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Estimation of serum magnesium levels in stable and acute exacerbation of bronchial asthma and its correlation with disease severity. A cross-sectional study

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ABSTRACT

Background

Magnesium sulfate ($MgSO_4$) is widely used in managing acute exacerbations of bronchial asthma, especially in refractory cases. However, hypomagnesemia remains an under recognized electrolyte abnormality, often overlooked in routine asthma care. This study aims to assess serum magnesium levels in patients with bronchial asthma—both in stable condition and during acute exacerbations—and to explore its correlation with asthma severity.

Materials and Methods

This cross-sectional study was carried out at a tertiary care center in Thrissur, Kerala, with a total of 80 participants. Patients were divided into two main groups: Group A (Stable Asthma): Subdivided into well-controlled, partially controlled, and uncontrolled asthma based on the GINA symptom assessment. Group B (Acute Exacerbation): Further classified into mild to moderate and severe asthma based on clinical assessment. Serum magnesium levels were measured at the time of presentation for all patients.

Results

The findings showed a statistically significant reduction in mean serum magnesium levels among patients with acute exacerbations (1.71 ± 0.16 mg/dL). Among those with stable asthma, patients with uncontrolled asthma had lower magnesium levels (1.85 ± 0.16 mg/dL) compared to those with partially controlled (2.06 ± 0.14 mg/dL) and well-controlled asthma (2.08 ± 0.14 mg/dL).

Conclusion

Serum magnesium levels were notably lower in asthmatic patients with higher disease severity. These findings suggest that monitoring and correcting magnesium deficiency could potentially improve asthma control and reduce exacerbations.

Keywords: Stable asthma, acute exacerbation of asthma, asthma control, Serum magnesium

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INTRODUCTION

Asthma is a significant non-communicable disease (NCD) affecting individuals across all age groups, and it remains the most prevalent chronic condition in the younger population. According to the latest Global Initiative for Asthma (GINA) guidelines, asthma is characterized as a heterogeneous condition defined by chronic airway inflammation and associated with variable expiratory airflow limitation [1]. The prevalence of asthma varies widely not only between countries and geographical regions but also within nations, influenced by differences in environmental and socioeconomic conditions [2]. Globally, it is estimated that approximately 300 million people currently suffer from asthma, and this number is increasing by nearly 50% every decade [3]. In India alone, around 34.3 million individuals are affected, accounting for about 13.09% of the global asthma burden, according to the Global Burden of Disease (GBD) estimates from 1990–2019. Asthma is also associated with significant mortality, contributing to approximately 13,200 deaths in India. Furthermore, it accounts for 27.9% of disability-adjusted life years (DALYs) among the Indian population, highlighting a disproportionately higher burden compared to global figures. India's asthma-related mortality is nearly three times higher, and its DALY rate is nearly double the global average [4]. A global review of asthma mortality across 46 countries, which included 36 high-income and 10 middle-income nations, showed a decline in the estimated mortality rate from 0.44 per 100,000 in 1993 to 0.19 per 100,000 in 2006. However, between 2006 and 2017, no significant changes in global asthma mortality rates were observed [5]. In recent years, the relationship between asthma and serum magnesium levels has garnered growing attention in both research and clinical practice. Magnesium plays a vital role in numerous physiological processes, including neuromuscular function and immune modulation—both of which are relevant in the pathophysiology of asthma [6]. As one of the most abundant intracellular cations, serum magnesium levels typically range from 1.8 to 2.3 mg/dL [7]. Magnesium contributes to bronchodilation by inhibiting smooth muscle contraction in the airways and blood vessels. It also reduces acetylcholine release from cholinergic nerve endings and enhances the synthesis of nitric oxide and prostacyclin, further aiding in airway relaxation [8]. Conversely, hypomagnesemia can lead to increased muscle contractility and bronchoconstriction. Several studies have highlighted the therapeutic benefits of magnesium, particularly in managing acute asthma exacerbations [9]. However, in spite of several research and recommendations, serum magnesium evaluation as a routine investigation has not been validated. Hence, it's important to correlate its association with severity of asthma control. This study aims to estimate the serum magnesium levels in bronchial asthma patients and to correlate it with the asthma severity.

Materials & Methods

A prospective hospital based cross-sectional study done in a period of 18months in the department of Respiratory Medicine, in a tertiary care center Thrissur, Kerala. A total of 80 patients were recruited from the inpatient and outpatient of our department and was further divided into two groups; Group A (Stable asthma) with 41 patients & Group B (Acute exacerbation) with 39 patients. Patients with other chronic pulmonary diseases, patients of age less than 18 years, and patients with history of smoking were excluded from the study. Stable asthma patients are those who came to the OPD for regular follow-up or with mild symptoms, this group was further subdivided into well controlled, partially controlled and uncontrolled asthma based on GINA symptom assessment. Those patients who presented to OPD or emergency department with worsening asthma symptoms were included under acute exacerbation of bronchial asthma (Group B) which was further subdivided into mild to moderate & severe exacerbation considering the worst presentation based on clinical evaluation including level of consciousness, speech, Spo2 ≤ 92%, pulse rate, respiratory rate, central cyanosis, wheeze intensity/ silent chest and lab investigations including arterial blood gas. For both groups for estimation of serum magnesium, 2ml of venous blood sample was collected, at the time of admission or during the hospital visits. The sample was then estimated using an auto-analyzer dry chemistry

method in vitreous 5600 machine. For assessment of Serum magnesium levels between 2 groups and its correlation unpaired T-test was applied and to assess their severity in each group Bonferroni multiple comparison test was used. A p value of 0.05 or less was considered statistically significant. The data was analyzed using IBM software Statistical Package for Social Sciences version 25.

Results

The mean age in Group A was 37.07 ± 10.15 years, while in Group B, it was 42.92 ± 13.43 years (Graph-1). Younger patients (19–34 years) had higher serum magnesium levels (Group A: 2.06 mg/dL, Group B: 1.74 mg/dL), whereas those ≥51 years had lower levels (Group A: 1.83, Group B: 1.72 mg/dL). Overall, Group B had lower magnesium levels across all age groups (Table-1). Regarding gender distribution, Group A had 80.49% females and 19.51% males, while Group B had 56% females and 44% males, with no significant difference in serum magnesium levels between males and females (Table-2). A significant variation in magnesium levels was observed among patients (well-controlled: 2.08 mg/dL, partially controlled: 2.06 mg/dL, uncontrolled: 1.85 mg/dL), with the lowest levels in uncontrolled asthma. Within Group B, the mean serum magnesium levels were significantly lower in severe acute exacerbation (1.65 mg/dL) than in mild to moderate exacerbation (1.757 mg/dL) (Table-3). Overall, Group B had a significantly lower mean serum magnesium level (1.71 ± 0.16 than Group A (2.01 ± 0.17, p = 0.0001)

Graph 1: Mean Age Distribution

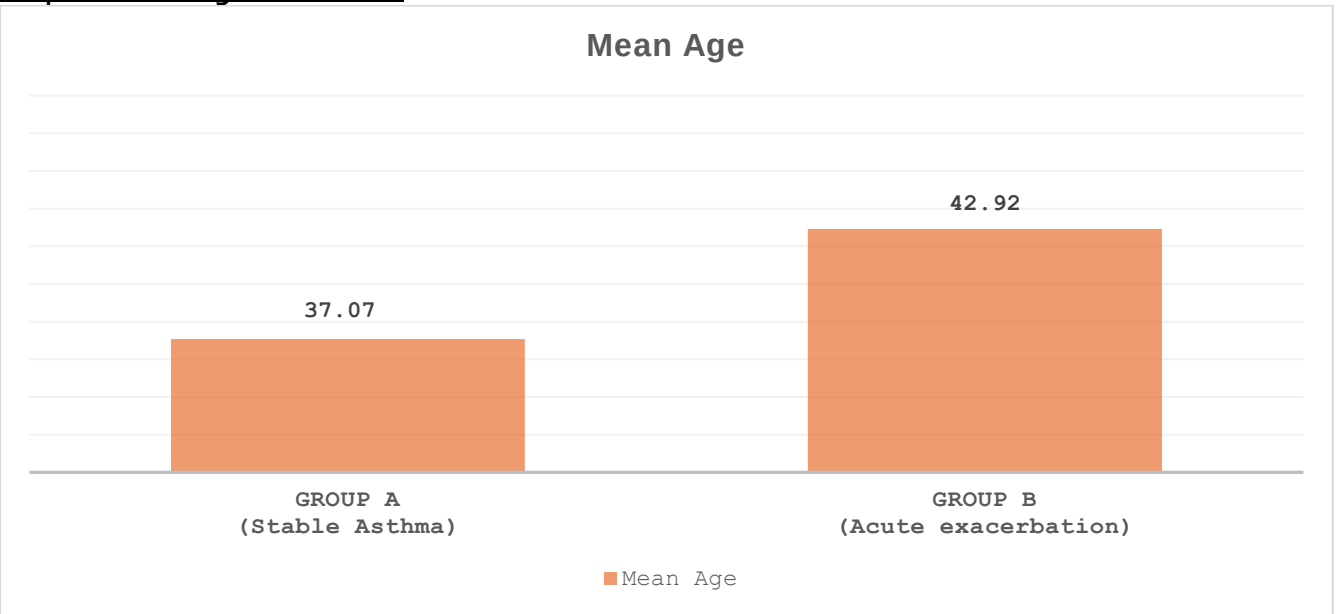

Table-1 Distribution of patients according to age group in stable and acute exacerbation with respect to mean serum magnesium.

	Stable asthma				Acute exacerbation of asthma			
Age group (in years)	N	%	Mean S. Mg^{2+}	SD	N	%	Mean S. Mg^{2+}	SD
19 -34 yr	18	43.9	2.06	0.16	13	33.3	1.74	0.19
35 -50 yr	19	46.3	2.02	0.15	12	30.7	1.66	0.12
>51 yr	4	9.76	1.83	0.24	14	35.9	1.72	0.18

Total	41	100	
Mean	37±10.15		42.92±13.43

Table-2: Distribution of patients according to gender in stable and acute exacerbation in comparison with mean serum magnesium

Stable asthma (group A)				
	N	%	Mean S. Mg^{2+}	SD
Male	8	19.57	2	0.19
Female	33	80.44	2.02	0.17
Total	41		1.71	0.16
Well controlled	15		2.08	0.14
Partially controlled	16		2.06	0.14
Uncontrolled	10		1.85	0.16
Acute exacerbation of asthma (group B)				
	N	%	Mean S. Mg^{2+}	SD
Male	17	19.51	1.71	0.18
Female	33	80.49	1.7	0.15
Total	41			0.22
Mild-moderate	21		1.757	0.1720
Severe	18		1.65	0.1383

Table-3 Comparison of serum magnesium among group A & group B

Mean S. Mg^{2+}	N	Mean	SD	P-value
Group A (Stable Asthma)	41	2.01	0.17	0.0001
Group B (Acute exacerbation)	39	1.71	0.16	

Discussion

Asthma remains a significant global health concern with high prevalence, morbidity, and mortality. The association between serum electrolytes and asthma has been well established. Magnesium has a role in bronchial smooth muscle relaxation, vascular contraction, and neurosynaptic function. It plays a crucial role in cardiac contractility, muscle function, DNA synthesis and repair, and cellular metabolism. Magnesium inhibits acetylcholine secretion, thereby exerting a bronchodilation effect.[10,11] Magnesium has a normal serum concentration ranging between 1.8 and 2.3 mg/dL.[7] The therapeutic utility of intravenous magnesium sulfate ($MgSO_4$) in the management of asthma exacerbations and refractory asthma has been recognized.[12,13] Although hypomagnesemia is frequently observed

in asthmatic patients, there is limited literature on the correlation between serum magnesium levels, asthma disease control and severity, and hence the current study aims to assess this association. In our study, 80 bronchial asthma patients meeting the inclusion criteria were classified into two groups: Group A (stable asthma patients) and Group B (acute exacerbation of asthma). A female predominance was observed in both groups (Group A: 80.49%, Group B: 56.41%). There are limited studies that have explored the correlation between serum magnesium levels and gender. Our study found no significant difference in mean serum magnesium levels between males and females. In group A of stable asthma patients, low serum magnesium levels were seen only in 9.76% of patients and they belonged to the age group ≥51 years. In group B of patients with exacerbation, lowest frequency of exacerbations 30.77% was noted in the 35–50-year age group along with hypomagnesaemia; this could be due to poor dietary intake, high consumption of processed food, high metabolic demands, poor hydration. Patients aged ≥51 years showed lower serum magnesium levels, which overall suggests hypomagnesemia is more prevalent in older age group in stable and acute exacerbation of asthma, this could be possibly due to underlying chronic diseases involving renal or gastrointestinal tract and or factors such as starvation or malabsorption, excessive urinary magnesium loss, excess alcohol consumption, and regular / over use of medication use (e.g., short-acting beta-2 agonists, long-term corticosteroids, theophyllines, diuretics, proton pump inhibitors and laxatives).[14] Based on GINA asthma symptom control, among Group A with total of 41 subjects, 15 had well controlled asthma, 16 had partially controlled asthma and 10 had uncontrolled asthma with a mean serum magnesium values of 2.08, 2.06 and 1.85 respectively, suggesting that uncontrolled group had significantly lower mean serum magnesium levels when compared to well controlled and partially controlled asthma group, This was consistent with the study done by Mohan et al who conducted a cross-sectional study on 160 asthma patients, had similar results.[15] Comparing blood magnesium levels with Group A (stable asthma) and Group B (acute exacerbation of asthma) in our study revealed mean serum magnesium levels to be 2.01 and 1.71 respectively, with lower levels of S. Mg^{2+} among the acute exacerbation group of asthma. Study by Ramadan et al had serum magnesium levels 1.74 in Group A and 1.37 in Group B. There was a significant difference in the serum magnesium level between asthmatic patients and healthy controls, as well as between asthmatic patients during an exacerbation and stable asthmatics.[13] In a study by Anand Agrawal et al. discovered that patients in an acute exacerbation had a statistically significant reduction in their blood ionic Mg^{2+} level when compared to stable and healthy subjects. They also observed low magnesium level in patients with type 2 respiratory failure.[16] There are limited studies that have assessed the severity of asthma exacerbation with mean blood Mg^{2+} levels, in this study to assess the relation with disease severity, we found that the mean blood Mg^{2+} levels were 1.757 among mild to moderate exacerbations and 1.65 among severe acute exacerbations. This shows the overall correlation of disease severity with levels of serum magnesium, suggesting that there is a direct link with the control and severity of asthma with hypomagnesaemia. This was consistent with study done by Brahma Reddy et al with 60 asthmatic samples had mean serum magnesium values of 1.86 and 1.53 in mild to moderate exacerbation and severe acute exacerbation respectively.[17] and study by Indranath had 50 asthma patients, with 28% of acute exacerbation patients who had hypomagnesemia.12 Alamoudi et al had 38% of severe asthma patients with hypomagnesemia.[18] As per our study hypomagnesemia is prevalent in all asthmatics, however its intensity varies based on severity and control of asthma which warrants an importance in assessing serum magnesium levels in all asthmatics as a baseline investigation. However, our study has limitations due to smaller sample size, lower proportion of males and elderly population, lack of baseline magnesium levels before an acute exacerbation, lack of dietary/ drug history and RBC magnesium levels were not assessed for accurate levels.

Conclusion

Serum magnesium levels were significantly low in asthmatics. This shows that serum magnesium has a direct link in correlation with disease control and

disease severity. Therefore, regular monitoring and optimization of serum magnesium can lead to enhanced well-being among asthmatics.

Clinical Significance

People with acute exacerbation of asthma had low serum magnesium levels compared to stable asthma and among stable asthmatics uncontrolled had lowest serum magnesium levels followed by partially controlled asthma with respect to well controlled asthma. Therefore, maintaining normal serum magnesium levels may help to achieve better asthma control and reduce the frequency of acute flare-ups, leading to an improved quality of life for patients and a more cost-effective approach by lowering hospitalization rates. Dietary supplementation of magnesium may also play a crucial role in asthma management. Magnesium in spite of being a crucial ion for the respiratory system, serum magnesium values are not assessed with routine investigations.

$MgSO_4$ therapeutic utility in acute exacerbation has been established several years ago, however monitoring serum magnesium may also have an important role in preventing asthma attacks. Hence regular monitoring of magnesium levels in asthmatics as a biomarker may be used as a predictor for disease control. Maintaining normal serum magnesium may help reduce hospital visits and flare-ups, ultimately improving quality of life and offering a more cost-effective approach in asthma care.

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