KJMS / OPEN ACCESS Print ISSN: 2790-0207 Online ISSN: 2790-0215

Original article

Study The Relation Between Serum Magnesium level and The Severity of Asthma

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DOI: 10.32894/kjms.2022.137484.1049
Received: 23-12-2022, Published online: 01-10-2023

Abstract:

- ***Background*:** Asthma is one of the most common chronic diseases globally and has been increasing in prevalence over the last few decades. The aim of this study is to assess the serum Magnesium levels in bronchial asthma patients in relation to severity stage.

- ***Methods:*** A case control study conducted at Baghdad Teaching Hospital at Baghdad Medical City complex of fifty patients were diagnosed as bronchial asthma according to GINA guideline and fifty healthy individuals as a control group.

- ***Result:*** Serum Magnesium levels were lower in asthmatic patients (36%), compared with healthy controls (4%), and significantly lower in asthmatic patients during exacerbation compared with stable asthmatics.

- ***Conclusions:*** Serum Magnesium levels have a positive correlation with the level of symptom control in asthma. In uncontrolled asthma, serum Magnesium is significantly low. Hence, it might be useful as a biomarker in assessing control or severity of asthma.

- **Keywords:** Asthma, exacerbation, magnesium.

Cite as: Hassan, Y., W. AL Obiady, M. Study The Relation Between Serum Magnesium level and The Severity of Asthma. *Kirkuk Journal of Medical Sciences*, 2023; 11(2): 51-63. doi: 10.32894/kjms.2022.137484.1049

INTRODUCTION

Bronchial asthma is a chronic condition characterized by recurrent bronchospasm resulting from reversible bronchial hyper responsiveness in response to stimuli of a level or intensity which usually does not cause such narrowing in most individuals. Globally bronchial asthma is one of the most common diseases which affect approximately ~330 million peoples. Asthma has great social impact, with a prevalence of about 10–12% in adults and 15% in children. It can be found at any age [(1)].

Asthma is widely distributed all over the globe including tropical countries like India. But it has variable prevalence among different populations. In India, its prevalence is about 2% [(1,2)]. Because of its potential role in preventing respiratory infections, vitamin D deficiency is an important public health issue. The key function of vitamin D is to regulate calcium and phosphorus homeostasis and in turn vitamin D metabolism is regulated by factors that respond to plasma concentration of calcium, phosphate, and magnesium. Calcitriol (active form of vitamin D) is involved in insulin secretion, inhibit interleukin production by T-lymphocytes and immunoglobulin by B-lymphocytes, differentiation of monocyte precursor cells, and modulation of cell proliferation. Cells of the immune system such as T-lymphocytes, activated B-lymphocytes, and Dendritic cells express vitamin D receptors (VDRs) [(3)].

Dendritic cells also express 1, α-hydroxylase, which suggests that 25-hydroxycholecalciferol (Calcitriol) can be converted to its active form (Calcitriol) locally and so it participates in immune response. Moreover, vitamin D is found to play a role in innate immunity against various microbial agents. It up regulates the synthesis of cathelicidin and immunoglobulin's [(4)]. Probably this can be the possible reason behind the curing effects of sunlight on tuberculosis and other infections.Thus, vitamin D is one of the important regulators of immunity. Its deficiency along with triggering stimuli may increase the risk of asthma, allergies, and exacerbation of diseases [(5)]. As per few earlier reports, magnesium (Mg) deficiency is associated with increased tracheobronchial hyper reactivity, pulmonary vascular drag, and ventricular arrhythmia. Treatment with β_2-agonists can reduce magnesium levels in serum by intracellular shift or urinary loss [(6)]. Magnesium causes relaxation of bronchial smooth muscles and dilatation of airways, most probably by altering calcium ion movement. In contrary, hypomagnesaemia may produce bronchoconstriction. It may disturb the neuromuscular mechanism to such an extent in certain individuals which may result in bronchial spasms [(7)]. Magnesium (Mg) as the second most plentiful intracellular cation and an important part of bone mineralization has a crucial function in synthesis and metabolism of vitamin D. Lower levels of serum magnesium are associated with hypovitaminosis D [(8)]. Hypomagnesaemia lowers the concentration of vitamin D in body which can worsen the clinical condition in asthma by tracheobronchial hyper reactivity and by increasing susceptibility to respiratory infection [(5-8)]. The aim of the study is to assess the relationship between serum magnesium level and asthma severity.

PATIENT and METHOD

The study took place at the Baghdad Teaching Hospital, within the Medical City complex, during a period spanning from June 2018 to December 2018. The research aimed to conduct a case-control study to explore the relationship between bronchial asthma and various factors. Patients diagnosed with bronchial asthma, according to the GINA (Global Initiative for Asthma) guidelines, were included in the study. However, individuals with certain conditions or habits that could potentially confound the results were excluded from both the patient and control groups. These exclusions encompassed chronic kidney disease, diabetes mellitus, ethanol use, diuretics and proton pump inhibitor use, hyperthyroidism, pregnancy, malabsorption syndrome, hypertension, and dyslipidemia.

A convenient sampling method was employed to select a group of 50 patients with bronchial asthma who met the inclusion and exclusion criteria. The researcher collected all the necessary data for the study through a structured questionnaire, which covered several aspects of the patients' medical history and demographics.

The questionnaire consisted of the following sections:

1. Demographic data, which included information about the patients' age, gender, and other relevant factors.

2. Medical and drug history, which provided insights into the patients' past and current health conditions and medications.

3. Body mass index (BMI), a measure of body weight in relation to height, which was determined by the researcher based on the patients' weight and height. The BMI values were classified according to the World Health Organization's guidelines, into normal (<25Kg/m2), overweight (25-29.9Kg/m2), and obese (>30Kg/m2).

4. Asthma duration, which indicated how long the patients had been living with asthma.

5. Asthma severity, measured using a peak flowmeter, which helps assess the airflow in the patients' lungs.

6. Asthma medications, detailing the types of medications the patients were using to manage their asthma.

7. Serum magnesium level, which was determined through venous blood samples collected from the participants. The blood samples were centrifuged, and the serum was then analyzed using ELISA (enzyme-linked immunosorbent assay). The reference range for serum magnesium levels in adult males was 1.8-2.6 mg/dl and 1.9-2.5 mg/dl in adult females. The ELISA kit used for analysis, called 'SIEMENS DIMENSION,' had been authorized by the Ministry of Health since 2015 and was stored at the appropriate temperature.

Before proceeding with the study, ethical considerations were carefully addressed. The approval of the Baghdad Teaching Hospital administration was obtained, and an oral informed consent process was conducted with all the participants, ensuring their voluntary participation. The patients' well-being was of utmost importance, and they were treated with care and respect by both the researcher and supervisor.

For statistical analysis, the data collected from the selected patients were organized and analyzed using the Microsoft Excel program and Statistical Package for Social Sciences (SPSS) version 23. The outcomes were presented in various scales and categorical variables. Fisher's exact test was utilized for comparing categorical data. A significance level (p-value) of ≤ 0.05 was considered to draw meaningful conclusions from the study's results.

RESULTS

This prospective study included 50 asthmatic patients with mean age of 40.7±13.8 years; 28% of them were less than 30 years age, 30% of them were in age group 30-39 years, 8% of them were in age group 40-49 years, 16% of them were in age group 50-59 years and 18% of them were in age 60 years and more. Female asthmatic patients were more than males with female to male ratio as 1.1:1. All these findings were shown in table 1.

Table 1: Demographic characteristics of asthmatic patients.

Variable	No.	%
Age	mean±SD (40.7±13.8years)	
<30 years	14	28.0
30-39 years	15	30.0
40-49 years	4	8.0
50-59 years	8	16.0
≥60 years	9	18.0
Total	50	100.0
Gender		
Male	24	48.0
Female	26	52.0
Total	50	100.0

Most (96%) of asthmatic patients were urban residents. The occupation of asthmatic patients was distributed as followings; housewife (32%), student (2%), self-employed (6%), public servant (38%) and retired (22%). Mean BMI of asthmatic patients was 27.8±5.4 Kg/m^2; 38% normal BMI, 26% overweight and 36% of them were obese. All these findings were shown in table 2.

Table 2: General characteristics of asthmatic patients.

Variable	No.	%
Residence		
Urban	48	96.0
Rural	2	4.0
Total	50	100.0
Occupation		
Housewife	16	32.0
Student	1	2.0
Self-employed	3	6.0
Public servant	19	38.0
Retired	11	22.0
Total	50	100.0
BMI mean±SD (27.8±5.4Kg/m^2)		
Normal	19	38.0
Overweight	13	26.0
Obese	18	36.0
Total	50	100.0

Mean asthma duration was 21.2±12.6 years; 30% less than 10 years, 34% 10-20 years and 36% of them had more than 20 years asthma duration. All these findings were shown in table 3.

Table 3: Asthma duration and vital signs of asthmatic patients.

Variable	No.	%
Asthma duration mean±SD (21.2±12.6years)		
<10 years	15	30.0
10-20 years	17	34.0
>20 years	18	36.0
Total	50	100.0

Mean medications number was 2.4±0.9; 26% of them had single medication, 16% of them two medications, 48% of them had three medications and 10% of them had four medications. Types of medications were commonly SABA inhaler (26%), SABA inhaler+ LABA/Steroid Inhaler + Methylxanthin derivative tab (18%), SABA inhaler+ SAMA inhaler + LABA/Steroid Inhaler (12%), SABA inhaler+Methylxanthin derivative tab +SAMA Inhaler (10%), etc. All these findings were shown in table 4.

Table 4: Medication characteristics.

Variable	No.	%
Medications number mean±SD(2.4±0.9)		
1	13	26.0
2	8	16.0
3	24	48.0
4	5	10.0
Total	50	100.0
Type of medications		
SABA inhaler+Methylxanthin derivative tab +SAMA Inhaler	5	10.0
SABA inhaler+ Steroid Inhaler+Methylxanthin derivatives tab	2	4.0
SABA inhaler +Steroid tab	4	8.0
SABA inhaler + Leukotriene receptor antagonist tab + LAMA/Steroid Inhaler	2	4.0
SABA inhaler+ SAMA inhaler+ LABA/Steroid Inhaler	6	12.0
SABA inhaler	13	26.0
SABA inhaler+ LAMA/Steroid Inhaler	1	2.0
SABA inhaler +Steroid Inhaler+ Methylxanthin derivatives tab	2	4.0
SABA inhaler +LABA/Steroid Inhaler+ Methylxanthin derivative tab	9	18.0
SABA inhaler + Leukotriene receptor antagonist tab	3	6.0
SABA inhaler + Leukotriene receptor antagonist tab + SAMA inhaler	1	2.0
SABA inhaler+ Steroid Inhaler	2	4.0
Total	50	100.0

The severity of asthma was classified to mild (30%), moderate (36%) and severe (34%). Exacerbation of asthma was recorded for 70% of asthmatic patients. Mean serum magnesium of asthmatic patients was 1.95±0.24 mg/dl; 36% of them had low serum magnesium level. All these findings were shown in table 5.

Table 5: Severity of asthma and serum magnesium level of asthmatic patients.

Variable	No.	%
Severity of asthma		
Mild	15	30.0
Moderate	18	36.0
Severe	17	34.0
Total	50	100.0
History of Exacerbation of asthma		
Yes	35	70.0
No	15	30.0
Total	50	100.0
Serum magnesium mean±SD (1.95±0.24mg/dl)		
Normal	32	64.0
Low	18	36.0
Total	50	100.0

No significant differences between asthmatic patients and controls regarding age (p=0.1) and gender (p=0.6). All these findings were shown in table 6.

Table 6: **Distribution of demographic characteristics according to asthmatic cases and controls.**

Variable	Asthmatic		Control		P Value
	No.	%	No.	%	
Age					0.1* NS
<30 years	14	28.0	11	22.0	
30-39 years	15	30.0	6	12.0	
40-49 years	4	8.0	5	10.0	
50-59 years	8	16.0	15	30.0	
≥60 years	9	18.0	13	26.0	
Gender					0.6** NS
Male	24	48.0	26	52.0	
Female	26	52.0	24	48.0	

**Fishers exact test, **Chi-square test, NS=Not significant.*

A highly significant association was observed between low serum magnesium level and asthmatic patients (p<0.001); 36% of asthmatic patients with low serum magnesium level in comparison to 4% of healthy controls with low serum magnesium. All these findings were shown in table 7.

Table 7: Distribution of serum magnesium level according to asthmatic cases and controls.

Variable	Asthmatic		Control		P Value
	No.	%	No.	%	
Serum magnesium level					**<0.001*S**
Normal	32	64.0	40	80.0	
Low	18	36.0	2	4.0	
High	0	-	8	16.0	

No significant differences in serum magnesium level were observed according to age groups of asthmatic patients (p=0.06). No significant differences in serum magnesium level were observed according to gender of asthmatic patients (p=0.3). No significant differences in serum magnesium level were observed according to BMI groups of asthmatic patients (p=0.5). All these findings were shown in table 8.

Table 8. Distribution of serum magnesium level according to age, gender and BMI groups of asthmatic patients.

Age groups (years)	<30	30-39	40-49	50-59	≥60	P Value
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
Serum magnesium level(mg/dl)	1.97±0.16	1.84±0.23	1.8±1	1.9±1	2.1±0.3	0.06*NS
Gender	**Male**		**Female**			**P**
	Mean±SD		**Mean±SD**			
Serum magnesium level (mg/dl)	1.98±0.26		1.98±0.19			0.3*NS
BMI (Kg/m^2)	**Normal**	**Overweight**	**Obese**			**P**
	Mean±SD	**Mean±SD**	**Mean±SD**			
Serum magnesium level (mg/dl)	1.94±0.21	1.9±0.2	1.899±0.26			0.5*NS

**One way ANOVA analysis, NS=Not significant.*

No significant differences in serum magnesium level were observed according to asthma duration groups of asthmatic patients (p=0.08). The mean serum magnesium of asthmatic patients was significantly reduced among patients with increased number of medications (p=0.02). All these findings were shown in table 9.

Table 9. Distribution of serum magnesium level according to asthma duration number of medications of asthmatic patients.

Asthma duration (years)	**<10**	**10-20**	**>20**	**P**
	Mean±SD	**Mean±SD**	**Mean±SD**	
Serum magnesium level (mg/dl)	1.94±0.19	1.86±0.18	2±0.27	0.08*[NS]

Number of medications	**1**	**2**	**3**	**4**	**P**
	Mean±SD	**Mean±SD**	**Mean±SD**	**Mean±SD**	
Serum magnesium level (mg/dl)	2±0.22	2.1±0.15	1.9±0.24	1.7±0.1	**0.02***[S]

**One way ANOVA analysis, NS=Not significant, S=Significant*

There was a highly significant reduction in serum magnesium level among patients with severe asthma (p<0.001). The mean serum magnesium of asthmatic patients was significantly reduced among patients with positive exacerbation history of asthma (p=0.03). All these findings were shown in table 10.

Table 10. Distribution of serum magnesium level according to severity asthma exacerbation of asthmatic patients.

Asthma severity	**Mild**	**Moderate**	**Severe**	**P**
	Mean±SD	**Mean±SD**	**Mean±SD**	
Serum magnesium level (mg/dl)	2±0.15	2.1±0.22	1.7±0.06	**<0.001***[S]

History of Asthma exacerbation	**Yes**	**No**	**P**
	Mean±SD	**Mean±SD**	
Serum magnesium level (mg/dl)	1.9±0.24	2.1±0.15	**0.03****[S]

**One way ANOVA analysis, **Independent sample t-test, S=Significant.*

DISCUSSION

The relationship between serum magnesium levels and bronchial asthma has been widely established over the years, with the most well-known association being the therapeutic use of magnesium sulfate in cases of acute severe asthma. In our current study, we classified the severity of asthma into three categories: mild (30%), moderate (36%), and severe (34%). The mean serum magnesium level of asthmatic patients was found to be 1.95 ± 0.24 mg/dl, falling within the normal range (1.8-2.5 mg/dl).

Compared to the control group, the asthmatic patients showed a significant decrease in serum magnesium levels (p value < 0.001), with 36% of asthmatic patients having low serum magnesium levels, in contrast to only 4% of the control group. Moreover, there was a highly significant reduction in serum magnesium levels among patients with severe asthma (Mean ± SD = 1.7 ± 0.06) when compared to those with chronic stable asthma (Mean ± SD = 2 ± 0.15).

Our study's findings align with previous research, such as the study conducted by Haury et al., which also reported lower serum magnesium levels in asthmatic patients compared to the control group [(9)]. Similar results were observed in studies conducted by Siebes KD et al., Mohammed NS et al., and Ahmed AA et al. [(10-12)]. Nevins et al. also reached a similar conclusion, emphasizing the lower serum magnesium levels in asthmatic patients compared to the control group [(13)].

However, there have been conflicting results, as seen in the study conducted by Karkish KS et al., which found no significant relationship [(14)]. Additionally, other studies on adults have failed to find a similar association [(15, 16)].

We also found that the mean serum magnesium level of asthmatic patients significantly decreased with an increased number of medications (p=0.02), consistent with the findings of Das et al. [(17)], who reported a statistically significant relationship between hypomagnesaemia and the use of ⩾3 medications. Furthermore, our results indicated that asthmatic patients with a positive history of exacerbations had a significantly reduced mean serum magnesium level (P = 0.03). This finding was similar to the report by Alamoudi [(18)], which found that chronic asthmatics with low magnesium levels experienced a higher number of exacerbations compared to those with normal magnesium levels. Das et al. [(17)] also observed a significant relation between serum magnesium levels and exacerbations.

No significant differences were found between asthmatic patients and the control group concerning age (p=0.1) and gender (p=0.6). Similarly, there were no significant differences between asthmatic patients and controls regarding residence (p=0.4) and occupation (p=0.6).

Based on our findings, this study sheds light on the potential role of magnesium supplementation therapy in the long-term management of asthma. Maintaining serum magnesium levels within the normal or high range may aid in achieving better asthma control. Furthermore, our study suggests that apart from being used as a therapeutic adjunct in managing severe acute asthma, magnesium might also play a crucial role in preventing asthma attacks. However, the regular dietary supplementation of magnesium for inducing asthma control requires further investigation.

In order to better understand the physiology of magnesium in the human body, including its intracellular stores and correlation with serum levels, more research is needed. Alternative methods of estimating magnesium levels, such as red blood cell storage, may prove useful. Additionally, it is essential to comprehend the potential side effects and complications of magnesium overdose thoroughly. Further studies are warranted to explore these aspects fully.

CONCLUSION

Low serum magnesium level was found in patients with chronic stable bronchial asthma compared to control. Its levels were found significantly lower in asthmatic patients during exacerbations compared with stable asthma. Serum magnesium levels found to have a positive correlation with the severity of asthma.

RECOMMENDATION

We recommend measuring serum magnesium level in all patients present with bronchial asthma. Hence, it might be used as a biomarker in assessing severity of asthma.
Whether regular dietary supplementation of Magnesium might help in inducing asthma control needs further study.
We need further studies in this field with a larger sample for further evaluation of relationship between serum magnesium level and the severity of asthma.

Financial support and sponsorship:
Nil.

Conflicts of interest:
There are no conflicts of interest**.**

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