

## Comparison of Serum Magnesium Levels in Well-Controlled and Poorly Controlled Bronchial Asthma Among Children and Healthy Controls at a Tertiary Care Hospital

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### KEYWORDS

asthma,  
magnesium,  
children.

### ABSTRACT:

**Background:** Asthma is one of the most common chronic diseases worldwide and has been increasing in prevalence over the last few decades. Magnesium ion has an inhibitory action on smooth muscle contraction, histamine release from mast cells and acetylcholine release from cholinergic nerve terminals. Magnesium has been shown to relax bronchial smooth muscles and influence the function of respiratory muscles. Hypomagnesemia have been associated with diminished respiratory muscle power.

**Objectives:** To compare the serum Mg levels in children with bronchial asthma in well controlled and poorly controlled and with healthy non asthmatic children in Vinayaka Mission Kirupananda Variyar Medical College and Hospital, Salem.

**Methodology:** Children with established asthma were to be identified in pediatric asthma clinic, at Vinayaka Mission Kirupananda Variyar Medical College and Hospital, Salem after obtaining written informed consent from parents- detailed history, clinical examination to be done. Using GINA guidelines cases were to be divided into well controlled and poorly controlled groups. A third group comprised of healthy children. Venous blood samples of 2ml were to be drawn and sent to laboratory.

**Results:** Serum Mg levels were significantly lower in poorly controlled asthmatic patients compared with well controlled and healthy controls. There was a positive correlation between serum Mg levels and control level of asthma in children.

**Conclusion:** Identifying lower magnesium levels earlier and avoidance of triggering factors can reduce the frequent exacerbations and control of asthma.

### Introduction-

Asthma is a long-lasting inflammatory disorder of the lung airways ensuing in sporadic airflow impediment. There is a extensive disparity of 1.6- 36.8% universally in asthma occurrence in various geographical areas. Although there has been a considerable advance in managing asthma, childhood asthma appears to be growing in prevalence.[1]

Numerous studies and existing literature show that asthma prevalence associated well with described allergic rhinitis and atopic eczema. Allergy has been identified as the surrounding environment with its allergens stimulates a genetically predisposed individual to activate his immune responses for a chronic inflammation.[2]

The various common environmental agents leading to such aberrant inflammatory repair include inhaled allergens etc.[3] In addition to the given standard treatments, mineral- supplementation therapies, such as magnesium, are being tried to maintain asthma control. Improvement in bronchial responsiveness and quality of life were reported with oral magnesium therapy in patients with asthma [4,5]. The basis of which lies on the important role

that magnesium plays in the activity of smooth muscles. Magnesium is the cofactor of more

than 300 enzymes and is involved in many physiological functions including protein synthesis, intracellular signal distribution and enzyme catalysis. Since it is the natural antagonist of calcium, it brings about smooth muscle relaxation. In addition, magnesium suppresses the excitability of muscle fibers by reduction of acetylcholine secretion from motor nerve terminals. It also inhibits production of inflammatory mediators by helping stabilization of T-cells and inhibiting mast cell degranulation. Further, it reduces the severity of inflammation in asthma by stimulating nitric oxide and prostacyclin synthesis.[6,7]

Magnesium is the fourth most abundant cation in the body and the second most common intracellular cation. Since magnesium intervenes in calcium transport mechanisms and intracellular phosphorylation reactions, it constitutes an important determinant of the contraction and relaxation state of bronchial smooth muscle. Magnesium deficiency is associated with increased contractility of smooth muscle cells. Since contractility of bronchial smooth muscle is important in patients with asthma, magnesium deficiency could lead to bronchial smooth muscle contraction or lack of bronchial muscle relaxation.[8]

Although clinical trials using magnesium as an adjunct to treating asthma exacerbation have been conducted in children, no work has yet been done to determine whether serum magnesium levels in asthmatic children differ from those of controls and whether asthma exacerbation in children is associated with low serum magnesium levels. Therefore, we undertook this study to assess whether magnesium deficiency exists in asthmatic children between attacks and during exacerbation. The above actions of magnesium suggest a possible role of magnesium deficiency and poor asthma control. However, studies conducted to establish this relationship have yielded conflicting results. Therefore, there is a need for a study to assess whether magnesium deficiency exists in asthmatic children.

#### **Materials and Methods-**

It was a Prospective observational study conducted at Vinayaka Mission Kirupananda Variyar Medical College and Hospital in the department of paediatric asthma clinic for a period of One year from Dec 2022 to Nov 2023. Children aged 1 to 12 years, who were diagnosed to have bronchial asthma based on GINA guidelines.

#### **Inclusion criteria:**

All children aged 1-12 years who were diagnosed to have asthma after therapeutic trial of ICS for children less than 5 years and children above 5 years by GINA guidelines, who are being followed up in the department of paediatrics as out-patient or admitted for in-patient care. Children with established asthma were identified in pediatric asthma clinic attached to pediatric department, Vinayaka Mission Kirupananda Variyar Medical College and Hospital.

#### **Exclusion Criteria:**

- Children of age <1 years
- Children with Congenital cardiac and lung abnormalities.
- Neurologically impaired children
- Children who satisfied inclusion criteria are taken up for the study.

After obtaining written informed consent from, detailed history from parents, clinical examination was done; anthropometry was measured. The level of control was assessed using GLOBAL INITIATIVE FOR ASTHMA (GINA) guidelines. Children were assigned into well controlled (group1) and poorly controlled (group 2). The poorly controlled group included both the partially controlled and uncontrolled group of GINA. Third group was healthy children. Venous blood samples around 2 ml were drawn before starting treatment and sent to laboratory. Serum magnesium was analysed by xylydyl blue method using Machine Biosystems BA 400 in full automated analyser.

Clinical data of these patients documented using a standard proforma and analyzed. Children who met the criteria are enrolled. Clinical data of these children were collected using a proforma sheet. Children with atopy had dermatology consultation and children with recurrent sneeze and nasal symptoms were evaluated by an ENT consultant. All children were followed up for the study period of 1 year. Patients were managed by the treating unit as per protocol.

All information regarding exacerbations requiring hospital admissions, including PICU, general ward admission were collected. Data of medications and prophylactic drug usage were collected and subjected to analysis.

Institutional ethics committee clearance obtained before the study.

### Sample size estimation-

Sample size was calculated using formula  $-4PQ/D^2$

Having a prevalence of 7.24 with an 95% confidence interval and 10 percent error, the sample size was 120. Clinical data of asthma children collected.

### Statistical Analysis-

Variables like age, sex, BMI, atopy, family history, previous hospitalisation, picu admission, exposure to smoking collected and entered in the Microsoft excel sheet. All analyses were done with IBM SPSS software Version 22.0. Proportions were compared by using ANOVA and Kruskal wallis test to find out the statistical significance. Value of  $p < 0.05$  is considered as statistically significant. Statistical analyses were made for all variables separately and they are analysed accordingly.

### Results-

**Table 1- Age and Sex wise distribution of study participants**

AGE IN YEARS	NO OF PATIENTS	PERCENTAGE
LESS THAN 5 YRS	36	30%
MORE THAN 5 YRS	84	70%

As per table 1 The proportion of cases in less than 5 years and more than 5 years were 30% and 70 % respectively. In our study the prevalence of cases in both age groups were almost equal. Among 120 cases 73 were male children and 47 were female children, which corresponds to 61% and 39% respectively. This shows that boys are more affected than girls.

**Table 2- Association Between BMI and Level of Control**

LEVEL OF CONTROL	BMI	
	MEAN	SD
WELL CONTROLLED	15.38	2.2
POORLY CONTROLLED	15.49	2.06
HEALTHY	15.39	2.06
ANOVA		
P VALUE - 0.967		
NON SIGNIFICANT		

As per table 2 this study does not show significant relation between overweight and asthma. Although some studies have shown association between them, yet their temporal relationship remain unclear.

Children were categorized into Well controlled, poorly controlled and healthy based on asthma control questionnaire. The proportions of cases in different categories were equally 40 children in each group respectively.

**Table 3- Serum Magnesium Levels**

SERUM MAGNESIUM	NO OF PATIENTS	PERCENTAGE
NORMAL	77	64.00%
ABNORMAL	43	36.00%

As per table 3 In our study 77 children had normal levels and rest had mostly higher level than reference range whereas only two cases were below normal levels, this was not statistically significant, But when we analysed the mean values of all these groups, the poorly controlled group had lower values compared to other groups which was also statistically significant.

**Table 4- Level of Control vs Magnesium levels**

LEVEL OF CONTROL	SERUM MAGNESIUM	
	MEAN	SD
WELL CONTROLLED	2.25	0.43
POORLY CONTROLLED	2.05	0.26
HEALTHY	2.32	0.54
ANOVA		
P VALUE - 0.016		
SIGNIFICANT		

As per table 4 Finally, we analysed the main part of this study the relation between serum magnesium levels and control of asthma. Serum levels of magnesium have been investigated in asthmatic patients based on its effects in asthma treatment. Low serum Mg levels in adult asthmatic patients have been described many years ago. Although it was within the normal range, serum magnesium levels were statistically significantly lower in patients with asthma symptoms versus the other groups.

**Table 5- ATOPY VS CONTROL**

LEVEL OF CONTROL	ATOPY	
	PRESENT	ABSENT
WELL CONTROLLED	7	33
POORLY CONTROLLED	17	23
HEALTHY	3	37
KRUSKAL WALLIS TEST		
P VALUE - 0.001		
SIGNIFICANT		

As per table 5 there as significant relation between history of atopy and control level of asthma in children in our study

**Table 6- SOCIOECONOMIC STATUS VS CONTROL**

SOIOECONOMIC STATUS	LEVEL OF CONTROL		
	WELL CONTROLLED	POORLY CONTROLLED	HEALTHY
CLASS I	3	5	7
CLASS II	17	13	3
CLASS III	17	16	23
CLASS IV	3	6	7
KRUSKAL WALLIS TEST			
P VALUE - 0.027			
SIGNIFICANT			

As per table 6 in our study nearly half of children belong lower socioeconomic status (47%) which is similar to previous studies which explains Several how socioeconomic status (SES) influences the development of asthma but with discrepant results.

**Table 7- EXPOSURE TO SMOKING VS CONTROL**

LEVEL OF CONTROL	EXPOSURE TO SMOKING	
	PRESENT	ABSENT
WELL CONTROLLED	2	38
POORLY CONTROLLED	7	33
HEALTHY	3	37
KRUSKAL WALLIS TEST		
P VALUE - 0.143		
NON SIGNIFICANT		

In our study among 120 cases, 12 children had exposure to tobacco smoke. The severity of asthma and serum IgE levels was found to be higher in these children compared to those without a history of passive smoking. Passive smoking influences on the severity of asthma by increasing the bronchial responsiveness. In our study the Proportion of cases with history of atopy was 22%.

**Table 7- Hospital Admission vs Level of Control**

LEVEL OF CONTROL	HOSPITAL ADMISSION	
	REQUIRED	NOT REQUIRED
WELL CONTROLLED	7	33
POORLY CONTROLLED	11	29
HEALTHY	0	40
KRUSKAL WALLIS TEST		
P VALUE - 0.001		
SIGNIFICANT		

Among 18 children who required hospital admission, most of them were poorly controlled

#### **Discussion-**

Asthma is a chronic inflammatory disease of airways with increasing number of hospitalizations in young children worldwide. It poses a significant burden to the patient, family, health care systems and government. With advancement in management protocols and health education there has been a dramatic reduction in morbidity and mortality.

We analysed 40 healthy cases with 80 cases with symptoms and signs suggestive of asthma, who were attending the Outpatient as well as admitted in the Department of Pediatrics of Vinayaka Mission Kirupananda Variyar Medical College and Hospital, Salem



The proportion of cases in less than 5 years and more than 5 years were 30% and 70 % respectively. In our study the prevalence of cases in both age groups were almost equal. Chhabra SK Gupta et al [9] in their study reported that prevalence of asthma is more in age group of 6-9 year which was 14.9% compared to 8.7% in 10-12 years and with 5.5 % in the 13-15 year groups. In the study by Chandra Madhur Sharma et al[10] the prevalence of asthma in children in various ages as 7.04 percent in 5 to 8years, 7.67 percent in the age group of 9 to 11 years, 9.67 percent in the age group of 12 to 15 years.

Among 120 cases 73 were male children and 47 were female children, which corresponds to 61% and 39% respectively. This shows that boys are more affected than girls. But Anupama et al[11] reported a female preponderance in asthmatic adults. Male predominance in our study may be due to narrow airways and increased tone of airways in children which prompt them to increased airflow obstruction in response to various stimuli. Around puberty the prevalence becomes higher in female due to alterations in the thoracic size that occurs in male but not in female.

In our study nearly half of children belong lower socioeconomic status (47%) which is similar to previous studies which explains how socioeconomic status (SES) influences the development of asthma but with discrepant results. Most studies have reported that children in families with low SES (measured by parental occupation, education or family income), have an increased asthma risk even after adjustment for known confounders such as prenatal maternal smoking, indoor allergens, and maternal stress[12]. Other studies, however, found no relationship with parental SES [13]. These diverse results could be due to different study designs, small sample sizes, or varying measures of SES.

In our study among 120 cases, 12 children had exposure to tobacco smoke. The severity of asthma and serum IgE levels was found to be higher in these children compared to those without a history of passive smoking. Passive smoking influences on the severity of asthma by increasing the bronchial responsiveness. In our study the Proportion of cases with history of atopy was 22%. There is significant relation between history of atopy and control level of asthma in children in our study. Study done by Sanja Dimitrijevic et al.[14] showed most of children with asthma had allergic rhinitis, followed by eczema; sometimes both eczema and allergic rhinitis at the same time.

Among 18 children who required hospital admission, most of them were poorly controlled, a few studies have analysed this which showed In the US, 2.3% of all emergency department (ED) visits and about 5.6% of all hospitalizations among children were attributed to acute asthma. In Saudi Arabia, one center reported that over 1 year, an average of 5.7% of all ED visits were secondary to acute asthma[15]. This ratio can rise to 13.7% during the winter season as reported by another study from a different hospital.

A proportion of children presenting to the ED with acute asthma are eventually admitted to the hospital with an estimated rate ranging from 7% to 23%. This is determined by several variables including age, sex, the baseline severity of exacerbation, early response to treatment in the ED (within the 1st h),[16] and the level of control of asthma symptoms in the past.

Finally, we analysed the main part of this study the relation between serum magnesium levels and control of asthma. Serum levels of magnesium have been investigated in asthmatic patients based on its effects in asthma treatment. Low serum Mg levels in adult asthmatic patients have been described many years ago. Contrarily, some studies reported no difference between asthmatic patients and normal individuals, in terms of serum magnesium levels

Although it has been a subject of research in adults for a long time, serum Mg levels of children has recently begun to be investigated. First, Kakish et al.[17] reported that serum Mg levels were not lower during and between attacks in asthmatic children aged between 6 and 18 years as compared to the control group without asthma. In one another study it was found that serum Mg levels were within the normal range in both patient groups including children with acute asthma attack and with stable asthma. However, although it was within the normal range, serum

magnesium levels were statistically significantly lower in patients with asthma attack versus the other groups.

In one another study done by Daliparthi et al [18] they screened 256 adult patients who met the inclusion criteria. After 96 patients were removed based on exclusion criteria, 160 patients were grouped into three based on the level of symptom control.

Forty-eight patients belonged to the “well controlled” group, 59 in “partly controlled” group, and the remaining 53 in “uncontrolled” group. The mean serum Mg level (mg/dl) was  $2.08 \pm 0.37$ ,  $2.07 \pm 0.28$ , and  $1.83 \pm 0.34$  in well, partly, and uncontrolled groups, respectively. As the level of control of asthma decreased from well controlled to uncontrolled, the level of mean serum Mg also decreased.

The findings of this study is similar to that in the study conducted by Haury et al[19]., who reported significantly lower level of serum magnesium in asthmatics compared to healthy subjects. This is also in concordance to the findings of the studies conducted by Siebes KD et al[20]., Mohammed NS et al[21]. also concluded that the mean serum magnesium levels are lower like the current study. Hence, this study shows that low serum magnesium can be an indicator of asthma.

### Conclusion

Asthma continues to be a chronic disease which is increasing in prevalence among children worldwide especially in developing countries like India. The morbidity and mortality due to asthma is still rising. Boys had higher incidence of asthma compared to girls in this study. Atopy, passive smoking, family history remains the major risk factors in childhood asthma. There is strong correlation between atopy and asthma control. Children with persistent exposure to passive smoking and with positive family history have poor control of asthma. These children should take necessary precautions to avoid the triggering factors that may contribute to morbidity. Identifying the disease earlier and avoidance of triggering factors can reduce the frequent exacerbations. This study demonstrated the serum magnesium levels are statistically lower amongst asthmatics. Many further larger multicentric studies needs to be performed in larger groups of children with asthma using more advanced testing methods like intracellular magnesium estimation are needed. Identifying lower magnesium level earlier and avoidance of triggering factors can reduce the frequent exacerbations and control of asthma.

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