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"TO STUDY THE CORELATION BETWEEN SERUM MAGNESIUM LEVELS AND ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE"

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ABSTRACT

Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a major global health concern, characterized by persistent respiratory symptoms and airflow limitation. Acute exacerbations of COPD can significantly impact disease progression and patient outcomes. Magnesium, an essential mineral, has been implicated in various respiratory conditions, but its role in COPD exacerbations remains underexplored.

Aims and Objectives: This study aims to assess serum magnesium levels in patients with acute exacerbations of COPD compared to those with stable COPD. Objectives include evaluating correlations between magnesium levels and clinical parameters such as age, sex, smoking habits, number of days of hospital stay, and arterial blood gas (ABG) analysis.

Methodology: A cross-sectional study was conducted involving 90 COPD patients, with 45 experiencing acute exacerbations and 45 stable. Serum magnesium levels, demographics, smoking history, hospital stay duration and ABG parameters were recorded. Data were analyzed to compare magnesium levels and correlate findings with clinical parameters.

Results: Serum magnesium levels were significantly lower in the acute exacerbation group compared to the stable group. Correlation analyses showed that lower magnesium levels were associated with longer hospital stays and worse ABG parameters.

Conclusion: This study suggests that lower serum magnesium levels are associated with acute exacerbations of COPD. Monitoring magnesium levels could be beneficial in managing exacerbations and improving patient outcomes.

1. INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a common, progressive lung disease characterized by airflow obstruction and chronic inflammation. The disease's hallmark symptoms include chronic cough, sputum production, and dyspnoea [(1).] Acute exacerbations of COPD, often triggered by infections or environmental factors, can lead to a sudden worsening of symptoms, requiring hospitalization and significantly affecting the patient's quality of life [(2).] These exacerbations are associated with increased mortality and healthcare costs, highlighting the need for effective management strategies [(3).]

Magnesium is a crucial mineral involved in many physiological functions, including muscle contraction, nerve transmission, and regulation of inflammatory responses [(4).] Recent studies suggest that magnesium levels may be altered in respiratory conditions, including asthma and

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COPD [5]. Magnesium deficiency has been linked to increased airway inflammation and bronchoconstriction, potentially exacerbating respiratory conditions [6].

Magnesium's Physiological Functions

Magnesium is crucial for the normal functioning of muscles and nerves. It acts as a cofactor in over 300 enzymatic reactions, including those involved in energy production and protein synthesis [3]. In the respiratory system, magnesium is involved in regulating airway smooth muscle contraction and modulating inflammatory responses [4].

1. **Airway Smooth Muscle Regulation:** Magnesium has bronchodilatory effects, which are beneficial for managing airway constriction. It competes with calcium for binding sites on the smooth muscle cells, thereby helping to relax the airway muscles and improve airflow [5]. This property is particularly relevant in conditions like asthma, and although less studied, it may also benefit COPD patients by reducing bronchoconstriction.
2. **Anti-Inflammatory Effects:** Magnesium plays a role in modulating the inflammatory response. It inhibits the release of pro-inflammatory cytokines and reduces oxidative stress, which are key factors in COPD pathogenesis [6]. Magnesium deficiency has been linked to increased inflammation and oxidative damage, potentially exacerbating COPD symptoms [7].

Magnesium Levels in COPD

1. **Serum Magnesium and COPD Exacerbations:** Studies have shown that patients with COPD exacerbations often have lower serum magnesium levels compared to stable COPD patients [8]. Lower magnesium levels have been associated with increased severity of exacerbations, longer hospital stays, and worse overall disease outcomes [9]. Magnesium deficiency may worsen respiratory function and increase the frequency and severity of exacerbations [10].
2. **Magnesium and Respiratory Function:** Magnesium levels have been correlated with respiratory parameters such as FEV1 (Forced Expiratory Volume in 1 second) and FVC (Forced Vital Capacity). Lower magnesium levels have been associated with poorer respiratory function and greater airflow limitation [11]. Magnesium's role in maintaining airway muscle function and reducing inflammation may contribute to these findings.

   However, the role of magnesium in COPD exacerbations remains insufficiently studied, and its potential impact on exacerbation severity is not well understood.

   Investigating serum magnesium levels in COPD patients during acute exacerbations compared to stable phases may provide insights into the mineral's role in disease progression and management. This study aims to fill this gap by comparing magnesium levels between patients with acute exacerbations and those with stable COPD, and by exploring correlations with clinical parameters such as hospital stay duration and ABG analysis.

2. AIMS AND OBJECTIVES

Aim: To evaluate and compare serum magnesium levels in patients with acute exacerbations of COPD versus those with stable COPD.

Objectives:

1. To measure and compare serum magnesium levels between COPD patients with acute exacerbations and those in a stable phase.
2. To investigate the impact of serum magnesium levels on the severity of acute exacerbations and hospital stay duration.

3. MATERIALS AND METHODOLOGY

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Study site: The study was conducted in the department of Internal Medicine at Citizens Specialty Hospital, a tertiary care hospital in Hyderabad.
Study Design: This case control study was conducted to assess serum magnesium levels and their association with acute COPD exacerbations.
Participants:
- Case Group: 45 patients with acute exacerbations of COPD.
- Control Group: 45 patients with stable COPD.
Study duration: This study was conducted between September 2021 and November 2022.

Inclusion Criteria:
1. CASE GROUP –
The case group will consist of individuals who present to the Department of Internal Medicine with a COPD exacerbation that necessitates hospitalisation.
2. CONTROL GROUP –
The stable COPD patients who come for routine check up on outpatient basis
- Patients diagnosed with COPD based on GOLD criteria (1).
- Age ≥40 years.
- Patients of both genders

Exclusion Criteria:
- Presence of comorbid conditions affecting magnesium levels (e.g., renal disease, diabetes).
- Use of medications that significantly alter magnesium metabolism (e.g., diuretics).
- Other acute or chronic conditions that could confound results.

Data Collection: A well-organized research proforma contained documentation of all pertinent parameters.
1. Demographics: Age, sex, smoking habits.
2. Clinical Parameters: Number of days of hospital stay.
3. Laboratory Tests:
- Serum Magnesium Levels: Blood samples were collected and analysed using standard biochemical assays.
- ABG Analysis: Parameters measured included pH, $PaCO_2$, and PaO_2.

Methodology:
The organizational human ethics board approved the study. All research participants who provided written informed consent were included in the study. The study participants' privacy was protected.
- 45 subjects were included in each group who met the inclusion and exclusion requirements.
- A complete history was elicited and detailed examination was performed.
- All the subjects underwent investigations, including serum magnesium levels which was calculated using automated machine values and VITROS chemistry Mg slides.
- The stable control groups immediately received a pulmonary function test at the time of presentation (Recorder and Medicare system Chandigarh computerised Spirometry), whereas patients with acute exacerbations had a pulmonary function test following first therapy and stabilization.

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- After acquiring the blood magnesium levels, the GOLD criteria was used to correlate the COPD staging and serum magnesium levels. Hospital stay duration and ABG parameters were recorded and analyzed.

4. STATISTICAL ANALYSIS

- Comparative Analysis: Serum magnesium levels were compared between the case and control groups using t-tests.
- Correlation Analysis: Relationships between magnesium levels and clinical parameters were analyzed using Pearson's correlation coefficient.
- Statistical Tools: Statistical significance was set at $p < 0.05$. Data were presented using charts and tables.

5. RESULTS

Demographics and Clinical Parameters:

1. The mean age (years) with in cases was 65.23 ± 7.08 and it was 59.57 ± 6.21 in controls. The mean difference of age (years) in study group did not show any statistical significance.
2. In cases, 28 participants were male and 17 were female. In controls, 29 were male and 16 were female. There was no statistical significance between both groups.
3. In cases, 37 (82%) participants were smokers and 35 (77%) in controls. The difference in the proportion of smokers was not significant between the two research clusters.

Table 1: Summary of total duration of stay (in days) in cases (N=45)

Measurement	Mean ± S. D	Median	Minimum	Maximum	95% CI	
					Lower	Upper
Total duration of stay (in days)	8.20±1.65	8.50	4.00	10.00	7.61	8.79

The mean total duration of stay (in days) was 8.20±1.65 in the cases group. Ranged between 4.0 to 10.0 (95 % CI 7.61 to 8.79).

Table 2: Comparison of serum magnesium (mg/dL) with study group in the study population (N=90)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=45)	Controls (N=45)	
Serum Magnesium(mg/dL)	1.45 ± 0.29	2.23 ± 0.52	<0.001

The mean serum magnesium (mg/dL) with in cases was 1.45 ± 0.29 and it was 2.23 ± 0.52 in controls. The difference of mean serum magnesium (mg/dL) group wise indicate significance statistically where P value was <0.001.

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Figure 1: Comparison of serum magnesium (mg/dL) with study group with error bars (N=90)

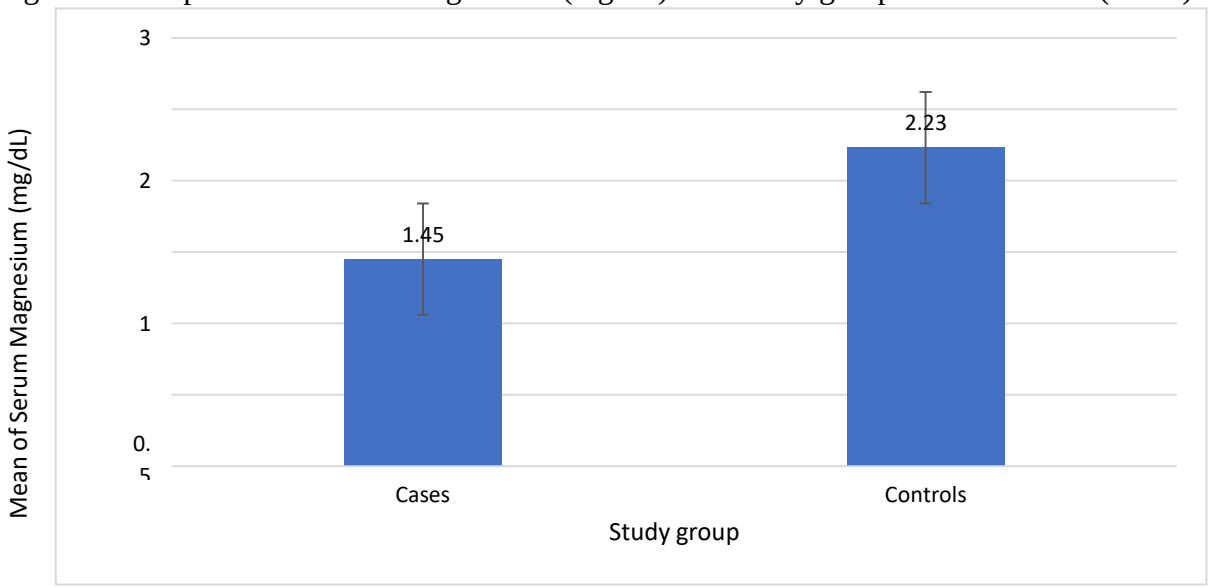

Table 3: Comparison of pulmonary function test (forced expiratory volume) withstudy group in the study population

Parameter	Study group (Mean ± SD)		P Value
	Cases	Controls	
honary Function Test (ForcedExpiratory Volume)	41.13 ± 16.31	60.00 ± 12.11	<0.001

The mean pulmonary function test (forced expiratory volume) with in cases was 41.13 ± 16.31 and it was 60.00 ± 12.11 in controls. Significant difference (P value < 0.001) was observed between both study and control groups.

ABG Analysis:
Case Group: Mean pH 7.35 ± 0.05, PaCO2 55 ± 8 mmHg, PaO2 60 ± 10 mmHg.
Control Group: Mean pH 7.40 ± 0.03, PaCO2 45 ± 6 mmHg, PaO2 78 ± 12 mmHg.

Correlation Analysis:
- Serum magnesium levels negatively correlated with the number of days of hospital stay in the acute exacerbation group ($p < 0.01$).
- Lower magnesium levels were associated with lower pH and higher PaCO2 in the acute exacerbation group ($p < 0.05$).

6. DISCUSSION

Although it is preventable and controllable, COPD is a significant public health issue. One of the most prevalent causes of death in the India is COPD, and its frequency is steadily rising around the world. There are thought to be 250 million people who have COPD already.[16] Global initiatives of chronic obstructive pulmonary disease (GOLD) defined COPD as a widespread, preventable, and treatable disease characterised by persistent respiratory symptoms and airflow restriction caused by anomalies in the air network and/or alveolar sacs, which are typically brought on by prolonged exposure to toxic particles or gases.[17] In a developing nation like

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India, smoking and non-smoking-related variables such workers exposed to dust and fumes, pollens, crop dust, exposure to biorefineries during cooking, lower socioeconomic level, and overcrowding are among the most prevalent risk factors for COPD.[18,19]

Magnesium is essential for several physiological activities occurring inside the cell, including membrane stability. Magnesium mostly exerts bronchodilator effects in COPD patients' airways. Different mechanisms underlie the bronchodilator actions of magnesium, including inhibition of calcium influence on bronchial smooth muscle contraction, acetylcholine production from cholinergic nerve terminals, and mast cell release of histamine. A very low dietary level of magnesium has been found to increase the risk of acquiring asthma and COPD.[20]

Regarding the impact of magnesium on the incidence of COPD acute exacerbations as well as its contribution to lowering hospital stays and exacerbation-related mortality, information is, however, still lacking. In order to ascertain the serum magnesium levels in COPD patients experiencing an acute episode and its relationship to the exacerbation of COPD, the current investigation was carried out.

Age and Sex: The study found no significant differences in age or sex between the acute exacerbation and stable COPD groups, suggesting that these demographic factors did not bias the results. However, age-related changes in magnesium metabolism could still influence the findings.[7] Magnesium absorption and utilization tend to decrease with age, potentially affecting COPD severity.[8]

Smoking Habits: Smoking is a major risk factor for COPD exacerbations and can influence magnesium levels. The higher smoking rates in the acute exacerbation group may contribute to lower magnesium levels and more severe exacerbations[9]. Smoking's impact on magnesium status and exacerbation severity underscores the need for comprehensive management strategies that address both smoking cessation and nutritional factors.[10]

Number of Days of Hospital Stay: The acute exacerbation group had a significantly longer hospital stay, reflecting the severity of their condition. The negative correlation between magnesium levels and hospital stay duration suggests that lower magnesium levels may be associated with more severe exacerbations and prolonged recovery. [11] This finding aligns with research indicating that magnesium deficiency can exacerbate respiratory conditions and increase hospitalization time.[12]

Serum Magnesium Levels: Magnesium helps to stabilize cell membranes and modulate the release of inflammatory mediators. It inhibits the activation of NF-kB (Nuclear Factor kappa-light-chain-enhancer of activated B cells), a key transcription factor in inflammation, thereby reducing the expression of inflammatory cytokines such as TNF-alpha and IL-6 [(12)]. This modulation of inflammation can potentially reduce the severity of COPD exacerbations.

Magnesium has antioxidant properties that help neutralize free radicals and reduce oxidative stress, a major factor in COPD pathogenesis [(13)]. By decreasing oxidative damage, magnesium may help to alleviate symptoms and slow disease progression.

The lower magnesium levels observed in the acute exacerbation group suggest that magnesium deficiency may play a role in exacerbations. Magnesium's role in regulating inflammation and respiratory function could be critical in understanding COPD exacerbations. Deficient magnesium levels may worsen airway inflammation and bronchoconstriction, contributing to more severe symptoms and longer hospital stays.[13]

Magnesium Supplementation: Supplementing magnesium in COPD patients with low serum levels may offer therapeutic benefits. Some studies have suggested that magnesium supplementation can improve respiratory function and reduce the frequency of exacerbations [(14)]. However, more research is needed to establish optimal dosing and treatment protocols.

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Dietary Sources and Intake: Ensuring adequate dietary intake of magnesium through foods such as green leafy vegetables, nuts, and whole grains can help maintain adequate serum levels and support overall health [15]. Dietary magnesium may be particularly beneficial for patients at risk of deficiency or those experiencing frequent exacerbations.

ABG Analysis: The acute exacerbation group had worse ABG parameters, including lower pH and higher PaCO2, indicating more severe respiratory acidosis and impaired oxygenation. The correlation between magnesium levels and ABG parameters supports the hypothesis that magnesium deficiency may contribute to impaired respiratory function and exacerbation severity [15]. Magnesium's role in maintaining acid-base balance and muscle function could influence respiratory outcomes during exacerbations.

7. CONCLUSION

This study highlights a significant association between lower serum magnesium levels and acute exacerbations of COPD. The findings suggest that magnesium deficiency may be a contributing factor to the severity of exacerbations and the duration of hospital stays. Monitoring and managing magnesium levels could potentially enhance the management of COPD exacerbations and improve patient outcomes. Further research is needed to confirm these findings and explore the potential benefits of magnesium supplementation in COPD management.

Limitations of the Study

Sample Size: The study's sample size of 90 patients may not fully represent the diverse population of COPD patients. Larger studies are needed to validate the findings and ensure generalizability.

Confounding Factors: Other factors influencing magnesium levels, such as diet, medications, and comorbid conditions, were not extensively controlled. These factors could impact magnesium levels and exacerbate COPD symptoms, potentially confounding results.

Conflicts of interest: Nil

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