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STUDY ON SERUM ELECTROLYTES AND SEVERITY OF COPD AS PER GOLD CRITERIA AT OUR TERTIARY CARE HOSPITAL

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ABSTRACT

Background: According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), chronic obstructive pulmonary disease (COPD) is distinguished by recurrent respiratory symptoms and airflow restriction that are caused by abnormalities in the airways and/or alveoli, which are typically brought on by protracted exposure to hazardous gases or particles. The social and economic burdens formed by acute exacerbations of COPD are very high. Depending on the severity of the condition, patients with COPD had a 5 year overall survival rate that varied from 56% to 92%.

Objectives: In this study, we aimed to correlate the serum electrolyte levels with the severity of COPD using GOLD criteria (2021).

Methods: A total number of 180 patients were included in the case control study. This includes 90 patients of stable COPD and 90 patients of acute exacerbation of chronic obstructive pulmonary disease (AECOPD) of age group of 30 to 60 years. 5 ml venous blood was drawn from patients; under aseptic precautions with a clot activator tube. Serum was separated by centrifugation and used for the following biochemical analysis. Serum Sodium, Serum Potassium, Serum Chloride, Serum Ionic Calcium were estimated using Unicorn Lyte 5 Analyzer and Serum Magnesium was estimated using Dimension EXL 200. Statistical analysis was analyzed using Student's t-test and Chi-Square test for the correlation of serum electrolyte levels with the severity of disease.

Results: There is significant decrease in the levels of serum sodium, chloride, ionized calcium, and magnesium in acute exacerbation (AE) COPD patients as compared to stable COPD patients ($p < 0.001$). There is no significant difference in the levels of serum electrolytes with the severity of the disease ($p > 0.05$).

Conclusion: In the present study, we found hyponatremia, hypochloremia, hypocalcemia, and hypomagnesemia in acute exacerbation (AE) COPD patients as compared to stable COPD patients. The present study did not find a statistically significant correlation between the levels of electrolytes and the severity of COPD.

Keywords: COPD, Electrolyte imbalance, Hypocalcemia, Hypomagnesemia, Hyponatremia.

INTRODUCTION

According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), chronic obstructive pulmonary disease (COPD) is distinguished by recurrent respiratory symptoms and airflow restriction that are caused by abnormalities in the airways and/or alveoli, which are typically brought on by protracted exposure to hazardous gases or particles.[1] COPD

causes gradual and enduring respiratory symptoms, such as coughing, breathing issues, and phlegm formation. The social and economic burdens formed by acute exacerbations of COPD are very high. Less information is known about the causes and indicators of prognosis in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD), particularly those from poor nations.[2]

As COPD progresses from an early stage to an advanced one, pulmonary hypertension, the alveolar wall, and the respiratory epithelial fibrosis all disappear. Depending on the severity of the condition, patients with COPD had a 5 year overall survival rate that varied from 56% to 92%.[3] The risk factors for chronic respiratory diseases (CRDs) include the use of tobacco, allergens, exposure to outdoor and indoor pollutants, unhealthy diet, obesity, physical inactivity, and occupational exposure, etc.[4] The target of assessment of COPD is to determine the airflow limitation level, its effect on the health of the patient, and risk of future procedures like hospital admissions, the patient's death, or exacerbations, to select the right therapy for management. The following things are considered in the assessment of COPD.[5]

Severity of the abnormalities of the spirometry

1. Signs and symptoms of the patient
2. Proper history of patients of moderate and severe exacerbations
3. Comorbidities

Mild events of exacerbations are managed by a rescue medication which is short-acting, but not recorded in clinical trials or practice. Moderate events need therapy with rescue medication that is short-acting along with oral steroids or antibiotics. Severe events need therapy in hospitalization and/or may lead to death.[6]

Electrolyte imbalances are common in COPD patients. Electrolyte imbalance causes COPD patients to have poor outcomes. The metabolic disturbances and their consequences in COPD are known but still data is limited regarding why considerable ratio of patients with COPD presents with significant electrolyte imbalances (EI) on the basis of severity (as per the GOLD criteria 2023). There are various endothelial factors and impairment of exchange of gas which induces various hormones such as vasopressin and atrial natriuretic peptide that lead to hyponatremia and water retention. A hyponatremia or low level of sodium (Na^+) is the most prevalent and significant electrolyte imbalance identified in patients with COPD. Other conditions involve hypokalemia, hypomagnesemia, and hypocalcemia.[7] Various researches compared the serum electrolyte levels in COPD patients, healthy controls, and acute exacerbation (AE) COPD patients. The present study is undertaken to determine and compare the serum electrolyte levels in stable and acute exacerbation (AE) COPD patients and correlate the serum electrolyte levels with the severity of COPD using GOLD criteria (2021).

The objectives of our study includes –

a) To estimate and compare the serum electrolyte levels in stable COPD and acute exacerbation (AE) COPD patients.
b) To correlate the serum electrolyte levels with the severity of COPD using GOLD criteria (2021).

MATERIAL & METHODS

Source of Data and Study Design:

It is a case control study, conducted at the National Institute of Medical Sciences & Hospital in Jaipur, (Rajasthan) in the Department of Biochemistry in association with the Department of Respiratory Medicine and General Medicine. Samples were analyzed for biochemical investigations in the Department of Biochemistry, National Institute of Medical Sciences & Research and Hospital, Jaipur.

Inclusion Criteria:

- Clinically diagnosed stable and AECOPD patients.
- Age between 30 to 60 years (both male and female).
- Patients who are willing to participate in the study.

Exclusion Criteria:

Patients with Diabetes Mellitus (DM), Hypertension, Cardiovascular Disease, Thyroid Dysfunction, Renal Disease (such as acute renal failure, chronic kidney disease), Pregnant and lactating women, Alcoholic were excluded from the study.

Sample Collection: 5 ml venous blood was drawn from patients; under aseptic precautions with a clot activator tube. Serum was separated by centrifugation and used for the following biochemical analysis. Serum Sodium, Serum Potassium, Serum Chloride, Serum Ionic Calcium were estimated using Unicorn Lyte 5 Analyzer and Serum Magnesium was estimated using Dimension EXL 200.

Statistical Analysis: All the data was presented in number % percentage. Mean and Standard Deviation were used to determine the data. Student's t-test was used for the comparison of serum electrolyte levels in stable and acute exacerbation (AE) COPD patients. Chi-square test was used for the correlation of serum electrolyte levels in stable COPD patients. A p-value less than 0.05 were considered statistically significant.

RESULTS

A total number of 180 patients were included in the study. This includes 90 patients of stable COPD and 90 patients of AECOPD of age group of 30 to 60 years. There are 68 (75.56%) and 22 (24.44%) were males and females patients in stable COPD group whereas 64 (71.11%) and 26 (28.89%) were males and females patients in AECOPD group.

It is evident from the Table No 1 that there were decreased levels of sodium, chloride, ionized calcium and magnesium levels in AECOPD patients compared to stable COPD patients, which was statistically highly significant (p- value < 0.00001). There was no statistically significant difference in the levels of potassium between the two groups.

It is evident from the Table No 2 that levels of serum electrolytes did not show statistically significant correlation with the severity of COPD as per GOLD criteria ($p > 0.05$).

DISCUSSION

In the present study, we included a total of 180 patients based on inclusion and exclusion criteria. These patients were divided into 90 stable COPD group and 90 AECOPD group. The mean age (years) in stable COPD and AECOPD patients was 52.2 ± 7.92 years and 53.87 ± 8.01 years respectively. The ratio of males was high as compared to females in stable COPD and AECOPD patients. Das P et al (2010) also showed the high ratio of males as compared to females in AECOPD (47: 17) and control group (15: 5).[2] Most of the patients (70%) were having normal BMI in both stable and acute exacerbation (AE) COPD condition.

We evaluated serum levels of sodium, potassium, chloride and ionized calcium in both the groups. The normal reference ranges used for these parameters were serum sodium is 135 – 145 mmol/L, potassium is 3.5 – 5.3 mmol/L, Chloride is 97 – 110 mmol/L, Ionized Calcium is 1.1 – 1.32 mmol/L, and magnesium is 1.6 - 2.4 mg/dL respectively. We found statistically significant decreased levels of serum sodium, chloride, ionized calcium and magnesium in acute exacerbation (AE) COPD patients as compared to stable COPD patients ($p < 0.001$). We found no statistically significant difference in the levels of serum potassium in acute exacerbation (AE) COPD patients as compared to stable COPD patients ($p > 0.05$).

In concordance with our findings, Maklad SF et al (2019)[8] find significantly abnormal levels of serum electrolyte (sodium, potassium, magnesium and chloride) levels in AECOPD patients as compared to healthy controls.

During AECOPD, lungs experience increase in mucus production, tightening of passages of airway and inflammation is triggered by immunological defense system activation in the body. Hyponatremia is developed due to hypercapnia, hypoxia, renal insufficiency, respiratory acidosis, SIADH are some factors responsible for it. Hypomagnesemia cause muscle fatigue as it is involved in muscle tones maintenance and contraction of muscle.

Hypochloremia is caused due to respiratory acidosis with metabolic alkalosis and chronic hypercapnia.[8] Rathore HK et al (2020) reported low serum levels of sodium, potassium, chloride, and magnesium in patients of AECOPD compared to stable COPD. Hypercapnia and Chronic hypoxias a result of primary lung pathology, renal or cardiac failure, malnutrition, and respiratory acidosis, use of steroids and bronchodilators, and SIADH may also contribute to hyponatremia in COPD patients. Patients with COPD are predisposed to electrolyte imbalance.[9] Rashid MHU et al (2019) also found low serum levels of sodium and potassium in patients of AECOPD as compared to stable COPD.[7] Sreekumar A et al (2021) also reported that low serum levels of magnesium had an association with COPD exacerbation.[10] Comert et al. (2016) reported that magnesium had positive effects on respiratory muscle functioning and might be utilized as a supplement to normal therapy since it helps patients with AECOPD regain their dyspnea.[11] Tandon S et al. found significantly decreased serum level of magnesium in patients with AECOPD as compared to stable COPD taking PPI and diuretics. More severe was the COPD exacerbation, more frequent was the hypomagnesemia.[12] It has been found that increasing hypoxemia during AECOPD causes intracellular magnesium ions to be depleted.[13] Airway hyperactivity and pulmonary dysfunction are both exacerbated by hypomagnesemia.[14]

Based on FEV1 post-bronchodilator, COPD is divided into four stages. In this study, we also found no significant correlation between serum electrolyte levels and severity of disease in stable COPD patients.

The limitation of the present study is that there may be a correlation between serum electrolyte levels and disease severity; it may not necessarily imply causality. Other factors may be contributing to both the electrolyte imbalance and

the disease severity. Electrolyte levels can vary throughout the day and may be affected by stress, physical activity, and other factors. Therefore, a single measurement may not be representative of a patient's overall electrolyte status.

CONCLUSION

Majority of the studies in our setup do not measure the electrolyte levels as a routine diagnostic test in COPD patients. Henceforth, the results of our study clearly indicate that electrolyte disturbances are quite common in COPD patients and the measurement of these electrolytes will mark significant difference between the two categories, i.e., stable COPD and AECOPD which will be helpful in early therapeutic intervention. Hence worth, the progress of the COPD to AECOPD and also acute exacerbation episodes can be minimized.

In our study, the decrease in the levels of serum sodium, chloride, ionized calcium, and magnesium was found to be more significant in acute exacerbation (AE) COPD patients. We find hyponatremia, hypochloremia, hypocalcemia, and hypomagnesemia in acute exacerbation (AE) COPD patients as compared to stable COPD patients. There is no correlation of serum electrolyte levels, i.e., sodium, potassium, chloride, ionized calcium, and magnesium in stable COPD patients on the basis of severity of disease and maximum number of patients is categorized in moderate (46%) category according to the GOLD criteria. Abnormal levels of electrolytes such as sodium, potassium, chloride, ionized calcium and magnesium have been linked to higher mortality rates in COPD patients. Therefore, the present study suggested that serum electrolyte levels help in assess the severity of the disease and provide appropriate treatment. It is recommended that there should be continuous monitoring of the electrolytes in stable as well as in acute exacerbation (AE) COPD patients and especially in the patients with comorbidities that increases the risk of electrolyte imbalances.

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TABLES

Variables	Stable COPD	AECOPD	t- test	P- Value
Age (years)	52.2 ± 7.92	53.87 ± 8.01	-1.404	0.16202
BMI (kg/m^2)	23.45 ± 2.68	22.99 ± 2.22	1.254	0.21140
Males	68 (75.56%)	64 (71.11%)	-	-
Females	22 (24.44%)	26 (28.89%)	-	-
Sodium(mmol/L)	141.14 ± 3.71	135.3 ± 5.93	7.975	0.00001
Potassium(mmol/L)	4.08 ± 0.47	3.93 ± 0.72	1.655	0.09959
Chloride (mmol/L)	102.62 ± 3.61	97.4 ± 5.77	7.276	0.00001
Ionized Calcium (mmol/L)	1.12 ± 0.15	0.77 ± 0.2	13.282	0.00001
Magnesium (mg/dL)	2.04 ± 0.27	1.74 ± 0.39	6.000	0.00001

Table 1: Shows Distribution of Variables in Stable and AECOPD Patients.
Not significant ($p > 0.05$) and Highly significant ($p < 0.001$)

Variables	Mild	Moderate	Severe	Very Severe	Chi-Square Test	P – Value
Hyponatremia (Na^+< 135)	0	3	0	0		
Normal (Na^+: 135 -145)	4	35	32	10		
Hypernatremia (Na^+> 145)	0	3	1	2	2.929	0.23116
Hypokalemia (K^+< 3.5)	1	1	1	1		
Normal (K^+: 3.5 - 5.3)	3	40	32	11		
Hyperkalemia (K^+> 5.3)	0	0	0	0	4.951	0.17545
Hypochloremia (Cl^-< 97)	0	2	1	0		
Normal (Cl^-: 97 - 110)	4	39	32	12	0.345	0.55708
Hyperchloremia (Cl^-> 110)	0	0	0	0		
Hypocalcemia (Ca^{2+}< 1.1)	1	15	10	6		
Normal (Ca^{2+}: 1.1 - 1.32)	3	25	23	6	1.704	0.63616
Hypercalcemia (Ca^{2+}> 1.32)	0	1	0	0		
Hypomagnesemia (Mg^{2+}< 1.6)	0	2	1	0		
Normal (Mg^{2+} : 1.6 - 2.4)	4	39	32	12	0.345	0.55708
Hypermagnesemia (Mg^{2+}> 2.4)	0	0	0	0		

Table 2: Shows Correlation of Serum Electrolyte Levels with the Severity of Disease. #Not significant ($p > 0.05$)

GOLD Stage	Severity	Spirometry
I	Mild	FEV1/FVC <0.7 and FEV1 ≥80% predicted
II	Moderate	FEV1/FVC <0.7 and FEV1 ≥50% but <80% predicted
III	Severe	FEV1/FVC <0.7 and FEV1 ≥30% but <50% predicted
IV	Very Severe	FEV1/FVC <0.7 and FEV1 <30% predicted

TABLE 3: Shows the Classification of COPD stages on the basis of severity.