ORIGINAL RESEARCH

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Chronic Obstructive Pulmonary Disease (COPD) and Magnesium Levels: Relationship Analysis

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Abstract

Objective

Identifying modifiable risk factors is very important for preventing acute chronic obstructive pulmonary disease (COPD) severity. This study was conducted to determine the role of serum magnesium levels in acute COPD exacerbation.

Material and Method

A total of 104 COPD patients with a mean age of 66.63 ± 8.79 years and female 17.3%(18) males 82.69%(86) were included in our study. Chest X-ray, respiratory function test, and biochemical blood tests were performed on the cases. The relationship between magnesium level and COPD severity was evaluated using appropriate statistical methods.

Results

Demographic data of the patients were collected, biochemical evaluation was performed, and the relationship between magnesium levels and respiratory parameters was investigated. Serum magnesium was found to be low in patients (25%). COPD evaluation test was compared with mMMR and CAT, dyspnea symptoms were observed to be more in hypomagnesemia cases, and the difference was found to be statistically significant (p:0.029, p:0.030, respectively). In terms of respiratory function tests, FEF25-75 was found to be lower and statistically significant in hypomagnesemia patients. Disease duration was found to be statistically significant in hypomagnesemia cases (p:0.033). When compared with male and female patients, smoking was observed more in male individuals, and this parameter was also found to be statistically significant (p:0.044).

Conclusion

It was concluded that hypomagnesemia may increase respiratory distress in COPD patients and contribute to COPD exacerbations.

Keywords: Chronic Obstructive Pulmonary Disease, Magnesium, Respiratory function test

Introduction

Chronic obstructive pulmonary disease (COPD) is a significant and prevalent respiratory condition that continues to present a growing global health challenge (1). Epidemiological data indicate that the worldwide prevalence of COPD is approximately 10%, with rates increasing with advancing age (2). The World Health Organization (WHO) projects that this trend will persist, leading to a further increase in cases by

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2030 (3). COPD is associated with high morbidity and mortality rates, which makes it a critical public health concern. Its etiology and pathogenesis involve a complex interplay between genetic predisposition and environmental factors, including tobacco smoke, air pollution, occupational exposure, and other environmental hazards (4).

Magnesium plays a crucial role in maintaining muscle strength and optimizing exercise performance, primarily through its effects on blocking calcium channels and inhibiting acetylcholine release (5). As a vital mineral, magnesium is involved in several physiological functions including smooth muscle relaxation, bronchodilation, and immune system regulation (6,7). It has been postulated to exert a protective effect against respiratory conditions owing to its contributions to processes such as bronchodilation, mast cell stabilization, regulation of neurohumoral mediators, and enhancement of mucociliary clearance in the airway smooth muscles (8,9). Moreover, magnesium demonstrates potent vasodilatory and bronchodilatory properties while also modulating the release of acetylcholine and histamine. Its anti-inflammatory actions make it a potential therapeutic agent for respiratory diseases such as asthma and COPD (7). While some studies indicate that hypomagnesemia may result in increased muscle contraction, others have highlighted the role of magnesium in alleviating bronchial muscle tension through its involvement in oxidative stress defense mechanisms and the regulation of leukocyte activation (10,11).

Material and Method

Purpose and Type of Research

This study aimed to assess the correlation between chronic obstructive pulmonary disease (COPD) severity and serum magnesium concentration in COPD patients presenting to the chest disease outpatient clinic.

Research Population and Sample

This study investigated the association between the severity of COPD and serum magnesium levels in patients diagnosed with COPD. Patients diagnosed with COPD for at least two years were included in the study. Patients with gastrointestinal disorders, pancreatitis, renal diseases, endocrine or metabolic conditions, hepatic dysfunction, or the use of thiazide diuretics were excluded. The study adhered to the principles of the Declaration of Helsinki and participation was voluntary. Data regarding patient demographics (age, disease duration, body mass index [BMI]), clinical details (comorbidities, smoking habits, and long-term oxygen therapy [LTOT] use), and medical records were collected through in-person interviews and patient files. Comorbidities, such as systemic arterial hypertension, heart disease, obstructive sleep apnea (OSA), and malignancies, were considered based on previous diagnoses. Diagnostics included plain chest radiographs (anterior, posterior, and lateral views), pulmonary function tests (PFT) using the BTL "CardioPoint-Spiro" module, and biochemical markers. COPD was classified according to severity: Mild: FEV1 ≥ 80%; Moderate: FEV1=50-80%, Severe: FEV1=30-50%, and Very Severe: FEV1 ≤ 30%. Pulmonary function tests were conducted, and patients with an FEV1/FVC ratio <70% and an FEV1 value ≤ 79% were included. Disease severity was assessed using the COPD Assessment Test (CAT) and the Modified Medical Research Council (mMRC) dyspnea scale. Biochemical markers such as calcium (Ca), magnesium (Mg), sodium (Na), potassium (K), and C-reactive protein (CRP) were measured using radioimmunoassays. Serum magnesium levels <1,7 mg/dL were defined as hypomagnesemia (12,13). Serum magnesium levels were assessed during acute COPD exacerbations and analyzed for respiratory distress, disease duration, and hospitalization frequency. The association between serum magnesium levels, COPD assessment tools (CAT and mMRC), respiratory parameters, and biochemical markers was investigated using the appropriate statistical methods.

Statistical Analysis

Data analysis was conducted using the SPSS software (version 22.0; IBM®, Chicago, USA). Normality was assessed using visual (histograms and probability plots) and analytical (Shapiro-Wilk test) methods. The descriptive statistics are reported as follows: Mean ± standard deviation for normally distributed continuous variables. Median (min-max) for non-normally distributed data. Frequency and Percentage of Categorical Variables. Comparisons between groups were performed using the independent t-test for normally distributed variables and Mann-Whitney U test for non-normally distributed variables. The chi-square test was used for nominal data. Linear regression analyses were conducted to examine the relationship between magnesium levels and respiratory parameters (FEF 25-75, FEV1, CAT score, and mMRC). Multivariate regression analyses were performed to assess the impact of magnesium levels on age, respiratory function, and biochemical markers. Statistical significance was set at $P < 0.05$. This study did not utilize artificial intelligence (AI) tools, including large language models (LLMs) or chatbots, at any stage of production.

Results

Data from all patients with COPD presenting to the chest disease outpatient clinic with acute exacerbations were analyzed. The study cohort comprised 104 patients (78 males (75%) and 26 females (25%). The mean age of the patients was 66.63 ± 8.79 years. Comorbidities were observed in 58% of the participants. Regarding smoking status, 15 patients (8%) were never-smokers, 53 patients (50.96%) were former smokers, and 36 patients (34.61%) were current smokers. Furthermore, 19% of patients received long-term oxygen therapy (LTOT). The frequency of acute exacerbations within a year was 68.26%, with 60.57% of these patients requiring inpatient treatment. When classified according to the GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria, the highest patient distribution was observed in GOLD Stage 3. Table 1 summarizes the demographic data, and the GOLD classification distribution is shown in Figure 1. Magnesium Levels and Their Impact In previous studies, serum magnesium (Mg) levels of <1,7 mg/dL

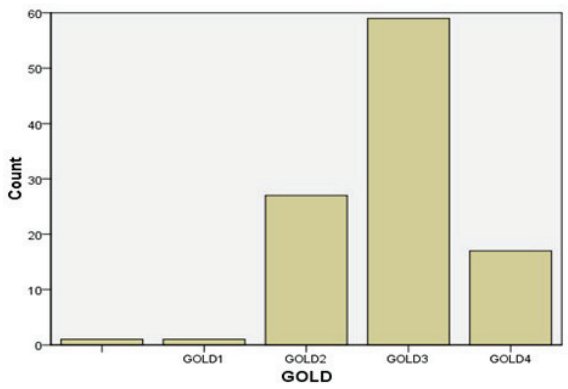

Figure 1
Distribution according to stages
GOLD:Global Initiative for Chronic Obstructive Lung Disease

were classified as hypomagnesemia (12,13). Based on this threshold, the patients in our study were categorized into hypomagnesemic (25%) and normomagnesemic (75%) groups. Serum magnesium levels were evaluated in relation to respiratory parameters, dyspnea scales, and biochemical markers. A negative correlation was observed between magnesium levels and mMRC (Modified Medical Research Council Dyspnea Scale) and CAT (COPD Assessment Test) scores, indicating that lower magnesium levels were associated with more severe symptoms. Conversely, a positive correlation was found between magnesium levels and FEF 25-75 (mid-expiratory flow rate), suggesting improved respiratory function with higher magnesium levels (Figures 2, 3, and 4; Table 2). FEF 25-75 is a marker of small airway obstruction and

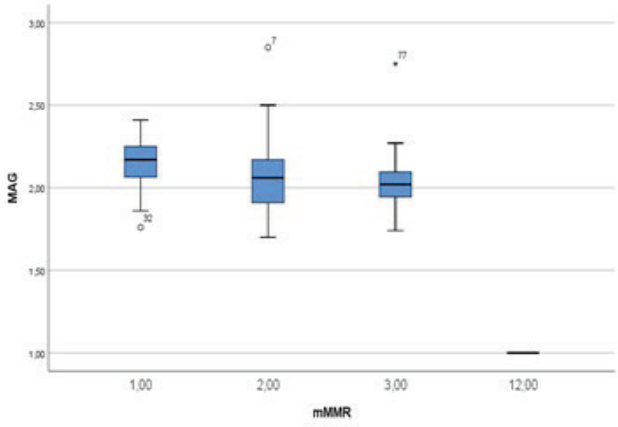

Figure 2
Relationship between magnesium and mMRC
MRC: Modified Medical Research Council
MAG:Magnezyum

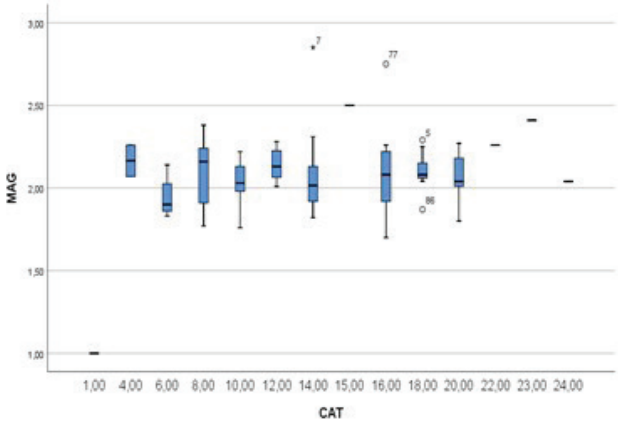

Figure 3
Relationship between magnesium and CAT
CAT: The COPD Assessment Test

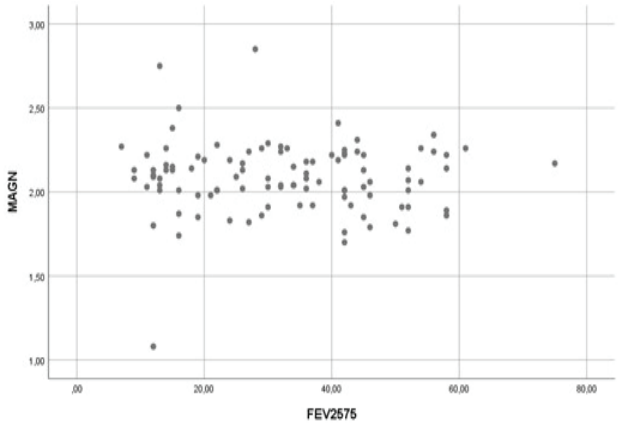

Figure 4
Relationship between magnesium and FEF25-75

Table 1 Demographic and clinical data of patients

All patients	**(min-mx) n mean %**
Age (mean ± SD) years	(44-89) 66.63 ±8.79
Sex (%) Female Male	 n:18 (%17.30) n:86 (%82.69)
Body mass index (BMI) (mean ± SD)	26.16 ± 5.89 (16.3-44.7)
Duration of COPD (years) (mean ± SD)	(2-20) 8.67 ± 4.585
The number of comorbidities median (min-max) no comorbidities comorbidity 1 comorbidity 2 comorbidity 3	2 (0-4) n:46(%41.3) n:48(%45) n:9(%5) n:1 (%2.5)
Smoking (pack/year) median (min-max) current smoker old smoker never smoker	40 (1-100) n:36(%34.61) n:53(%50.96) n:15(%14.42)
Number of patients who are NONE LTOT Number of patients who are on LTOT	n: 85 (%57.5) n:19(%36.3)
No hospitalizations in 1 year 1 hospital stay in 1 year 2 hospital stays in 1 year Number of hospitalizations in 1 year ≥3	n:41 (%39.42) n:32 (%30.76) n:20 (%19.23) n:9 (%8.65)
1 year No exacerbation 0 Number of exacerbation in 1 year: 1 Number of exacerbation in 1 year: 2 Number of exacerbation in 1 year: 3 Number of exacerbation ≥4 per year	n:33 (%31.73) n:37 (%35.57) n:20(%19.23) n:9 (%8.65) n:5 (%4.80)
GOLD1 Mild GOLD2 Moderate GOLD 3 Severe GOLD 4 Very Severe	n:1(%0.96) n:27 (%25.96) n:59 (%56.73) n:17 (%16.34)

GOLD:Global Initiative for Chronic Obstructive Lung Disease, LTOT:long term oxygen therapy BMI: Body mass index
Comorbidity: The coexistence of two or more diseases or disorders.

indicates that it is a candidate for COPD in the early period before COPD occurs. This allows us to take precautions against COPD.

Additional Findings A statistically significant negative correlation was identified between disease duration and magnesium levels (p=0.033). The group with more years of smoking has lower magnesium. The result was not statistically significant (p=0.55) CRP value was found to be higher in the group with low magnesium value. It was not statistically significant. (p=0,868) (Table 2). Sex comparisons revealed that smoking rates and serum calcium levels were significantly higher in males than in females (p=0.044 and p=0.001, respectively) (Table 3). Our findings suggest that magnesium may play a protective role in patients with COPD, potentially mitigating disease severity. These results underscore the importance of Mg in the management of COPD, warranting further research to explore its therapeutic implications.

Discussion

Magnesium, a crucial intracellular cation, plays a significant role in regulating bronchial tone and respiratory muscle function. Its deficiency has been associated with bronchospasm and respiratory distress, underscoring its importance

Table 2 Parameters of patients according to magnesium value

	n	low magnesium	n	Normal Magnesium	p
Age	26	65,23±10,38		67,10±8,21	0,106
Cigarette	26	19.74±9.80	78	18.85±10.517	0.55
BDI	26	26.15±5.51	78	26.16±6.02	0.819
Comorbidity	26	0.70±0.80	78	0.66±0.79	0.932
hospitalization	26	1.35±1.02	78	1.27±0.211	0.698
disease year	26	10.73±6.32	78	9.01±4.65	0.033
Attack	26	2.833±1.418	78	2.769±1.557	0.624
CAT	26	13.92±4.739	78	12.230±4.607	0.030
MRC	26	2.079±0.627	78	1.576±0.724	0.029
Calcium	26	9.117±0.552	78	9.278±0.498	0.718
CRP	26	17.471±30.171	78	16.874±29.708	0.868
WBC	26	9.936±5.271	78	9.897±2.821	0.109
neutrophil	26	69.250±13.422	78	64.910±1.219	0.068
Calcium	26	9.11±0.55	78	9.27±0.49	0.718
FEV1	26	42.423±13.546	78	45.579±13.676	0.753
FEV1/FVC	26	67.076±5.999	78	64.679±6.657	0.845
FVC	26	70.42±18.47	78	67.32±19.46	0.693
FEF25-75	26	31.34±15.26	78	35.53±14.69	0.013

FEF25-75: Mid-expiratory flow rate, FEV1: 1. Forced expiratory volume per second,
FVC: Forced vital capacity, CAT: The COPD Assessment Test, MRC:Modified Medical Research Council
Comorbidity: The coexistence of two or more diseases or disorders.

Table 3 Distribution of patients' parameters according to gender

	n	Male	n	Female	p
Age	87	66.72±8.94	18	65.77±8.14	0.617
Cigarette	87	20.17±9.32	18	15.28±12.65	0.044
comorbidity	87	0.67±0.78	18	0.67±0.79	0.663
Attack	87	2.92±1.44	18	2.22±1.53	0.724
Magnesium	87	2.093±0.19	18	1.99±0.29	0.411
Calcium	87	9.26±0.45	18	8.72±183	0.001
Hospitalization	87	1.46±1.00	18	0.83±0.98	0.652

Comorbidity: The coexistence of two or more diseases or disorders.

in chronic respiratory conditions, such as COPD (14). Magnesium also contributes to membrane stabilization and supports various physiological processes, including modulation of inflammation and smooth muscle relaxation (13). Previous studies suggested a potential correlation between insufficient magnesium intake and the development of asthma or COPD (9). The present study, with a mean patient age of 66.63 ± 8.79 years, aligns with findings by Singh et al., where the mean patient age was reported as 60.4 ± 6.5 years (15). The male-to-female ratio in this study (82.69% male, 17.30% female) contrasts with Singh et al.'s study, in which the proportions were 58% and 42%, respectively (15). The prevalence of hypomagnesemia varies considerably across studies. Rajjab et al. reported hypomagnesemia in 33.76% of patients with COPD (16), while Kumar et al. and Makwana et al. found higher rates of 45% and 57%, respectively (13,17). In the current study, 25% of COPD patients exhibited hypomagnesemia during acute exacerbations, which was relatively low but still significant. The wide variation in hypomagnesemia prevalence may reflect differences in the study populations, dietary magnesium intake, and comorbid conditions. Consistent with other studies, this study observed that hypomagnesemia was more prevalent in advanced COPD stages (GOLD stages 3 and 4). This finding corroborates those of Shah et al., who associated hypomagnesemia with advanced disease stages and frequent exacerbations (18). In the present cohort, 59% of the patients were in GOLD Stage 3, and hypomagnesemia was correlated with worsening COPD severity indicators, such as higher CAT and mMRC scores ($p = 0.030$, $p = 0.029$). Different studies have found that magnesium levels are low in advanced stages and acute exacerbations of COPD. (19,20). The association between low magnesium levels and increased frequency of exacerbations has been highlighted in previous studies. They reported a negative correlation between FEV1 and magnesium levels, with lower magnesium levels being associated with higher rates of exacerbations (21,22). Similarly, in this study, a negative correlation between magnesium and FEV1 was observed, although this was not statistically significant. However, a significant positive correlation was found between magnesium levels and FEF 25-75, suggesting a primary impact of hypomagnesemia obstruction ($p = 0.013$).

Several factors may contribute to hypomagnesemia in COPD patients. These include heavy smoking, poor dietary intake, and the use of medications such as corticosteroids and beta-agonists, which can promote magnesium depletion (23). In our study, 93% of the patients were current or former smokers and all were on corticosteroids and beta-mimetics. Although cigarette pack-years were higher among hypomagnesemia patients, the difference was not statistically significant ($p = 0.55$). Underweight and malnutrition are commonly reported in patients with COPD. Previous studies have reported malnutrition rates of 20-40% in patients with COPD (24). In our study, 8.65% of patients were underweight, a lower proportion than anticipated, with a mean BMI of 26.16 ± 5.89, indicating that most patients were of normal weight or overweight. No significant relationship was observed between BMI and magnesium levels. Magnesium deficiency may exacerbate systemic inflammation by promoting histamine release and neutrophil activation (25). Although our study found a negative correlation between magnesium and CRP levels, consistent with other findings (26), this was not statistically significant. Low magnesium levels are associated with prolonged hospital stays and increased mortality in patients with COPD (13,15). Although our study observed a higher attack frequency and hospitalizations among hypomagnesemic patients, these findings were not statistically significant ($p = 0.624$, $p = 0.698$). Our results suggest that magnesium deficiency in COPD exacerbations is associated with worsened dyspnea (MRC) and higher symptom scores (CAT), potentially indicating its role in disease progression and symptom severity. These findings underscore the importance of regular monitoring of magnesium levels in patients with COPD, particularly during exacerbations, as a potential marker for disease severity and prognosis. The protective role of magnesium in respiratory health emphasizes its importance in COPD management. Addressing hypomagnesemia through nutritional or pharmacological interventions may improve outcomes in patients with COPD, especially those with frequent exacerbations or advanced disease stages. Further studies are warranted to explore Mg supplementation as a therapeutic option for COPD.

Conclusion

This study highlights the importance of monitoring serum magnesium levels in patients with COPD during acute exacerbations, especially upon admission and throughout hospitalization. Our findings suggest that in addition to standard bronchodilator therapy, magnesium supplementation may safely and effectively reduce dyspnea in patients with COPD exacerbations. Our results also indicated that both pharmacological and non-pharmacological magnesium support could play a role in decreasing the frequency of COPD exacerbations and reducing the length of hospital stay. This study contributes to the growing literature on the role of magnesium in COPD management. However,

further multicenter studies with larger sample sizes and extended follow-up periods are necessary to establish the therapeutic efficacy of magnesium in COPD treatment and to provide more comprehensive guidelines for its use in clinical practice.

Conflict of Interest Statement
The authors declare that they have no conflicts of interest.

Ethical Approval
Ethics Committee approval for this study was obtained from Harran University, as evidenced by a letter dated 12.12.2022- HRÜ/22.24.28. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki.

Consent to Participate and Publish
Written informed consent for participation and publication was obtained from all the participants or their legal guardians included in the study.

Funding
No external funding was received for the study.

Availability of Data and Materials
Data available on request from the authors.

Authors Contributions

İMH: Data curation; Formal analysis; Investigation; Methodology; Visualization; Conceptualization; Funding acquisition; Data curation; Resources; Supervision; Writing-original draft. Writing-review & editing.

FG; Conceptualization; Validation Supervision; Methodology Writing-review & editing.

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