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Original Article

A Comparison of Serum Magnesium Levels in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease (COPD) and Stable Chronic Obstructive Pulmonary Disease Patients

Laibah Safdar, Tariq Ismail, Fuad Ahmad Siddiqi, Ahmar Rashid, Ammara Amjad, Sidra Saeed

Department of Medicine, Combined Military Hospital, Rawalpindi/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To compare serum magnesium (Mg) levels in patients with stable Chronic Obstructive Pulmonary Disease (COPD) and those presenting with acute exacerbation of COPD.
Study Design: Comparative cross-sectional study.
Place and Duration of Study: Combined Military Hospital, Rawalpindi Pakistan, from Jun to Dec 2024.
Methodology: This study was conducted on 120 cases of COPD, already diagnosed on the basis of dynamic pulmonary function test results (post bronchodilator FEV1/FVC ratio less than 0.7 or 70%). Patients selected through non-probability convenience sampling were divided into two groups on the basis of their presentation. 60 patients were those presenting with symptoms of acute exacerbation of COPD (Group-A), identified on the basis of Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, and 60 were those with stable COPD (Group-B). Serum magnesium levels were measured in both groups and compared.
Results: The mean serum magnesium level in patients with stable COPD was 0.93±0.19 mmol/L and in those with acute exacerbation of COPD, the mean was 0.65±0.08 mmol/L. The difference in the serum magnesium levels between these two groups was statistically significant.
Conclusion: In patients with acute exacerbation of COPD, serum magnesium levels are less than those with stable COPD, showing that low levels of serum magnesium in COPD patients are associated with increased risk of acute exacerbations, therefore serum magnesium level can be used for monitoring COPD patients for acute exacerbations.

Keywords: Acute Exacerbation, Chronic Obstructive Pulmonary Disease, Serum Magnesium.

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) has been identified as a major cause of death worldwide.[1,2] As per WHO 2024 data, it the fourth most common cause of death, causing approximately 5% of all global deaths.[3] The leading risk factors are tobacco smoking, occupational pollutants, indoor air pollution (from biomass combustion) and ambient air pollution.[4]

There is growing evidence about the association between serum magnesium (Mg) and prevalence of COPD, therefore in the prevention and management of COPD, magnesium supplementation might play an important role.[5] Also, IV magnesium supplementation during episodes of COPD exacerbation has been found to significantly improve pulmonary function tests, therefore it has been advocated to be used, in addition to bronchodilators, in COPD exacerbations.[6,7] The most important function that magnesium plays in the respiratory system is its role as a bronchodilator.[8] This is done by causing the blockade of calcium channels in the airway smooth muscles and reducing airway excitability.[9] A study conducted in Indian state Odisha showed serum magnesium levels of 1.88±0.19 mg/dL in acute exacerbation of COPD, compared to 2.06±0.18 mg/dL in stable COPD patients.[10]

The purpose of our research was to study this relationship between serum magnesium levels and COPD exacerbations in our population, by comparing the serum magnesium levels of stable COPD patients with the serum magnesium level of patients presenting with acute COPD exacerbation.

METHODOLOGY

This cross-sectional comparative study was conducted at Combined Military Hospital (CMH) Rawalpindi, Pakistan, from Jun to Dec 2024. The study was initiated after getting approval from hospital's

Correspondence: Dr Laibah Safdar, Department of Medicine, Combined Military Hospital, Rawalpindi Pakistan
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Ethical Review Committee (ERC letter no.856 CMH Rawalpindi, dated 17/04/2024).

Inclusion Criteria: COPD patients of either gender, with age ranging from 45 to 75 years, who had already been diagnosed with COPD on the basis of dynamic pulmonary function test results (post bronchodilator FEV1/FVC ratio less than 0.7 or 70%) were included.

Exclusion Criteria: Patients with history of ischemic heart disease, renal failure, heart failure and asthma, those using any magnesium supplements or magnesium lowering drugs (like PPIs and digoxin) were excluded.

WHO calculator was used to calculate sample size. Using published detectable mean difference of 0.18 mg/dL, it came to be 17 participants per group.[10] To increase precision and allow for between-population variability and potential missing data, we enrolled 60 participants per group (n=120), which provides substantially greater than 80% power to detect the assumed difference. Non-probability convenience sampling was used to collect data, and informed consent was obtained.

Among these 120 patients, 60 were presenting with acute exacerbation of COPD (Group-A), and 60 were stable COPD patients, with no signs and symptoms of acute exacerbation (Group-B). Acute exacerbation of COPD was identified on the basis of GOLD (Global Initiative for Chronic Obstructive Lung Disease) 2024 guidelines.[11] Exacerbation has been defined as an event characterized by dyspnea and/or cough and sputum that worsens over less than 14 days, and classified as mild, moderate or severe:1) Mild if they are treated with short-acting bronchodilators only; 2) moderate if they are treated with antibiotics and/or oral corticosteroids plus short-acting bronchodilators; and 3) severe if because of the exacerbation, the patient visits the emergency room or requires hospitalization.[11]

After taking informed consent from patients or their attendants, information of all participants was recorded. This included their age, gender, body mass index (BMI), smoking history, comorbid conditions, family history, drug history, years since diagnosis of COPD and history of pervious admissions with acute exacerbation of COPD (AECOPD). Under aseptic measures, blood sample of all the participants was drawn and the samples were sent to Armed Forces Institute of Pathology (AFIP) laboratory for serum magnesium levels. Reports were collected through keeping a record of patients' hospital/lab ID. The reference range of serum magnesium in the laboratory at AFIP is 0.6-1mmol/L.

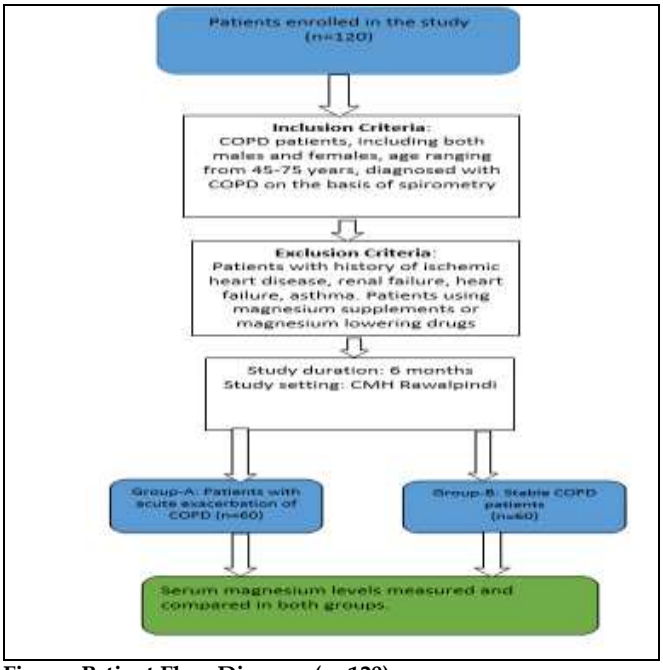


Figure: Patient Flow Diagram (n=120)

Data was analyzed using Statistical Package for the Social Sciences (SPSS) version 23. Frequency along with percentage was calculated for variables like gender, comorbid conditions, smoking status, medications used for COPD treatment, duration of COPD diagnosis, severity of COPD exacerbation and history of previous exacerbations. Mean along with standard deviation was calculated for continuous variables like age, BMI, oxygen saturation, total leucocyte count (TLC), CRP, serum creatinine, hemoglobin and serum magnesium levels. Among these variables that were compared between these two groups, all of the variables (oxygen saturation, TLC, CRP, serum creatinine, hemoglobin and serum magnesium levels) were not normally distributed. Therefore Mann-Whitney U test was applied to find any statistically significant difference across groups. To compare the serum magnesium levels of the two groups, independent sample t-test was applied. A *p*-value ≤0.05 were considered statistically significant.

RESULTS

Out of 120 COPD patients, 60 patients were those who presented with signs and symptoms of AECOPD (Group-A), and 60 patients were those who had stable COPD (Group-B). Mean age of our participants was 63.4±7.3 years. Among these 120 patients, 100(83.3%)

were male and 20 (16.7%) were female. Characteristics of study participants are shown in Table-I.

Table-I: Patient Characteristics (n=120)

Patient Characteristics	Values
Age in years (Mean ± SD)	63.4 ± 7.3
Gender	
Male	100 (83.3%)
Female	20 (16.7%)
Body mass index in kg/m2 (Mean ± SD)	28.31± 4.62
Comorbidities	
Diabetes Mellitus	58 (48.3%)
Hypertension	73 (60.8%)
Smoking status	
Current smoker	41(34.2%)
Ex smoker	68(56.7%)
Never smoked	11(9.2%)
Duration of COPD diagnosis	
Within the period of last 10 years	74(61.7%)
Before last 10 years period	46(38.3%)
History of previous Exacerbations	
Yes	45(37.5%)
No	75(62.5%)
Medications used for COPD treatment	
Inhaled LAMA	36(30%)
Inhaled LABA and ICS	55(45.8%)
Inhaled LABA+LAMA+ICS	29(24.2%)

**COPD: Chronic Obstructive Pulmonary Disease, LAMA: Long-acting muscarinic agonist, LABA: Long-acting beta-agonist, ICS: Inhaled Corticosteroid*

Out of the patients presenting with acute exacerbation of COPD, 22(36.6%) presented with mild severity, 17(28.3%) with moderate severity of exacerbation and 21(35%) presented with severe exacerbation of symptoms.

Table-II: Comparison of Clinical Parameters of Patients across Groups (n=120)

Clinical Parameters	Group-A (n=60) Mean±SD	Group-B (n=60) Mean±SD	*p*-value
Oxygen Saturation (SpO2 in %age)	88.0±5.0	95.0±1.2	<0.001
Serum Creatinine (umol/L)	78.9±14.2	89.3±66.0	0.34
Hemoglobin (g/dL)	12.3±1.6	12.5±2.0	0.76
Total Leucocyte Count (TLC) x109/L	12.6±2.9	7.1±1.4	< 0.001
C Reactive Protein CRP (Q)	56.9±39.8	7.7±2.2	< 0.001
Serum Magnesium Levels (mg/dL)	0.6±0.0	0.9±0.1	< 0.001

The mean value of serum magnesium levels in Group-B was 0.93±0.19 mmol/L and ingroup-A was 0.65±0.08 mmol/L (p≤0.05). The difference in the serum magnesium levels of patients presenting with different severity of exacerbations was not statistically significant (*p*=0.30).

DISCUSSION

Serum magnesium plays an important role in maintaining normal airway function, which makes it understandable that why deficiency of magnesium leads to acute exacerbation episodes in COPD patients.

There are different mechanisms by which magnesium carries out the function of regulating normal airway function. This is done by causing mucociliary clearance, bronchodilation of respiratory tract smooth muscle, release of neurohormonal mediators and stabilization of mast cells. On the other hand, impaired pulmonary function and increased airway hyperactivity are associated with hypomagnesemia.[12] There is found to be a decreased bioavailability of magnesium in patients with COPD, which can be attributed to increased incidence of smoking, and the use of certain drugs in COPD patients that decrease serum magnesium (like steroids and beta agonists).[13] Therefore, due to its effect in alleviating bronchospasm, magnesium has a role in COPD related QoL (quality of life) by causing improvement in respiratory symptoms, and orally administered magnesium has found to play an anti-inflammatory role in stable COPD patients.[14,15]

Our study that compared the serum magnesium levels in patients of COPD, presenting in either stable state or with acute exacerbation, demonstrated these levels to be significantly low in acute exacerbation group i.e. 0.6±0.0 mmol/L, in comparison to patients with stable COPD (0.9±0.1 mmol/L).

The mean age of our patients was 63.42, with male predominance, which is in accordance with previous studies.[13] The male predominance can be attributed to smoking being the most common cause of COPD and greater prevalence of smoking in males in our society.[16] The progression of COPD symptoms over the years leads to more presentations in older age groups.[17]

The mean serum magnesium levels in patients with stable COPD came out to be 0.93±0.19mmol/L and in those with acute exacerbation, it came out to be 0.65±0.08 mmol/L. A 2022 Pakistani study also confirmed increased number of exacerbations associated with serum Mg levels less than 1.8 mg/dl. It also reached the conclusion that 40% of COPD patients presenting with acute exacerbation had hypomagnesemia (serum Mg <1.80 mg/dl).[13] This is

also in accordance with a 2024 Indian study by Panwar *et al*., in which most of the patients with stable COPD had serum magnesium levels greater than 1.60 m g/dl and those with acute exacerbation had less than 1.60 mg/dl.[18]

Our results are comparable with a study conducted by Shubankar *et al*., which showed serum magnesium levels of 1.88±0.19 mg/dL in acute exacerbation, compared to 2.06±0.18 mg/dL in stable state.[10]

Makwana *et al*. carried out a study in which 57% of patients with acute exacerbation had hypomagnesemia (serum magnesium <1.7mg/dL) and duration of hospital stay was also significantly higher (80.7%) in hypomagnesemia patients, as compared to 55.8% in normomagnesemia patients.[19] A 2022 study by Kshirsagar *et al*. demonstrated that patients with serum magnesium levels <1.7mg/dL have 9.34 times higher risk of acute exacerbations.[20] A Turkish study by Hayat *et al*. showed increased severity of dyspnea symptoms and increased decline in respiratory function tests in COPD patients with hypomagnesemia.[21]

LIMITATIONS OF STUDY

Our study has few limitations. For acute exacerbation, other factors responsible for exacerbation could not be ruled out. In addition to this, COPD patients who presented with acute exacerbation should have been advised oral magnesium supplementation (during home disposal from Emergency Department or upon discharge from hospital in case of admission), and should have been followed up at 3-monthly and 6-monthly intervals for their serum magnesium levels and for further exacerbations. Moreover, a larger sample size would also yield more reliable results. Further studies on this topic are suggested to keep these points in view.

CONCLUSION

Serum magnesium levels in patients with acute exacerbation of COPD are less than those with stable COPD. This shows that serum magnesium level is an important modifiable risk factor for COPD exacerbation. Therefore, patients with COPD should be monitored with serum magnesium levels for acute exacerbation.

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Authors Contribution

Following authors have made substantial contributions to the manuscript as under:

LS & TI: Conception, study design, drafting the manuscript, approval of the final version to be published.

FAS & AR: Data acquisition, data analysis, data interpretation, critical review, approval of the final version to be published.

AM & SS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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