

Research Article

Serum Magnesium Level is Associated with Exacerbation of Bronchial Asthma

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Abstract

Bronchial asthma is one of the most common respiratory disorder with increasing prevalence among children and adults. During ionic study of disease Mg^{++} was found to be associated with exacerbation as well as treatment of the disease. Magnesium causes inhibition of smooth muscle contraction by competing with Ca^{++} , histamine release from mast cells by stabilizing outer membrane and acetylcholine release from cholinergic nerve terminals. All these processes results in relaxation of smooth muscles of bronchi which ultimately relieves the symptoms of asthma. Low magnesium level has been associated with asthma

Objective : To determine the serum magnesium (Mg) concentration in asthmatics in acute attack, stable stage of asthma and its comparison with healthy individuals.

Material and methods: 110 Subjects were enrolled in the study after their written consent, Among them 60 patients diagnosed as asthma (study group), 30 subjects with chronic stable asthma, 30 subjects with acute severe attack of asthma and 50 normal individuals as a control group..

Results: There was a significant decrease in Serum Mg levels in study group as compared to control group. It was further observed that there is decrease in serum Mg^{++} in asthmatic patients during acute attack of asthma as compared with stable stage of asthma. Moreover a positive correlation between serum Mg levels and lung function test especially FEV1 and FEV1/FVC ratio was observed in the present study.

Conclusion: There is a strong relationship between asthma and serum magnesium level. It was further concluded that in asthmatics there is further decrease in serum Mg in acute exacerbation of the disease as compared to chronic stable asthma.

Received | 14-02-2018: **Accepted** | 27-09-2019

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Keywords | Asthma, stable, exacerbation, Magnesium, FEV1

Introduction

Magnesium, an important inorganic element of body is present in many foods available as supplement, and frequently used in medicines. Magnesium acts as a cofactor in cellular enzymatic system and responsible for regulation of different chemical reactions,¹⁻³. Mg^{++} plays a vital role in

glycolysis oxidative phosphorylation and energy production, .This is also responsible for development of different structures of body like bone, genetic material (DNA, RNA,) and the antioxidant glutathione. Mg^{++} plays an important role in the transportation of ions like calcium and potassium across cell membranes which causes conduction of impulse in nerves, contraction of muscle, and

maintenance of normal heart conduction.³

The total amount of magnesium in an adult is about 25g. Among this 50% to 55% is in the bones and remaining in tissues.⁴ The serum total magnesium is less than 1%, and kept under control. The concentrations of serum magnesium range from 0.75 to 0.97 millimoles (mmol)/L.^{1,5} When serum Mg level is less than 0.75 mmol/L it is termed as hypomagnesaemia.⁶ The homeostasis of Mg⁺⁺ is controlled by the renal system and kidneys, excretes about 125mg magnesium in the urine in 24 hours.² The urinary excretion of Mg is reduced when its serum level is low.¹ There are many methods of assessment of Mg⁺⁺ but it very difficult to get the level as most magnesium is intracellular or in bone.³ The most common method for magnesium estimation is serum magnesium concentration but interesting to note that there is a little relationship between serum Mg⁺⁺ levels and total body Mg or its concentrations in tissues⁶. There are many other methods for determination of magnesium level. Among these Mg concentrations can be measured in red blood cells, saliva, and urine. The ionized Mg level in blood / plasma, or serum can be measured. Moreover magnesium-load or Tolerance test (an infusion of magnesium is given parentally and its urinary excretion is measured and from this its level in serum is determined) can be used to assess its level. It has been observed that among all methods mentioned above no single method is considered up to the mark.⁷ Some researchers⁴ but not all³ take the Magnesium Tolerance test the best method for assessment of magnesium in the body. In order to evaluate body Mg status, both lab tests and a clinical observation might be taken into an account.⁶ Low Mg⁺⁺ level make the person prone to many diseases and asthma is one of them. Asthma is a disorder defined by its clinical and pathological symptoms in which there is breathlessness, particularly at night, often associated cough.⁸ It has been observed that Mg⁺⁺ has potent effects on rabbit airways and causes smooth muscle relaxation of bronchial system results in broncho dilation.⁹ So main action of Magnesium is to cause relaxation of smooth muscles of respiratory bronchi. It also has anticholinergic effects which results in stabilization of mast cells and inhibits the release of acetylcholine.⁹ Many studies have proved that low intake of magnesium in diets causes impairment of pulmonary

function tests, bronchial hyper-sensitivity, and hyper-resonant wheezing. Researchers have observed that high magnesium intake results in improvement in symptom in asthmatic.¹⁰ Keeping this association in view a study was designed to assess and compare the serum Mg levels in asthmatics during stable (symptoms free) and exacerbations (acute attack) stages of the disease and its comparison with normal healthy individuals as controls.

Methods

This study was conducted in Emergency department (ED) of Mayo Hospital Lahore / Physiology department KEMU and outdoor of East Medical Ward. A total number of 110 (60 asthmatics as study group and 50 normal subjects without asthma as control group) patients were included in the study after informed consent and approval from ASRB of King Edward Medical University. Mainly there were two groups, the asthmatics were in study group & normal without any history of asthma were in Control Group. There was further division of Study Group (asthmatics) into two sub-Groups on the basis of Intensity of disease. The asthmatics were further divided into two groups. Group (I) included 30 patients with chronic stable bronchial asthma who used to come for regular follow up in the outdoor of East Medical Ward. Group (II) was consisted of 30 patients who presented in the emergency with acute severe attack of asthma with $FEV_1 \leq 50\%$ of predicted value. The asthmatic groups were compared with 50 age and gender match healthy subjects without asthma. As far as exclusion criteria was concerned patients with IHD, chronic renal disease, diabetes mellitus, diarrhea and alcoholics were excluded from the study. After enrollment detailed history was taken. Then general physical examination (GPE) and in the last respiratory examination was done. A venous sample was taken to determine Mg concentration

Spirometry was carried using Spirolab-III (MIR, Italy) to assess the pulmonary Function Tests (PFT). The significant reference spirometric values with airflow obstruction are $FEV_1 < 80\%$ and $FEV_1/FVC < 70\%$. In order to diagnose asthma the degree of reversibility in FEV_1 is 12% and 200 ml from the pre-bronchodilator value after treatment with bronchodilator agents.

Magnesium Estimation

Serum Mg⁺⁺ levels were determined in duplicate using Magnesium Liquicolor kit (Human) by photometric method on UV-VIS Spectrophotometer UVALB-280 (Bio Com Ltd UK). Magnesium in alkaline medium forms a colored complex with xylydyl blue and absorbance of this compound is checked by UV photometer. The absorbance is directly proportional to the concentration of the colored complex formed. The presence of calcium can affect the results and to inhibit it Glycoetherdiamine N,N,N,Ntetraacetic acid (GEDTA) is used to inhibit effect of calcium.^{12,13}

Three plastic test tubes were taken and labeled as standard, blank and test. One ml of magnesium test reagent was added in each test tube. 10 µl of serum was added in the tube labeled as test, 10µl of standard in test tube labeled as standard and 10µl of deionized water was added in blank tube. All tubes were placed at 37°C in water bath for 15min. After 15min, the results were recorded by placing the tubes in spectrophotometer. The normal range of serum magnesium in adult male is 1.8–2.6 mg/dl and 1.9–2.5 mg/dl in adult female adult male^[11].

Statistical Methodology

The data was analyzed by SPSS (version 17). The student t-test was applied to compare two groups to analyze quantitative data. The analysis of qualitative data was done by using chi-square test. As far as correlation between one qualitative variable and one quantitative variable or two quantitative variables of not normally distributed data is concerned it is Person's correlation which was used and $p < 0.05$ was considered as significant.

Results

The data of the study compiled in three tables as shown below.

Table 1 shows that male gender among the participant of the study is about 80% in study group and 75% in control group which was not of statistical significance. It was also observed that as far as age and BMI are concerned there was no statistically significant differences between two groups.

When Lung Function Tests were studied a significant

Table 1: Demographic Data of the Study Participants

	Asthmatics (Study Group) (n = 60)		Control (n = 50)		P value
	No.	%	No.	%	
Male	48	80	35	75	0.658
Female	12	20	15	25	
Age	51.65 ± 7.66		45.85 ± 9.70		0.057
BMI	26.81 ± 4.46		26.15 ± 4.91		0.602

BMI, Body mass index,

difference statistically was observed between study and control groups. As far as Forced expiratory volume in 1st second, Forced vital capacity ratio (FEV1/FVC) and FEV1 were concerned a significant difference was observed as shown in Table 2. Both FEV1/FVC ratio and FEV1 were lower in the study group as compared to the control.

It was further observed that serum Mg level was lower in study group as compared to control group as shown in Table 2 below.

Table 2: Lung Function Tests and Serum Mg Level

	(Study Group (n = 60)		Control (n = 50)		P value
	No.	%	No.	%	
FEV1/ FVC ratio	53.14 ± 8.71		86.68 ± 7.90		<0.001*
FEV1	51.93 ± 12.45		89.57 ± 12.89		<0.001*
Serum Mg	1.53 ± 0.34		2.11 ± 0.20		<0.001*

FEV1, Forced expiratory volume in the 1st second; FVC, Forced vital capacity

Table 3 shows that there is a significant difference in serum Mg level in stable and acute exacerbation of asthma. It was observed that there was decrease in Mg level during acute attack of asthma as compared to stable state as shown in Table 3. So it was concluded that as far as serum Mg level and each of FEV1/FVC ratio, FEV1 in both the stable asthmatics and exacerbation groups a positive correlation was there between serum Mg level and each of FEV1/FVC ratio, FEV1. A significant negative correlation was observed between serum Mg level and acute exacerbation of asthma. As far as FEV1/FVC ratio, FEV1 is concerned it was seen that there was a significant difference statistically during acute exacerbation and stable state of asthma.

Serum Mg level was significantly lower in asthmatic

patients compared with healthy controls and significantly lower in asthmatic patients during exacerbation compared with stable asthmatics. There was a positive correlation serum Mg level and each of FEV1/FVC ratio and FEV1.²⁵

Table 3: Demographic Data, Spirometric Values and Serum Mg Levels of Asthmatic Patients whether in Stable State or during Exacerbation.

	Stable (n = 30)		Exacerbation (n = 30)		P value
	No.	%	No.	%	
Male	24	75	26	85	0.429
Female	6	25	4	15	
Age	49.80 ± 7.86		52.50 ± 8.27		0.180
BMI	27.30 ± 4.42		26.33 ± 4.56		0.497
FEV1/FVC ratio	55.80 ± 6.48		47.48 ± 9.58		0.001*
FEV1	62.68 ± 6.78		40.18 ± 9.06		<0.001*
Serum Mg	1.74 ± 0.33		1.37 ± 0.24		<0.001*

Discussion

In this present study a significant decrease in magnesium levels was observed in study group (asthmatics) as compared to the control group. The mean of serum Mg levels in patients of study group was 1.53 ± 0.34 and in healthy control 2.11 ± 0.20 mg/dl (Table 2). This low serum Mg was confirmed by research done by Agin et al.¹⁴ In a study performed by Oladipo et al.¹⁶, it was observed that the serum Mg level were markedly on lower range in asthmatic patients compared to their normal healthy control. Hypomagnesaemia was commonly seen in asthma, the exact cause of which was unknown.¹⁵ It may be due to either low magnesium intake by the patients or excessive urinary loss of magnesium due to drugs like β_2 -agonist, steroid, and theophylline.^{17,18}

Our research confirmed that there was a significant decrease in FEV1/FVC ratio in asthmatics during acute attack than in asthmatics in stable stage (p value = 0.001). The value of this ratio in stable asthmatics was 55.80 ± 6.48 and in exacerbation was 47.48 ± 9.55 (TABLE 3). As far as, FEV1 was concerned it was decreased significantly in asthmatics when they suffered from acute illness than in stable stage (p value < 0.001). The value of FEV1 in asthmatics during stable stage was 61.68 ± 6.78 and during acute attack of asthma was 40.18 ± 9.06 (Table 3). This was confirmed by Sorkness et al in his study,¹⁹

In our study serum Mg levels were significantly

lower in asthmatics with acute exacerbation as compared to stable asthmatics, (p value < 0.001) This was observed that the mean serum Mg level in stable asthmatics was 1.74 ± 0.33 while during acute exacerbation it was 1.37 ± 0.24 (Table 3). The results of this study match with study conducted by Mohammad et al.¹²⁰¹, The same results were reported by, Alamoudi¹²¹¹ in his research. This relationship of low Mg level and asthmatic symptoms are due to an increased airway hypersensitivity. It has been seen that magnesium ions are involved in many physiologic processes which influence lung function. The mechanisms involved are competition of Mg with Ca ions results in decrease in contractility of bronchial smooth muscle function, increase in mast cells stability and immune function. Low magnesium level also causes neuromuscular irritability which results in bronchial spasms. The individuals with low dietary magnesium intake were prone to wheezes and hypersensitivity of bronchi as compared to normal intake subjects^{22,23,24}

In conclusion hypomagnesaemia was a significant finding in subjects with asthma either it is chronic stable asthma or it is in acute severe stage as compared to control. Serum Mg levels were significantly lower in asthmatic patients during exacerbations compared with stable asthmatics.

Conclusion

The above mentioned facts after the research concluded that Hypomagnesaemia has a major role in Asthma specially during acute stage of the disease. There is decrease in Mg level in Asthma when we compared level of Mg in asthmatics and normal subjects. It was further observed that there is decrease in Serum Mg levels in asthmatic subjects when comparison was done between stable and acute exacerbation of the disease. On the basis of these observations it is recommended that Mg level should be taken into account while treating asthma.

References

1. Hurley D, Binkley N, Camacho P, Diab D, Kennel K, Malabanan A et al. The Use of Vitamins And Minerals In Skeletal Health: American Association Of Clinical Endocrinologists And The American College Of Endocrinology Position Statement. *Endocrine Practice*. 2018; 24(10):915-924.
2. Betz J, Blackman M, Coates P, Cragg G, Levine M,

- Moss J et al. Encyclopedia of Dietary Supplements. 2nd ed. CRC press; 2010.
3. Ross A. Modern nutrition in health and disease. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2014.
 4. John W. Erdman, MacDonald, Ian A and Zeisel, Steven H. Present Knowledge in Nutrition. 10th ed. Chicester John Wiley & Sons; 2012.
 5. Workinger J, Doyle R, Bortz J. Challenges in the Diagnosis of Magnesium Status. *Nutrients*. 2018; 10(9):1202.
 6. Bruno A, Uasuf C, Insalaco G, Barazzoni R, Ballacchino A, Gjemarkaj M et al. Nutritional status and physical inactivity in moderated asthmatics. *Medicine*. 2016; 95(31):e4485.
 7. Gohil PR, Parmar M, Korvadiya A, Patel P, Patel JN. A Study of Serum Sodium, Potassium, Chloride Abnormalities In Chronic Stable Asthmatic Patients. *PIJR*. 2019; 8(7).
 8. Hamdan AJ, Wali S, Salem G, Al-Hameed F, Almotair A, Zeitouni M, Aref H, Nadama R, Algethami MM, Al Ghamdy A, Dihan T. Asthma control and predictive factors among adults in Saudi Arabia: Results from the Epidemiological Study on the Management of Asthma in Asthmatic Middle East Adult Population study. *Ann. Thorac. Med*. 2019; 14(2):148.
 9. Altinisik HB, Kirdemir P, Altinisik U, Gokalp O. Effects of magnesium sulfate on airway smooth muscle contraction in rats. *Medicinski Glasnik*. 2016;13(2).
 10. Garcia-Larsen V, Del Giacco SR, Moreira A, Bonini M, Charles D, Reeves T, Carlsen KH, Haahtela T, Bonini S, Fonseca J, Agache I. Asthma and dietary intake: an overview of systematic reviews. *Allergy*. 2016;71(4):433-42.
 11. 14. Lehmann C. Saunders manual of clinical laboratory science. Philadelphia: W.B. Saunders Co.; 1998.
 12. Jordan B, Mitchell C, Anderson A, Farkas N, Batrla R. The clinical and health economic value of clinical laboratory diagnostics. *EJIFCC*. 2015 Jan;26(1):47.
 13. Ouf FM, Ahmed F, Ahmed H, Ahmed E, Mohammed A. Electrolyte Disturbances And Their Impact On Mechanically Ventilated Patients With Acute Exacerbation Of Chronic Obstructive Pulmonary Disease. *Al-Azhar Assiut Med J*. 2015;3:27-34.
 14. Goyal K, Ahir GC, Bansal SK. Evaluation Of Serum Electrolyte Concentration Disturbances Among Asthmatic Patients. *JAMDSR*. 2016;4(4):56.
 15. Rashid MH, Chowdhury MR, Faraji MA, Rahman S. Assessment of Serum Magnesium Level in Patients with Bronchial Asthma. *Journal of National Institute of Neurosciences Bangladesh*. 2019 Jul 12;5(1):38-41.
 16. Mohamed AM. Plasma Levels of Magnesium and Copper Among Sudanese Patients with Bronchial Asthma (in Khartoum State) (Doctoral dissertation, Sudan University of Science & Technology).
 17. Ali AA, Bakr RM, Yousif M, Foad RE. Assessment of serum magnesium level in patients with bronchial asthma. *Egypt J Chest Dis Tuberc*. 2015;64(3):535-9.
 18. Papakonstantinou E, Klagas I, Karakiulakis G, Tamm M, Roth M, Stolz D. Glucocorticoids and β 2-agonists regulate the pathologic metabolism of hyaluronic acid in COPD. *Pulmonary pharmacology & therapeutics*. 2018;48:104-10.
 19. Sorkness RL, Kienert C, O'Brien MJ, Fain SB, Jarjour NN. Compressive air trapping in asthma: effects of age, sex, and severity. *J Appl Physiol*. 2019 Mar 7;126(5):1265-71.
 20. Gohil PR, Parmar M, Korvadiya A, Patel P, Patel JN. A Study Of Serum Sodium, Potassium, Chloride Abnormalities In Chronic Stable Asthmatic Patients. *PIJR*. 2019 Aug 31;8(7).
 21. Kılıc H, Kanbay A, Karalezlı A, Babaoglu E, Hasanoglu HC, Erel O, Ates C. The relationship between hypomagnesemia and pulmonary function tests in patients with chronic asthma. *Med Prin Pract*. 2018;27(2):139-44.
 22. Motamed H, Verki MM, Pooladzade M, Majidi A. Efficacy Evaluation of Nebulized Magnesium, as an Additional Complementary Treatment, in Clinical and Peak Flow Metric Improvements of Acute Asthma Attack: A Randomized Double-Blinded Clinical Trial. *Jundishapur J Nat Pharm Prod* . 2017;12(4).
 23. Ash SY, Cardet JC, Kusa T, Camargo C, Israel E. Insulin Resistance Modifies the Association Between Obesity and Current Asthma in Adults. *J.Allergy Clin. Immunol*. 2016;137(2):AB10.
 24. Ceylan Ayada ÜT, Genç O, Şahin S, Bulut İ, Arık Ö, Acat M. Evaluation of Serum Levels of Renin Angiotensin System Components in Asthmatic Patients. *Correspondance*. 2015 Jun 19.
 25. Ayada C, Toru Ü, Genç O, Şahin S, Bulut İ, Arık Ö, Acat M. Evaluation of Serum Levels of Renin Angiotensin System Components in Asthmatic Patients. *EMJ*. 2015;37(3).
 26. 2. Ali A, Bakr R, Yousif M, Foad R. Assessment of serum magnesium level in patients with bronchial asthma. *Egypt J Chest Dis Tuberc* . 2015;64(3):535-539.