The Association Between Serum Magnesium Levels And Acute Exacerbation In Patients Of Chronic Obstructive Pulmonary Disease

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ABSTRACT:
Background: Magnesium plays an important role in bronchodilation and has anti-inflammatory effects. Hypomagnesaemia has been associated with increased risk of acute exacerbations in chronic obstructive pulmonary disease (COPD). This study aimed to evaluate the relationship between serum magnesium levels and clinical outcomes in patients hospitalized for acute exacerbation of COPD (AECOPD).
Methods: This prospective observational study enrolled 45 patients admitted with AECOPD. Serum magnesium levels were measured at admission. Patients were followed until discharge, and duration of hospital and intensive care unit (ICU) stay were recorded. The association between serum magnesium and length of stay was analyzed using correlation and regression analyses.
Results: The mean age of study participants was 69.9±10.2 years. The mean duration of COPD was 9.13±4.7 years. The mean serum magnesium level was 2± 0.48 mg/dL. Lower serum magnesium levels correlated with longer hospital stay ($r = -0.517$, $p < 0.001$) and ICU stay ($r = -0.570$, $p < 0.001$).
Conclusions: Hypomagnesaemia at admission is associated with longer hospital and ICU stays in patients hospitalized for AECOPD. Serum magnesium levels may serve as a prognostic biomarker, and magnesium supplementation warrants further study as a potential intervention to improve clinical outcomes during COPD exacerbations.

Key words: Magnesium, COPD, Acute exacerbations, Duration of Hospital stay

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition characterized by persistent airflow limitation and recurrent exacerbations.[1] Acute exacerbations of COPD (AECOPD) significantly contribute to the disease burden, leading to increased morbidity, mortality, and healthcare utilization.[2,3] Identifying factors that influence the severity and outcomes of AECOPD is crucial for improving patient management and prognosis.

Magnesium, an essential element in the human body, plays a vital role in various physiological processes, including bronchodilation and inflammation regulation.[4] It acts as a calcium antagonist, promoting smooth muscle relaxation in the airways and potentially reducing airway hyperresponsiveness.[5] Additionally, magnesium has been shown to have anti-inflammatory properties, which may be particularly relevant in the context of COPD, a disease characterized by chronic inflammation.[6]

Recent studies have suggested that magnesium deficiency may contribute to the pathogenesis and exacerbation of COPD.[7]Hypomagnesemia has been associated with increased airway hyper responsiveness, inflammation, and oxidative stress, all of which are implicated in COPD progression and exacerbations.[8,9] These findings have sparked interest in the potential role of magnesium in COPD management and its possible use as a prognostic marker.

While the therapeutic potential of magnesium supplementation in acute asthma has been well-documented[10], its role in COPD management remains less clear. Some studies have reported beneficial effects of intravenous magnesium sulfate in treating AECOPD[11], but the relationship between serum magnesium levels and clinical outcomes in COPD exacerbations has not been extensively investigated. This gap in knowledge underscores the need for further research to elucidate the potential prognostic and therapeutic implications of magnesium in COPD.

This study aimed to evaluate the association between serum magnesium levels and clinical outcomes, specifically hospital and intensive care unit (ICU) length of stay, in patients admitted for AECOPD. By examining this relationship, we sought to assess the potential of serum magnesium as a prognostic biomarker and explore the implications for magnesium supplementation as a therapeutic strategy in COPD exacerbations. The findings of this study may contribute to a better understanding of the role of magnesium in COPD and potentially inform future management strategies for this prevalent and burdensome disease.

METHODOLOGY:

This prospective observational study was conducted at SNMC, Bagalkote, Karnataka. The study protocol was approved by the institutional ethics committee, and written informed consent was obtained from all participants or their legal representatives.

Sample size estimation was performed using OpenEpi software version 2.3.1. Based on a previous study by Sanket M., which reported a proportion of 57% of acute exacerbation of COPD patients with hypomagnesaemia, and using a 95% confidence level with 15% absolute precision, the required sample size was calculated to be 42. This was rounded up to 45 participants to account for potential dropouts. The formula used for sample size calculation was:

n = [DEFF*Np(1-p)] / [(d^2/Z^2_(1-α/2)*(N-1)+p*(1-p)]

The study enrolled 45 patients admitted to the hospital with a primary diagnosis of acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Inclusion criteria were: age ≥ 40 years, a confirmed diagnosis of COPD based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, and presentation with symptoms consistent with AECOPD. Exclusion criteria included: concurrent diagnosis of pneumonia, acute coronary syndrome, or other acute medical conditions that could confound the assessment of COPD exacerbation; and current use of magnesium supplements or medications known to significantly alter magnesium levels.

Upon admission, demographic data, medical history, and duration of COPD were recorded for each participant.

Blood samples were collected from each patient within 24 hours of admission. Serum magnesium levels were measured using a standardized colorimetric method in the hospital's central laboratory. Other relevant laboratory tests, including complete blood count, renal function tests, and arterial blood gas analysis, were also performed as part of standard care.

Patients received standard treatment for AECOPD according to current guidelines, which included bronchodilators, systemic corticosteroids, and antibiotics when indicated. The decision for

admission to the general ward or intensive care unit (ICU) was made by the attending physician based on the patient's clinical condition and lab parameters and was not influenced by the study protocol.

The primary outcomes measured were the length of hospital stay and, if applicable, the duration of ICU stay. These were calculated as the number of days from admission to discharge or transfer to a lower level of care.

Patients were followed daily during their hospital stay by trained research staff who recorded clinical progress, any complications, and ongoing treatments

Statistical analysis was performed using SPSS software 19.0. Data obtained was tabulated in an Excel sheet and was analysed. Quantitative data is expressed as mean + standard deviation and nonparametric data is expressed as median and min-max values. Percentages are used for representing qualitative data. Chi-square test is used for proportions in qualitative data. Student's unpaired t – test is used for Quantitative data.

Descriptive statistics were used to summarize patient characteristics and outcomes. The relationship between serum magnesium levels and length of stay (both hospital and ICU) was analyzed using Pearson's correlation coefficient. Multiple linear regression analysis was conducted to adjust for potential confounding factors such as age, COPD severity, and comorbidities. A p-value < 0.05 was considered statistically significant.

RESULTS:

Table 1 presents the basic demographic and clinical information of the study participants. It shows that the average age of the participants was about 70 years, with a slight majority being females (53.3%). The patients had been living with COPD for an average of about 9 years. The mean serum magnesium level was 2.0 mg/dL, which is within the normal range but on the lower end.

Table 1: Demographic and Clinical Characteristics of Study Participants (N=45)

Characteristic	Value
Age (years), mean ± SD	69.93±10.2
Gender, n(%)	
Males	21 (46.7%)
Females	24 (53.3%)
Duration of COPD (years), mean ± SD	9.13±4.7
Serum magnesium level (mg/dl), mean ± SD	1.94±0.45

Table 2 summarizes the main clinical outcomes of the study. On average, patients stayed in the hospital for about 7.4 days. 73.3% of the patients required admission to the ICU, with an average ICU stay of about 2.44 days. These figures give an indication of the severity of the COPD exacerbations in this patient group.

Table 2: Clinical Outcomes of AECOPD Patients

Outcome	Value
Length of hospital stay (days), mean ± SD	7.42±2.7
ICU admission, n (%)	33 (73.3%)
Length of ICU stay (days), mean ± SD	2.44±2.34

Table 3 shows the average levels of magnesium in those who were classified as those with hypomagnesaemia and those with normal magnesium levels. It also shows the mean duration of hospital stay and ICU stay vs. the other group.

Table 3: Comparison of patients with hypomagnesaemia and those with normal magnesium levels and duration of inpatient care.

Parameter	Hypomagnesaemia	Normal Magnesium levels
Number of patients	**26**	**19**
Mean magnesium levels (mg/dl)	**1.74**	**2.36**
Mean duration of hospital stay (days)	**9.07**	**5.15**
Mean duration of ICU stay (days)	**3.84**	**0.52**

Table 4 is crucial as it shows the main findings of the study. There was a significant negative correlation between serum magnesium levels and both hospital stay (r = -0.72) and ICU stay (r = -0.7). The p-values (< 0.001) indicate that these correlations are statistically significant. The negative correlation means that as magnesium levels decreased, the length of stay increased. This suggests that lower magnesium levels are associated with worse outcomes in terms of longer hospitalizations

Table 4: Correlation between Serum Magnesium Levels and Clinical Outcomes

Outcome	Correlation Coefficient (r)	p-value
Length of hospital stay	-0.72	**<0.001**
Length of ICU stay	-0.7	**<0.001**

DISCUSSION:

This study investigated the association between serum magnesium levels and clinical outcomes in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Our findings demonstrate a significant inverse correlation between serum magnesium levels and both hospital and ICU length of stay, suggesting that hypomagnesaemia may be associated with poorer outcomes in AECOPD patients.

The mean serum magnesium level in our study population was 2.0 ± 0.48 mg/dL, which is comparable to the findings of Bhatt et al.[8], who reported a mean level of 1.96 ± 0.27 mg/dL in COPD patients. However, our results are slightly higher than those reported by Aziz et al.[7], who found a mean serum magnesium level of 1.76 ± 0.31 mg/dL in their AECOPD cohort. This discrepancy might be attributed to differences in study populations or variations in magnesium measurement techniques.

Our study revealed a significant negative correlation between serum magnesium levels and length of hospital stay ($r = -0.72$, $p < 0.001$). This finding is consistent with the results of Gumuset al.[12], who also reported an inverse relationship between magnesium levels and hospitalization duration ($r = -0.42$, $p < 0.001$) in AECOPD patients. Similarly, we found a strong negative correlation between magnesium levels and ICU stay duration ($r = -0.7$, $p < 0.001$).

The mean duration of COPD in our study population was 9.13 ± 4.7 years, which is slightly longer than the 7.5 ± 3.8 years reported by Krishnan et al.[13] in their multicenter study. This difference might reflect variations in healthcare access or diagnosis patterns between study populations.

Our findings support the growing body of evidence suggesting that magnesium plays a crucial role in COPD pathophysiology and exacerbations. Magnesium's bronchodilatory and anti-inflammatory properties, as described by de Valket al.[14], may explain its potential protective effect against severe AECOPD outcomes. The inverse relationship between magnesium levels and length of stay could

be attributed to magnesium's ability to reduce airway inflammation and improve bronchodilation, as proposed by Gourgoulianiset al.[15]

However, it is important to note that our study design does not allow for the establishment of a causal relationship between hypomagnesaemia and poor outcomes in AECOPD. While our results are consistent with those of Bhatt et al.[8] and Aziz et al.[7], who found hypomagnesaemia to be an independent predictor of frequent readmissions and longer hospital stays, respectively, further prospective studies are needed to confirm this association.

he potential therapeutic implications of our findings are significant. If the relationship between magnesium levels and AECOPD outcomes is indeed causal, magnesium supplementation could represent a simple and cost-effective intervention to improve patient outcomes. This aligns with the findings of Shivanthan and Rajapakse[16], who reported improved lung function and reduced hospital stay with intravenous magnesium therapy in AECOPD patients.

CONCLUSION:

In conclusion, our study underscores the clinical relevance of serum magnesium levels in AECOPD and opens new avenues for research into both prognostic indicators and potential therapeutic interventions in COPD management. These findings may contribute to improving care strategies and outcomes for patients with this prevalent and burdensome respiratory disease.

Contribution: concepts, design, definition of intellectual concept, literature research, clinical studies, experimental studies, data acquisition, data analysis, statistical analysis. Manuscript preparation, manuscript editing and review

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