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ORIGINAL ARTICLE

Serum magnesium levels and its association with severity of asthma.

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ABSTRACT… Objective: To determine the serum magnesium levels and its association with asthma severity among children presenting with asthma. **Study Design:** Cross-sectional study. **Setting:** Department of Pediatrics, National Institute of Child Health, Karachi, Pakistan. **Period:** October 2024 to March 2025. **Methods:** A total of 151 children aged 6–15 years with asthma were enrolled using non-probability consecutive sampling. Serum magnesium was measured using atomic absorption spectrophotometry. Asthma severity was categorized according to GINA guidelines. Data were analyzed using SPSS version 26.0. Frequencies and percentages were calculated for categorical variables, whereas numerical variables were presented as mean ± standard deviation or median with inter-quartile range (IQR), as per normality distribution. ANOVA/Kruskal-Wallis, and chi-square/Fisher's exact tests assessed associations, with $p<0.05$ considered significant. **Results:** Of 151 children, 103 (68.2%) were male, and the median age was 10 years. Cough (70.9%), shortness of breath (14.6%), and difficulty in breathing (12.6%) were common. The median serum magnesium level was 2.10 (IQR: 2.00-2.30) mg/dl. Asthma severity was mild in 61 (40.4%), moderate in 68 (45.0%), and severe in 22 (14.6%) cases. Serum magnesium levels declined significantly with increasing asthma severity as median 2.12 mg/dl in mild, 2.10 mg/dl in moderate, and 2.00 mg/dl in severe asthma ($p=0.004$). Allergic rhinitis ($p=0.016$), and inpatient care ($p<0.001$) were associated with significantly lower magnesium concentrations. **Conclusion:** The present study demonstrates that lower serum magnesium levels are significantly associated with greater severity of asthma among children.

Key words: Allergic Rhinitis, Asthma, Cough, Serum Magnesium, Shortness of Breath.

INTRODUCTION

Asthma is one of the most prevalent chronic respiratory diseases, commonly presenting with symptoms such as wheezing, cough, breathlessness, and reversible airflow obstruction that can significantly interfere with everyday activities.[1,2] The widespread nature of asthma, coupled with its detrimental effects on quality of life and the associated economic burden on healthcare systems, underscores its importance as a major pediatric health issue.[3] The global prevalence of asthma stands at 11% for children aged 6–7 years, and 9.1% for 13–14 years.[4] In Pakistan, asthma is estimated to affect roughly 15 million children and 7.5 million adults.[5,6] Poorly controlled asthma can result in frequent nighttime awakenings, restrictions in physical activity, increased absenteeism from school or work, hospital admissions, and even mortality in severe cases.[7]

Bronchodilators are prescribed to enhance airflow in patients with compromised lung function.[8] These agents are routinely used to provide symptomatic relief in asthma and to improve pulmonary outcomes. Magnesium, a naturally occurring mineral, exhibits multiple properties that contribute to its bronchodilatory effects.[9] It plays a critical role in numerous physiological processes, including cellular metabolism and the regulation of cardiac and muscular activity. Of particular interest is magnesium's impact on smooth muscle tone, where it exerts a relaxing effect by inhibiting the contraction of bronchial and vascular smooth muscle, as well as by reducing acetylcholine release from cholinergic nerve endings.[9]

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Magnesium deficiency can result in decreased vitamin D levels, which may further exacerbate asthma severity by increasing airway hyperresponsiveness and susceptibility to respiratory infections.[10,11] The recent literature reports the correlation of magnesium levels and asthma as decreasing trend of Mg is seen in asthma. Average Mg levels were highest among well-controlled asthma patients, which found to be lower in partly controlled disease, and lowest in uncontrollable disease (2.08±0.37, 2.07±0.28, and 1.83±0.34, respectively).[12] The local literature on this subject is scarce from Pakistan due to which this study was planned. The objective was to determine the serum magnesium levels and its association with asthma severity among children presenting with asthma.

METHODS

This cross-sectional study was performed at the department of pediatrics, National Institute of Child Health, Karachi, Pakistan, from October 2024 to March 2025, after obtaining approval from Institutional Ethical Review Board (letter: 17/2024, dated: 3-2-2024). The sample size was calculated using online OpenEpi sample size calculator. Sample size of 151 was calculated considering the proportion of poorly controlled asthma among children as 11%[14], with 95% confidence level, and 5% margin of error. Non-probability consecutive sampling technique was adopted. Inclusion criteria were children of either gender, aged 6 to 15 years, diagnosed with asthma, and visiting asthma clinic or admitted in hospital for asthma management. Exclusion criteria were children with other respiratory or systemic diseases, severe acute malnutrition, or those having kidney diseases, malignancy, or gastroenteritis. Children using medications that could affect their magnesium levels, or those receiving magnesium supplements were also excluded. Children were also not enrolled if their parents/guardians refused participation. Informed written consents were obtained from parents/guardians of all participants.

Detailed medical history was documented and clinical examination was performed by the attending pediatrician. Venous blood sample, 2-3 ml, was collected for each child in a plain specimen bottle that was coagulated for 30 minutes before centrifugation. The supernatant fraction, the serum of about 0.8-1 ml, was immediately separated and stored in plain bottles in a refrigerator at temperature 2-8 ºC. Serum ionized magnesium analysis was performed using spectrophotometer. All the investigations were performed through institutional laboratory Patients admitted in hospital for asthma management were managed as per the hospital protocol. Pulmonary function test (PFT) by spirometry were obtain including forced expiratory volume (FEV1), FVC, and peak expiratory flow rate (PEFR). The disease severity of asthma was categorized based on GINA guideline.[13] Mild disease was labelled when patient was prescribed inhaled corticosteroid (ICS) or not prescribed any medications (Step1 and Step 2 of GINA). Moderate disease was considered when patient was prescribed a low-dose or high-dose ICS/LABA inhaler, but not tiotropium or low-dose oral corticosteroids (OCSs). Severe disease was defined if a patient was prescribed an ICS/LABA inhaler and receiving at least one prescription of tiotropium or a low-dose OCS. Severe acute malnutrition (SAM) was labeled as per World Health Organization.[15] Socioeconomic status was categorized as low (family income < 50,000 PKR), middle (>50,000 to 100,000 PKR), and high (>100,000 PKR). A special proforma was designed to record all relevant study data.

Data were analyzed using IBM-SPSS version 26.0. Frequencies and percentages were calculated for categorical variables like gender, residence, socioeconomic status, asthmatic symptoms, allergic rhinitis, asthma severity, need for tracheostomy, and family history of asthma and atopy. Numerical variables like age, disease duration, FEV1/FVC ratio, FEV1(%), PEFR, and Mg levels were presented as mean ± standard deviation (SD) or median with inter-quartile range (IQR), as per normality distribution. Analysis of variance (ANOVA), or Kruskal-Wallis test was applied to determine association of magnesium levels with asthma severity. Chi-square or Fisher exact test was applied to determine association of categorical variables with asthma severity.

P<0.05 was taken as statistically significant.

RESULTS

In a total of 151 children, 103 (68.2%) were male, and 48 (31.8%) female. The median age, height, and weight were 10.00 (IQR: 7.00-11.00) years, 127.00 (IQR: 112.00-135.00) cm, and 24.00 (20.00-31.00) kg, respectively. There were 134 (88.7%) children who resided in urban areas, whereas 71 (47.0%) belonged to a middle socio-economic background. The distribution of asthma severity was mild in 61 (40.4%), moderate in 68 (45.0%), and severe in 22 (14.6%) children. Cough, shortness of breath, and difficulty in breathing were the most frequent presenting complaints, noted in 107 (70.9%), 22 ((14.6%), and 19 (12.6%) children, respectively.

Male gender was significantly more prevalent in the mild (67.2%), and moderate (79.4%) asthma children, but less in the severe (36.4%) asthma children (p=0.001). Urban residence was significantly associated with increased asthma severity (p=0.004). Socio-economic status showed a significant difference, with low status more common in the moderate group (66.2%) compared to severe (18.2%) asthma (p<0.001). Family history of asthma was having significant association with the severity of asthma (p<0.001). Associated allergic rhinitis (p=0.016), and atopy (p<0.001) were more common in moderate and severe asthma. Regarding clinical presentation, cough was significantly associated with mild to moderate severity of asthma (p<0.001). Noisy breathing (p<0.001), and shortness of breath (p<0.001) were significantly more frequent in severe asthma cases. All mild and moderate cases were managed as outpatients, while the majority of severe cases (86.4%) required inpatient care (p<0.001), ash shown in Table-I shows the association of asthma severity with demographic and clinical characteristics.

Characteristics		Asthma Severity			P-Value
		Mild (n=61)	Moderate (n=68)	Severe (n=22)	
Gender	Male	41 (67.2%)	54 (79.4%)	8 (36.4%)	0.001
	Female	20 (32.8%)	14 (20.6%)	14 (63.6%)	
Age (years)		8.00 (8.00-11.00)	10.00 (7.00-11.00)	9.00 (7.00-12.00)	0.457
Height (cm)		127.00 (112.00-132.00)	127.00 (115.00-135.00)	120.00 (111.00-145.00)	0.595
Weight (cm)		23.00 (20.00-30.00)	23.00 (20.00-31.00)	24.00 (20.00-38.00)	0.471
Residence	Urban	48 (78.7%)	64 (94.1%)	22 (100%)	0.004
	Rural	13 (21.3%)	4 (5.9%)	-	
Socio-economic status	Low	22 (36.1%)	45 (66.2%)	4 (18.2%)	<0.001
	Middle	39 (63.9%)	23 (33.8%)	18 (81.8%)	
Family history of asthma		29 (47.5%)	43 (63.2%)	3 (13.6%)	<0.001
Family history of atopy		-	23 (33.8%)	4 (18.2%)	<0.001
Associated conditions	Allergic rhinitis	27 (44.3%)	46 (67.6%)	15 (68.2%)	0.016
	Atopy	17 (27.9%)	46 (67.6%)	12 (54.5%)	<0.001
Frequency of presenting complaints	Cough	37 (60.7%)	59 (86.8%)	11 (50.0%)	<0.001
	Difficulty in breathing	9 (14.8%)	9 (13.2%)	4 (18.2%)	0.848
	Shortness of breath	12 (19.7%)	-	7 (31.8%)	<0.001
	Noisy breathing	-	3 (4.4%)	8 (36.3%)	<0.001
	Fever	3 (4.9%)	4 (5.9%)	-	0.517
	Allergic rhinitis	3 (4.9%)	-	-	0.105
Place of care	Outpatient	61 (100.0%)	68 (100.0%)	3 (13.6%)	<0.001
	In-patient	-	-	19 (86.4%)	

Table-I. Association of asthma severity with demographic and clincial characteristics (n=151)

The median serum magnesium level was 2.10 (IQR: 2.00-2.30) mg/dl. Serum magnesium levels were inversely associated with asthma severity (figure-1), with the median (IQR) being 2.12 (2.10–2.40) mg/dl in mild, 2.10 (2.00–2.30) mg/dl in moderate, and 2.00 (2.00–2.20) mg/dl in severe asthma (p=0.004).

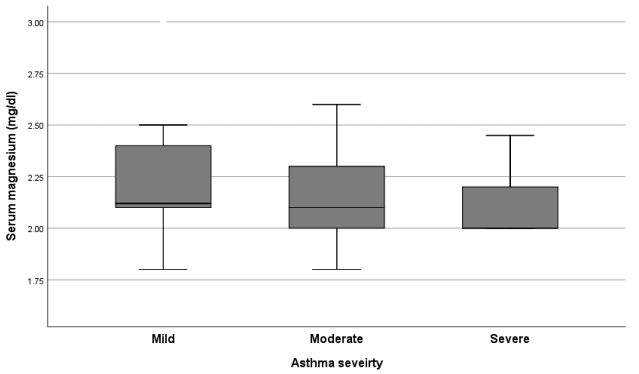

Figure-1. Association of asthma severity with serum magnesium levels

There was no significant correlation between serum magnesium and pulmonary function indices, including FEV1/FVC ratio (r=–0.022, p=0.788), FEV1% (r=0.103, p=0.209), or PEFR (r=0.089, p=0.278). No significant differences in serum magnesium were observed based on gender (p=0.161), residence (p=0.364), socio-economic status (p=0.053), or family history of asthma (p=0.456), or atopy (p=0.914). Children with allergic rhinitis had lower magnesium levels compared to those without [2.01 (2.00–2.30) vs 2.20 (2.10–2.40) mg/dl, p=0.001]. Outpatients had higher serum magnesium levels than inpatients [2.11 (2.00–2.32) vs 2.00 (2.00–2.00) mg/dl, p<0.001]. Table-II summarizes the association of serum magnesium with demographic and clinical variables.

DISCUSSION

The observation of lower serum magnesium levels among children with more severe asthma highlights the role of magnesium in airway physiology and bronchial hyperresponsiveness. This study found median serum magnesium level of 2.12 (2.10–2.40) mg/dl, those with moderate asthma 2.10 (2.00–2.30) mg/dl, and those with severe asthma 2.00 (2.00–2.20) mg/dl (p=0.004). This aligns closely with findings by Gaber et al.[16], who reported significantly lower serum magnesium in children with severe persistent asthma compared to those with milder forms and healthy controls, indicating a strong relationship between magnesium status and asthma severity. Alkholy et al.[17], also demonstrated significantly lower serum magnesium in children with more severe asthma, with the severe persistent subgroup having markedly lower levels than intermittent or mild persistent groups.

Charactsitics			Serum Magensium Level (mg/dl)	P-Value
Gender	Male		2.10 (2.00-2.30)	0.161
	Female		2.16 (2.02-2.32)	
Residence	Urban		2.10 (2.20-2.30)	0.364
	Rural		2.10 (2.05-2.30)	
Socio-economic status	Low		2.10 (2.23-2.20)	0.053
	Middle		2.20 (2.02-2.32)	
Family history of asthma	Yes		2.10 (2.00-2.32)	0.456
	No		2.10 (2.00-2.24)	
Family history of atopy	Yes		2.10 (2.00-2.25)	0.914
	No		2.10 (2.00-2.30)	
Associated conditions	Allergic rhinitis	Yes	2.01 (2.00-2.30)	0.001
		No	2.20 (2.10-2.40)	
	Atopy	Yes	2.10 (2.00-2.32)	0.085
		No	2.16 (2.10-2.30)	
Frequency of presenting complaints	Cough	Yes	2.10 (2.00-2.25)	0.439
		No	2.12 (2.00-2.30)	
	Difficulty in breathing	Yes	2.10 (2.00-2.30)	0.888
		No	2.10 (2.00-2.42)	
	Shortness of breath	Yes	2.11 (2.00-2.32)	0.041
		No	2.10 (2.00-2.10)	
	Noisy breathing	Yes	2.10 (2.00-2.30)	0.431
		No	2.20 (2.00-2.60)	
	Fever	Yes	2.10 (2.00-2.30)	0.595
		No	2.10 (2.10-2.10)	
Place of care	Outpatient		2.11 (2.00-2.32)	<0.001
	In-patient		2.00 (2.00-2.00)	

Table-II. Association of serum magnesium levels with demographic and clinical characteristics of children with asthma

Shaikh et al.[18], further corroborated the relationship between lower serum magnesium and increased

asthma severity. Saeed et al.[19], examining both acute and stable asthma, observed that children with acute severe asthma attacks had significantly lower serum magnesium compared to those with stable asthma and healthy controls, and also identified positive correlations between serum magnesium and lung function. These converging lines of evidence support the present finding that as asthma severity increases, serum magnesium levels decrease.

Khanna and Kundan[20], found no significant correlation between serum magnesium and asthma severity, even as vitamin D3 levels showed a clear inverse relationship with increasing severity. Chittamani et al.[14], reported no significant association between magnesium levels and asthma symptom control, as assessed by the ACT score. Their results also showed no significant correlation between magnesium and pulmonary function parameters. These findings suggest that the relationship between magnesium and asthma severity may be more apparent in populations with a higher burden of moderate or severe disease, or may depend on the criteria used for defining asthma control and severity. Differences in study design, population characteristics, and methods of measuring magnesium may account for discrepancies in the literature. The current study excluded children with comorbidities such as malnutrition, kidney disease, and those receiving magnesium supplements, which might have reduced potential confounders impacting magnesium status. Local dietary patterns and the prevalence of nutritional deficiencies may also play a role in population-specific magnesium status.

Gaber et al.[16], also reported significant positive correlations between serum magnesium and FEV1% ($r=0.712$) and FEV1/FVC ratio ($r=0.680$), suggesting a role for magnesium not only in disease severity but also in pulmonary function. In contrast, the current study did not find a statistically significant relationship between serum magnesium and pulmonary function tests, which may reflect differences in study design, population characteristics, or the distribution of asthma severity. Studies such as Khanna and Kundan.[20] and Chittamani et al.[14], found no signifiant association between serum magnesium levels and lung function tests, underscoring the possibility that magnesium's role may be more relevant in acute exacerbations or in severe persistent asthma rather than in mild or stable cases.

The current study found that allergic rhinitis and in-patient status were associated with lower magnesium levels. Children with allergic rhinitis had median serum magnesium of 2.01 (2.00–2.30) mg/dl compared to 2.20 (2.10–2.40) mg/dl in those without ($p=0.001$). This supports the concept that magnesium deficiency may be associated not only with asthma severity but also with the broader atopic diathesis, as also proposed by Alkholy et al.[17], and Shaikh et al.[18], who demonstrated that magnesium deficiency was more common among children with comorbid atopic diseases.

The clinical relevance of the inverse association between magnesium and asthma severity is multifold. Magnesium has well-documented bronchodilatory and anti-inflammatory properties and is used intravenously in acute severe asthma exacerbations as an adjunct to standard therapy.[21] The consistent observation of lower serum magnesium in more severe asthma and during acute attacks suggests a role for magnesium in modulating bronchial smooth muscle tone, airway inflammation, and bronchial hyperresponsiveness. From a clinical standpoint, the measurement of serum magnesium may offer prognostic value in assessing children at risk for more severe asthma or poor disease control. Identifying serum magnesemia levels provides an opportunity for targeted nutritional or therapeutic interventions, potentially improving asthma outcomes and reducing the frequency of severe exacerbations. This is especially relevant in resource-limited settings where asthma morbidity and mortality remain high, and modifiable risk factors such as micronutrient deficiencies are prevalent. Paul et al.[22], and Ogbuka et al.[23], both reported that higher serum magnesium was associated with better ACT scores and asthma control. On the other hand, Chittamani et al.,

found no significant association. The current study did not directly assess asthma control scores but did find that magnesium levels were lower in those requiring hospitalization, which may serve as a proxy for poorly controlled or more severe asthma. Chowdhary et al.[24], found that hypomagnesemia was associated with longer hospitalization, lower oxygen saturation, and increased need for mechanical ventilation, further highlighting the prognostic significance of magnesium in acute asthma management.

Several limitations of this study merit consideration. The cross-sectional design precludes establishing causality between hypomagnesemia and asthma severity. Longitudinal studies are needed to determine whether magnesium deficiency contributes to worsening asthma or is a consequence of severe disease or its management. The study relied solely on serum magnesium measurements, which may not reflect total body or intracellular magnesium status. Future studies should consider measuring red blood cell or ionized magnesium, as well as dietary intake, to provide a more comprehensive assessment. Selection bias may have occurred due to the non-probability consecutive sampling method and the predominance of urban, middle-income children. Multi-center studies with stratified random sampling are recommended to enhance generalizability. Another limitation is the lack of direct assessment of asthma control scores, which would have allowed comparison with studies specifically addressing symptom control. Future research should integrate objective and subjective measures of asthma control alongside biochemical parameters to better inform clinical practice.

CONCLUSION

The present study demonstrates that lower serum magnesium levels are significantly associated with greater severity of asthma among children. The monitoring serum magnesium may offer valuable insight into asthma severity and risk stratification in pediatric populations. Future studies employing longitudinal, multi-center designs and incorporating diverse biochemical and clinical endpoints are warranted to elucidate the mechanistic pathways and therapeutic potential of magnesium in pediatric asthma.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION	
1	**Syeda Ayesha Rehman:** Data collection, final approval.
2	**Muhammad Ashfaq:** Conception design, proof reading.
3	**Syed Muhammad Wahaj:** Methodology, critical revision.
4	**Khatidja Ally:** Literature review.
5	**Bader u Nisa:** Study design.
6	**Saima Ibbad:** Analysis.