

## ASSOCIATION OF SERUM MAGNESIUM LEVEL IN PATIENTS WITH STABLE AND EXACERBATED CHRONIC OBSTRUCTIVE PULMONARY DISEASE - A COMPARATIVE STUDY IN A TERTIARY CARE CENTRE OF NORTHERN KERALA

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Received : 22/11/2024  
Received in revised form : 08/01/2025  
Accepted : 24/01/2025

**Keywords:**  
Chronic obstructive pulmonary disease; Serum magnesium.

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DOI: 10.47009/jamp.2025.7.1.57

Source of Support: Nil,  
Conflict of Interest: None declared

*Int J Acad Med Pharm*  
2025; 7 (1); 292-295



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### Abstract

**Background:** Many evidence suggests that Mg<sup>2+</sup> deficiency contributes to exacerbations of asthma and Mg<sup>2+</sup> is useful in alleviating bronchospasm in these patients. Although the mechanism of this action is unknown, it has been suggested that Mg<sup>2+</sup> plays a role in the maintenance of airway patency via relaxation of bronchial smooth muscle. The objective is to determine the association of Serum Magnesium level with acute exacerbation of COPD. **Materials and Methods:** This was a cross-sectional study which included patients with COPD with age more than 40 years admitted in pulmonary medicine ward, intensive care units and patients came for follow up for 12 months (n=114) divided into two groups (n=57). After obtaining informed consent detailed history and pulmonary function test were done. Samples for serum magnesium were collected from study subjects and estimation was done using colorimetric method. Statistical analysis was performed using SPSS version 22.0 software. **Result:** The test results demonstrated that the mean serum Magnesium levels in case group was significantly lesser [ $1.807 \pm 0.234$ ] as compared to control group [ $1.982 \pm 0.173$ ] and the difference was statistically significant at  $P < 0.001$ . **Conclusion:** Serum magnesium level was found to be significantly decreased in patients with acute exacerbation of chronic obstructive pulmonary disease as compared to stable COPD patients. Hypomagnesemia increased with increasing severity of COPD exacerbation. The test results demonstrated that the mean serum Magnesium levels in Gold category B and C were significantly lesser as compared to category A and the difference was statistically significant. However, no significant difference was noted in the serum magnesium levels between Grade B & C.

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) represents an overlap of chronic bronchitis and emphysema. Bronchospasm is a contributing factor in their inability to clear secretions. This may result in reduced pulmonary gas exchange which resulted in decreased quality of life of the patient and repeated hospitalization.<sup>[1-3]</sup>

There are many modifiable and non-modifiable risk factors for COPD. Identification and correction of modifiable predictors may help in reduction of frequency of exacerbations. Few studies have investigated the factors leading to exacerbations. Magnesium plays a role in airway smooth muscle

relaxation and bronchodilation, stabilization of mast cells, neuro humoral mediator release and mucociliary clearance. So hypomagnesemia is one of the correctable risk factor.<sup>[4]</sup>

## MATERIALS AND METHODS

**Study Design:** Cross sectional study

**Duration of study:** 12 months (October 1, 2020 to October 1, 2021)

**Study setting:** Pulmonary Medicine ward, ICU & OPD of Govt. medical college, Kozhikode

**Study subjects:** Patients admitted with COPD in Pulmonary Medicine ward & ICU and patients came

to OPD for follow up at Govt. medical college, Kozhikode

**Sample size:** Sample size calculation was done using the formula

$$n = \frac{(Z\alpha + Z\beta)2SD2X}{d^2}$$

As the mean values are taken, SD2 is taken.

So n=57

Sampling Procedure

Study subjects included patients who are more than 40 years. They were divided into two groups

**Group 1:** 57 patients admitted with acute exacerbation of COPD.

**Group 2:** 57 patients having stable COPD came for follow up.

Informed consent was taken from all study subjects. Detailed history was taken about the duration of the illness and other significant medical illnesses. Pulmonary function test results were collected from the case records which were done during the admission to assess severity. Samples for serum magnesium were collected from study subjects and estimation was done using colorimetric method for serum ADA.

**Statistical Analysis:** Statistical Package for Social Sciences [SPSS] for Windows, Version 22.0 was used to perform statistical analysis. Mann Whitney Test was used to compare the mean serum magnesium levels and mean between the study groups. Furthermore, mean serum magnesium levels were compared among the study groups of different categories according to severity was performed using Chi-square test. The level of significance (p-Value) was set at  $p < 0.05$ .

## RESULTS

A cross sectional study was conducted among 114 COPD patients, 57 where patients with COPD exacerbation and 57 were stable COPD patients. These patients were further segregated according to Gold criteria.

The level of significance was set at  $p < 0.05$

$p < 0.05$  -Significant

$p < 0.01$  -Very significant

$p < 0.001$  - Highly significant

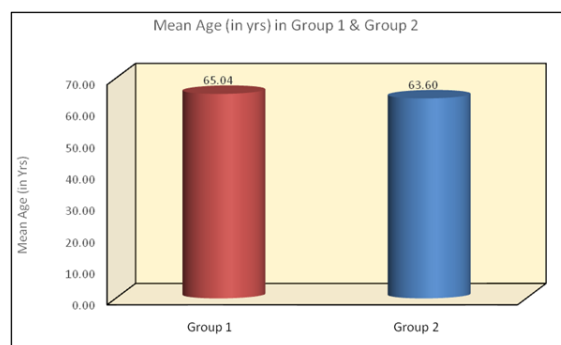
The mean age of the study patients were with a range of 45–80 years. Majority of the Group 1 were distributed in the age group of 45–79 years (mean of 65.04) and Group 2 were between 50–80 years (mean is 63.60) [Table 1].

The test results demonstrated that the mean serum Magnesium levels in case group was significantly lesser [ $1.807 \pm 0.234$ ] as compared to control group [ $1.982 \pm 0.173$ ] and the difference was statistically significant at  $P < 0.001$ . [Table 2]

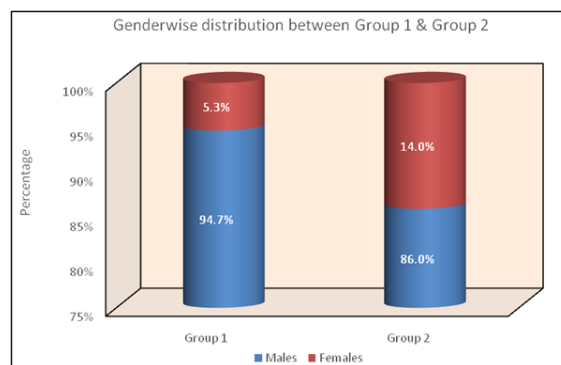
Majority of patients were in Gold category A. Among total patients 45.6% of cases were Gold category A, 19.3% were Gold category B, 35.1% Grade C. [Table 3]

The test results showed the mean serum magnesium levels in Grade A was  $1.916 \pm 0.268$ , Grade B was  $1.763 \pm 0.171$  and Grade C was  $1.691 \pm 0.143$ . This difference in the mean serum magnesium levels between different gold category grades in case group was statistically significant at  $P = 0.001$ .

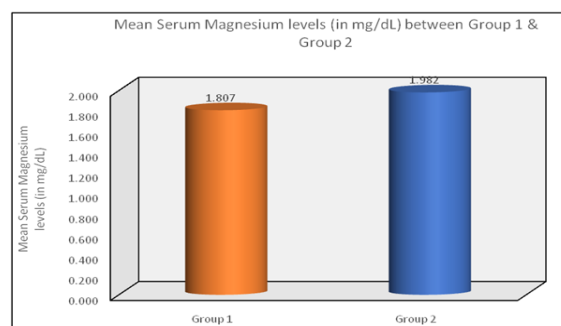
Multiple comparison of mean serum magnesium levels between different group showed that Grade A showed significantly higher serum magnesium levels as compared to Grade B & C at  $P = 0.04$  &  $P < 0.001$ . However, no significant difference was noted in the serum magnesium levels between Grade B & C [ $P = 0.08$ ].



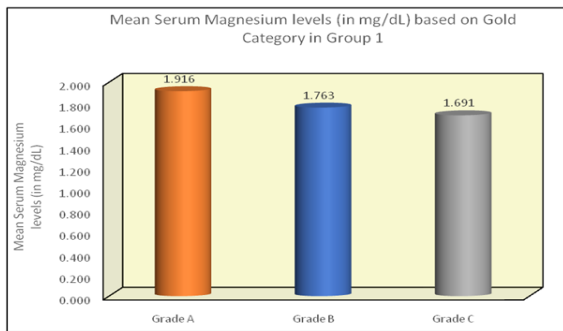
**Figure 1: Age distribution in Group 1 & Group 2**



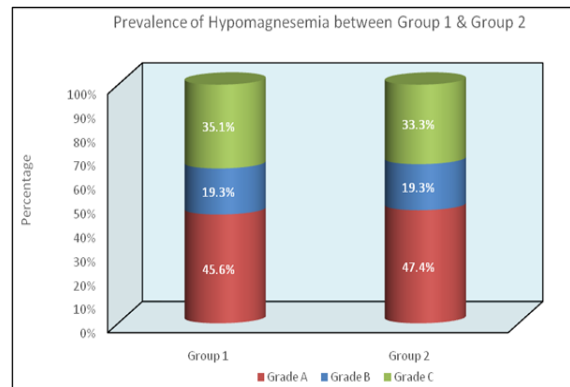
**Figure 2: Gender Wise distribution between Group 1 & Group 2**



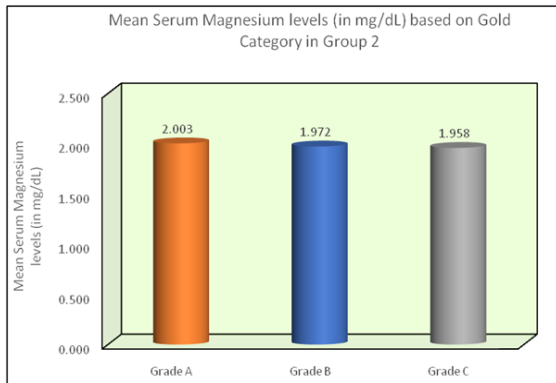
**Figure 3: Comparison of mean Serum Magnesium levels (in mg/dL) between study groups**



**Figure 4: Mean serum Mg level(mg/dL) based on Gold category in Group 1**



**Figure 6: Prevalence of hypomagnesemia between Group 1 & 2**



**Figure 5: Mean serum Mg level(mg/dL) based on Gold category in Group 2**

**Table 1: Age and gender distribution among 2 groups.**

Variable	Category	Group 1		Group 2		P-Value
		Mean	SD	Mean	SD	
Age	Mean & SD	65.04	8.15	63.60	7.87	0.26a
	Range	45 - 79		50 - 80		
Sex		n	%	n	%	0.11b
	Males	54	94.7%	49	86.0%	
	Females	3	5.3%	8	14.0%	

**Table 2: Comparison of mean Serum Mg levels (in mg/dL) between Group I and Group 2**

Parameter	Groups	N	Mean	SD	Mean Diff	P-Value
Serum Magnesium	Group 1	57	1.807	0.234	-0.175	<0.001*
	Group 2	57	1.982	0.173		

**Table 3: Comparison of Gold Category grading of patients between Group 1 & Group 2 using Chi Square Test**

Gold category	Group 1		Group 2		P-Value
	n	%	n	%	
Grade A	26	45.6%	27	47.4%	0.98
Grade B	11	19.3%	11	19.3%	
Grade C	20	35.1%	19	33.3%	

**Table 4: Comparison of mean Serum Mg levels based on Gold Category in Group 1**

Parameter	Gold Category	N	Mean	SD	Min	Max	P-Value a	Sig. Diff	P-Value a
Serum Mg	Grade A	26	1.916	0.268	1.22	2.28	0.001*	A vs B	0.04*
	Grade B	11	1.763	0.171	1.60	2.20		A vs C	<0.001*
	Grade C	20	1.691	0.143	1.60	2.20		B vs C	0.16

Parameter	Gold Category	N	Mean	SD	Min	Max	P-Value
Serum Mg	Grade A	27	2.003	0.174	1.71	2.31	0.62
	Grade B	11	1.972	0.204	1.68	2.30	

	Grade C	19	1.958	0.159	1.70	2.21	
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## DISCUSSION

We compared serum magnesium levels of patients with acute exacerbation of Chronic obstructive pulmonary disease with stable COPD patients visiting the Out Patient Department for follow up. Out of 114 patients participated in the study, 57 (50.0%) were patients with acute exacerbation of COPD and 57 (50.0%) were stable COPD patients.

Mean serum magnesium level was significantly lower in acute exacerbation of COPD patients than in the stable COPD group. Mean serum magnesium in acute exacerbation patients was 1.80 and stable patients was 1.98. These findings were similar to the findings of Sanowara et al.<sup>[5]</sup> and Aziz et al.<sup>[3]</sup> Mean serum magnesium levels in their studies were significantly lower in acute exacerbation of COPD than in stable COPD. ( $1.68 \pm 0.27$  vs  $2.09 \pm 0.12$  mg/dl,  $13.88 \pm 1.8$  vs  $17.8 \pm 0.10$  mg/dl respectively).

In our study increasing severity of COPD exacerbation was associated with higher prevalence of hypomagnesemia. Mean serum magnesium levels in different Gold categories were , Grade A - 1.916, Grade B - 1.763 and Grade C - 1.691. Cao et al determined a correlation between FEV1% <50% and frequent hospitalization due to acute exacerbations.<sup>[6]</sup> Our study also shows the number of attacks rises as predicted FEV1% decreases.

Stable COPD patients are often managed with inhaled corticosteroids and inhaled beta-2 agonist. Some studies show that these could be possible explanations for hypomagnesemia in COPD patients. Treatment with beta-2 agonists may reduce serum magnesium level. However, Alamoudi did not find any association between asthma medicines and hypomagnesemia.<sup>[7]</sup> Intravenous theophylline therapy can induce urinary excretion of calcium and magnesium in patients with recurrent asthma attacks and consequently increase risk of exacerbation.

## CONCLUSION

Serum magnesium level was found to be significantly decreased in patients with acute exacerbation of chronic obstructive pulmonary disease as compared to stable COPD patients.

Hypomagnesemia increased with increasing severity of COPD exacerbation. The test results demonstrated that the mean serum magnesium levels in Gold category B and C were significantly lesser as compared to category A and the difference was statistically significant. However, no significant difference was noted in the serum magnesium levels between Grade B & C.

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