of developing COPD.\(^12\) Most people with COPD are at least 40 years of age or older, and they mostly have a history of smoking.\(^13\) People suffering from COPD are at a higher risk of being diagnosed with other heart problems, lung cancer, and various other conditions.\(^14\) Due to airflow obstruction, low oxygen levels occur in the blood, which causes additional stress on the heart. It further develops into cardiovascular disease.\(^15\) Though
COPD patients mostly present with the features of acute respiratory infections (productive cough, dyspnea, etc.), there may be a number of metabolic disorders arising out of the disease process or as a consequence of the therapy, like electrolyte disorders, type-2 diabetes mellitus, hypertension, dyslipidemia, hyperbilirubinemia, elevated transaminase, elevated blood urea, and creatinine. 

**Materials and Methods**

A hospital-based study was conducted in the Department of Respiratory Medicine, SRMS Medical College, Bareilly, and the Department of Respiratory Medicine, Santosh Medical College, Ghaziabad during the period of November 2017 to November 2020.

Sample Size: Prevalence of COPD lies between 6.5 to 7.7%. We assumed a 6.5% prevalence of COPD with a 5% absolute error and a 10% non-response rate, the estimated sample size comes to be 105.

Inclusion Criteria: Confirmed COPD patients in the age group of 40 to 80 years.

Exclusion Criteria: Patients suffering from pneumonia, tuberculosis, interstitial lung disease, lung carcinoma, other cancers, and HIV are excluded. The study participants were subdivided into four categories: mild, moderate, severe, and very severe COPD according to GOLD guidelines. All the study participants were asked about their socio-economic status, smoking habits, history of dyspnea, duration of breathlessness, family history of respiratory disease, and diabetes mellitus with a well-defined questionnaire. Written consent has been obtained from all the participants prior to the data collection. COPD was diagnosed by spirometry machine-schiller SP-1. Prior to spirometry all the precautions were strictly followed by the technical staff. With spirometry FVC (Forced vital capacity), FEV1 (Forced expiratory volume in 1st second), and FEV1/FVC ratio were measured.

To confirm the cardiovascular disease two-dimensional echocardiography was done by Siemens Acuson X-300 Premium edition. All the patients underwent electrolyte analysis. Collection of blood sample: A blood sample was collected using a pre-heparinized syringe by arterial puncture by a phlebotomist.

**Results**

In the present study, we investigated a total of 109 patients of which 91 were males and 18 were females. Patients were 61.49 years old on average. The mean BMI of patients was 20.73 kg/m2. Out of 109 patients, 85 patients (77.98%) were smokers. Most of the smokers were having 10 or more than 10 pack-year smoking history. Based on COPD severity 39 patients were included in the moderate, 50 patients in the severe, and 20 patients in the very severe COPD group. We had no patients with mild COPD. (Table-1)

Echocardiography results in COPD patients show that 57(52.29%) cases had normal echocardiography. While remaining patients were to be having different stages of cardiac dysfunction. The majority of patients (52 patients; 47.71%) were found with pulmonary arterial hypertension.33 patients (30.28%) with dilated RA/RV, 25 patients (22.94%) with LVDD, and 24 patients (22.02%) with low
LVEF. (Table-2)

Sodium: In the present study 69 patients (69/109; 63.30%) with or without CVD were found with normal serum sodium levels, from this majority of patients (40/69; 70.18%) were included in the without CVD group. 32 patients (32/109; 29.36 %) were found to be having hyponatremia, from which 13 patients (13/32; 40.63%) were included in without CVD group and 19 patients (19/32; 59.38%) were included in with CVD group. Only 8 patients (8/109; 7.34%) were found to be having hypernatremia. 4 out of 57 without CVD (4/57; 7.02%) were found with hypernatremia, and 4 out of 52 with CVD (4/52; 7.69%) were found with hypernatremia. There were no major changes in hypernatremic patients with or without CVD. [Table-3]

Potassium: In the present study 43 patients (43/109;39.45%) with or without CVD were found with normal serum potassium levels, from this majority of patients (28/43 ;65.12%) were included in the without CVD group. 66 patients (66 /109; 60.55%) were found to be having hypokalemia, of whom 37 patients (37/66; 56.06%) had COPD with CVD and 29 patients (29/66; 43.94%) had COPD without CVD. No one of the COPD patients with or without CVD was found with hyperkalemia. It may also be noted that 56 patients (out of these 66 hypokalemic patients) were having severe (36) to very severe (20) COPD. [Table-3]

Table 1: COPD patient distribution

<table>
<thead>
<tr>
<th>COPD stages according to GOLD criteria</th>
<th>No of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
<td>FEV1/FVC (% of predicted)</td>
</tr>
<tr>
<td>GOLD 1</td>
<td>≥80</td>
</tr>
<tr>
<td>GOLD 2</td>
<td>50-79</td>
</tr>
<tr>
<td>GOLD 3</td>
<td>30-49</td>
</tr>
<tr>
<td>GOLD 4</td>
<td>&lt; 30</td>
</tr>
</tbody>
</table>

Table 2: Echocardiography findings in COPD patients

<table>
<thead>
<tr>
<th>Distribution of 109 COPD patients</th>
<th>Echocardiography results in 109 COPD patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of COPD patients without CVD</td>
<td>Pulmonary arterial hypertension</td>
</tr>
<tr>
<td>57</td>
<td>52</td>
</tr>
</tbody>
</table>
Graph 1: Diagnosis of study population

Table 3: Serum electrolyte imbalance in patients

<table>
<thead>
<tr>
<th>Serum electrolytes</th>
<th>Serum electrolyte imbalance in study patients</th>
<th>Statistical analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>COPD without CVD (n=57)</td>
<td>COPD with CVD (n=52)</td>
</tr>
<tr>
<td>Serum sodium level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal 135≤145 meq/L</td>
<td>40</td>
<td>29</td>
</tr>
<tr>
<td>Hyponatremia &lt;135 meq/L</td>
<td>13</td>
<td>19</td>
</tr>
<tr>
<td>Hypernatremia &gt;145 meq/L</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Serum potassium level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal 3.5≤ 5.5</td>
<td>28</td>
<td>15</td>
</tr>
<tr>
<td>Hypokalemia &lt;3.5 meq/L</td>
<td>29</td>
<td>37</td>
</tr>
<tr>
<td>Hyperkalemia &gt;5.5 meq/L</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Discussion

COPD is a chronic lung disease of the elderly group that usually affects people after the 4th decade of life. According to the Economic Times Health World report published in October 2019, COPD is the world’s third leading cause, and more than 90% of people are unaware of it. Smoking prevalence is very high among COPD patients. The prevalence of smoking is much greater in men than in women. COPD is the result of cumulative exposure for decades. The prevalence of COPD is often closely tied to the prevalence of tobacco smoking, although, in many countries, outdoor, occupational, and indoor air pollution (resulting from the burning of wood and other biomass fuel) are major COPD risk factors. The
single most important identified etiological component in COPD is cigarette smoking.

In the present study, among the 109 COPD patients, 92 patients (84.40%) were smokers. The American lung association reported the same as our study, about 85% of people with COPD develop the disease because of cigarette smoking. Age is a risk factor for COPD. As age advances, FEV1 declines, and other risk factors add to the disease process. As well, in COPD patients, cardiovascular disease findings increase with age also. There are various cardiac manifestations due to COPD. These infestations aggravate COPD, increasing morbidity and mortality among COPD patients. The findings of cardiovascular disease increase with the severity of COPD.

In the present study population, pulmonary arterial hypertension has been a major finding. One possible reason for this high prevalence of pulmonary hypertension could be selection bias that favoured ordering echocardiograms in patients with clinical features of pulmonary hypertension. The findings of our study appear to be like previous studies in respect of PAH, which increase with the severity of COPD. In the present study, PAH was found in 52 patients (47.70%). The mean age of COPD patients without PAH is 58.49, while those with PAH are 64.77. It shows that the incidence of cardiovascular disease increases with age among COPD patients. It is reviewed in another study also by Ann D. Morgan et al.

In the present study, there was no change in BMI among the patients with or without CVD. CVD in COPD does not differentiate between males and females. COPD is an umbrella term that represents airflow blockage and breathing-related disorders. COPD is also classified as a systemic disease because it affects the entire body rather than just one organ. As a result, COPD causes a variety of comorbidities. Common comorbidities in association with COPD are pulmonary infections, skeletal muscle abnormalities, hypertension, diabetes, cancer, and pulmonary vascular disease.

Chronic conditions of these diseases affect the health of COPD patients. Due to various comorbidities among COPD patients, several biochemical parameters get altered. Biochemical parameters change in COPD, which is also related to CVD. On the assessment of serum electrolyte, dyselectrolytemia was found in COPD patients. This is also reported by Cosimo Marcello Bruno et al. In the comparison of CVD patients, maximum number of non-CVD patients were maintaining the normal serum sodium and potassium level. It is also noted that the incidence of hyponatremia is higher in CVD patients than in non-CVD patients. One reason for hyponatremia is that COPD can cause SIADH due to renal tubules vasoconstriction and antidiuresis in response to hypercapnia. Such a type of response by the renal tubules leads to hyponatremia due to the retention of water. Liviu klein et al also reported the low serum sodium level in cardiac patients, which is similar to our findings. A vast majority of COPD with or without CVD patients (60.55%) were found with hypokalemia. It is also noted that incidence of hypokalemia is higher in COPD with CVD patients than in those without CVD. Potassium deficit can induce breathing problems since potassium is necessary for lung function. No patients were found with hyperkalemia. More
than ¾ PAH patients (42/52;80.77 %) were found with < 4 meq/L potassium level. As well as, out of 70 severe to very severe COPD patients, 63 patients (63/70;90%) were found with <4 meq/L potassium level. 36 patients of them (36/63;57.14%) had PAH. It implies that hypokalemia is a serious complication in COPD patients which also further develop in cardiovascular diseases. So it narrates that dyselectrolytemia increases with the severity of COPD. Dyselectrolytemia with the hypoxemia, hypercapnia and acidosis ultimately leads to cardiovascular disease. Which is also reported by Md. Haroon et al. 21 Incidence of cardiovascular disease in COPD patients increases with the severity of COPD. It is previously discussed also that PAH is a major finding in among the COPD patients in this study. One possible reason for the PAH findings is pulmonary vascular remodeling in COPD due to increase in pulmonary artery pressure, which is thought to result from the combined (cumulative) effect of hypoxia, inflammation and loss of capillaries.

Our study results appear to be similar with previous studies. 22,23 PAH findings increase with the severity of COPD. The treating physician frequently advised echocardiography to exclude the presence of cardiac failure rather than diagnose PAH, dilated RA/RV, and LVDD. It is felt that when COPD patients progress towards comorbid CVD, the diagnosis of PAH is important, and treatment should be started immediately.

**Conclusion**

COPD and CVD cause several pathophysiological and biochemical changes. Which alter the several biochemical parameters. Dyselectrolytemia occurs in COPD patients with or without CVD. The present study showed that in comparison to cardiovascular patients, the maximum number of COPD without CVD patients were maintaining the normal serum sodium level. It is also noted that the finding of hyponatremia is higher in CVD patients than in non-CVD patients.

More than 60% of COPD with or without CVD patients were found to have hypokalemia. The incidence of hypokalemia is higher in COPD with CVD patients than without CVD patients. So, the early diagnosis of CVD among COPD patients is necessary. It will reduce complications in COPD patients. If by treatment, the serum electrolyte level is maintained then the incidence of cardiovascular events also decreases in COPD patients. COPD has no permanent cure, but with proper management and appropriate treatment, a person by changing in lifestyle can achieve control over the symptoms, reduce the risk of other associated diseases, and also lead a quality life.

Ethical approval and consent to the participate: Prior to beginning research work ethical committee permission was taken from Santosh deemed to be university. As well as before collection of data patients or their caretaker written consent has been obtained and all things was explained to him in the local language.

**Abbreviations**

COPD: Chronic Obstructive Pulmonary disease
CVD: Cardiovascular disease
FEV1: Forced Expiratory Volume in 1 second
FVC: Forced Vital Capacity
GOLD: Global Initiative of Obstructive Lung Disease
LVDD: Left ventricular diastolic dysfunction
LVEF: Left Ventricular Ejection Fraction
PAH: Pulmonary Arterial Hypertension
RA: Right Atrium
RV: Right Ventricle
SIADH: Syndrome of inappropriate antidiuretic hormone secretion

References

20. Liviu Klein et al 2005 Lower Serum Sodium Is Associated With Increased Short-Term Mortality in Hospitalized Patients With Worsening Heart Failure Circulation vol.111, No 19 https://www.ahajournals.org/doi/10.1161/01.cir.0000165065.82609.3d