

## STUDY OF PREVALENCE OF HYPOMAGNESEMIA AND ITS IMPACT ON THE SEVERITY OF ACUTE ASTHMA

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**ABSTRACT: AIMS:** The purpose of the study is to determine the prevalence of Hypomagnesemia among patients presenting with acute exacerbation of asthma and during its standard treatment and to know its clinical significance. **SETTINGS AND DESIGN:** This is a prospective study done on inpatients admitted with acute exacerbation of asthma. **METHODS:** A total of 50 patients admitted with acute asthma were enrolled in the study with random selection. Treatment started according to GINA (Global Initiation of Asthma) protocol. Serum Magnesium levels were measured at intervals of 0 min, 90 minutes and 180 minutes and 24hrs after starting nebulization. **STATISTICAL ANALYSIS:** The Excel and SPSS 10.5 (SPSS Inc, Chicago) software packages were used for data entry and analysis. The student 'T' test was used to differentiate gender parameters Proportions were compared using Chi-square test. One-way analysis of variance was used to test the difference between groups. **RESULTS:** Hypomagnesemia at the time of admission (0 min) was found in 15(30%) subjects and it increased to 22(44%), 16(32%) and dropped to 7(14%) at 90min, 180min and 24 hours respectively after starting treatment. Maximum drop in magnesium level was noted at 90min (by 0.162 mg/dl). Severity of asthma was statistically and clinically significant with hypomagnesemia (P=0.04). **CONCLUSION:** As Hypomagnesemia was significantly associated with severe asthma attack, an effort should be made to check and correct serum magnesium level during admission and at least after 2 hours of nebulization.

**KEY WORDS:** Acute asthma, GINA,  $\beta_2$ -agonists, Hypomagnesemia.

**INTRODUCTION:** Magnesium is the fourth most abundant ion in the body and second most abundant intracellular cation. Total magnesium content is 24 gram (1000 mmol), maximum in bone and soft tissue. Total plasma concentration is 1.8-2.4mg/dl. Cellular shift and urinary excretion balance magnesium. Magnesium serves as a cofactor for more than 3000 enzyme reactions that involve adenosine triphosphate.<sup>1</sup> Magnesium also regulates the movement of calcium into smooth muscle cells, which is involved in the maintenance of cardiac contractile strength and peripheral vascular tone.

Hypomagnesemia is defined as concentration of serum magnesium <1.8mg/dl. Hypomagnesaemia is the most common electrolyte disturbances in chronic and hospitalized patients, which is usually concomitant with other electrolyte disturbances.

Hypomagnesemia was found to be a common disorder in patients with chronic asthma.<sup>2</sup> Patients with low magnesium was found to have more severe asthma and higher incidence of asthma exacerbations and hospitalization.<sup>3</sup> Few earlier reports showed an association between magnesium deficiency and increased airway hyperreactivity, pulmonary vascular resistance, and ventricular arrhythmia.<sup>4,5</sup> Treatment with  $\beta_2$ -agonists can reduce serum magnesium levels through urinary loss or intracellular shift.<sup>6</sup> Low dietary magnesium was also found to be associated with

# ORIGINAL ARTICLE

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wheezes and impairment of lung function in normal subjects,<sup>7</sup> while magnesium supplementation can reduce asthma symptoms.<sup>8</sup> In recent studies, the cause of hypomagnesemia in patients with acute asthma has been related to the use of  $\beta$ 2-agonists either orally<sup>9</sup> or IV,<sup>10</sup> or by nebulization.

The mortality rate in patients with asthma is still rising and has been partly attributed to adverse effects of  $\beta$ 2-agonists during acute asthma management.<sup>11</sup> In 1970s increased incidence of deaths in asthma were noted due to non-selective  $\beta$ -agonists (Isoproterenol) and Fenosterol.<sup>12</sup> There is limited data on prevalence and clinical significance of hypomagnesemia in acute asthma. Hence present study was carried out to determine the prevalence of hypomagnesemia during acute exacerbation and after standard treatment.

**MATERIALS AND METHODS:** This prospective study was carried out on randomly selected patients who were admitted to hospital with acute exacerbation of asthma from March 2007 to August 2008. A total of 50 subjects were selected randomly after they met all inclusion and exclusion criteria. Inclusion criteria: Patient admitting with acute exacerbation of mild, moderate, severe degree according to GINA, Patients of both sexes aged  $\geq 18$  years and Patients who were treated with  $\beta$ -2-agonists, anticholinergic drugs and Intra-venous steroids were taken for study. Exclusion criteria: Patients with life threatening asthma according to GINA, Patients treated with IV Aminophylline, Diuretics, Penicillin, Laxatives, Enema, Aminoglycosides, digitalis, heparin, Blood transfusion and Total Parenteral nutrition, Patients with diabetes mellitus, patients with ABG showing metabolic and respiratory alkalosis, and Patients with sepsis and starvation. Ethical clearance was obtained from the institutional ethical committee. Informed consent was obtained from each subject. The study was conducted in compliance with ICH-GCP guidelines.

Salbutamol nebulization was given at admission (0 min) and repeated at every 30 min intervals for first 2 hrs and then every fourth hourly up to 24 hrs and then repeated according to need. IV steroids were administered according to GINA protocol. Unresponsive patients were given nebulize Anticholinergics. Serum magnesium levels were measured at the time of admission (0 min), 90 minutes, 180 minutes and 24 hrs after starting nebulization. Other lab investigations done were: CBC, ESR, Creatinine, ECG, Chest X-ray (PA-view), PEF using peak flow meter at the time of admission and after one hour and Pulmonary function test once patient stabilizes.

The Excel and SPSS 10.5 (SPSS Inc, Chicago) software packages were used for data entry and analysis. The results were averaged (mean + standard deviation) for each parameter for continuous data and numbers and percentage for categorical data are presented in Table and Figure. The student 'T' test was used to determine whether there was a statistical difference between male and female subjects in the parameters measured. Proportions were compared using Chi-square test. One-way analysis of variance was used to test the difference between groups.

In all the above tests a "p" value of less than 0.05 was accepted as indicating statistical significance.

**RESULTS:** In the present study overall mean age was  $54 \pm 18$  years. Mean age of onset was  $28 \pm 16$  yrs. Out of 50 cases 29 (58%) were females, with female to male ratio of 3:1. Among males 13 out of 21 were below 40 yrs and among females 23 out of 29 were above 40 yrs. Female were affected more at older age and male at relatively younger age (Fig I). However severity of exacerbations were not statistically significant with respect to age (p value=0.182) and gender (p value=0.760).

## **Changes in Magnesium levels at various intervals with nebulization:**

Mean concentrations of Magnesium are plotted on figure-II. Mean magnesium concentration was 1.970 mg/dl at 0 min which was dropped by 0.162(1.808) mg/dl at 90 min, 0.064(1.906) mg/dl at 180 min and increased to 2.052 mg/dl after 24 hours of starting nebulization.

As shown in Table 1 Hypomagnesemia (<1.8mg/dl) was found in 15(30%) of patients, and it increased to 22(44%), 16(32%) and 7(14%) at 90min and 180min and 24 hours respectively. Table 2 shows changes in magnesium levels at various intervals with nebulization. Mean magnesium concentration was 1.970 mg/dl at 0 min. Maximum drop in magnesium level was noted at 90min (by 0.162 mg/dl). It dropped by 0.064 at 180 min and increased to 2.052 mg/dl at 24 hours. In 2 cases of severe hypomagnesaemia recovery delayed, first patient discharged after 6 days, second patient was ventilated and recovered with magnesium correction and discharged on 10<sup>th</sup> day.

## **Multiple logistic regression analysis showed significant association of severity of asthma with hypomagnesaemia (p=0.04).**

Mean duration of hospital stay was 4 days; maximum number [24(48%)] of patients were discharged on 3<sup>rd</sup> day and by 4<sup>th</sup> day 43(86%) patients were discharged. Number of days of hospital stay was statistically significant with respect to severity (p value=0.001) as shown in Table-3.

**DISCUSSION:** Hypomagnesaemia is usually associated with other electrolyte disturbances. Hypokalemia that accompanies Magnesium depletion is refractory to potassium replacement therapy and should be treated with Magnesium replacement therapy even before treating hypokalemia. Magnesium is an intracellular ion. Serum Mg ++ levels correlate poorly with the total body store and serum Mg ++ may appear normal in spite of depletion of body store. The estimation of Mg ++ level in RBC, WBC, or muscle cell will be more representative of the body store but it is expensive. Hence we have measured only serum Mg ++ level in our study.

International guideline recommends the use of intravenous magnesium sulfate in the treatment of acute severe asthma, especially if FEV<sub>1</sub> is between 25-30% of predicted at presentation, or if there is poor response with Beta-2 agonists.<sup>13</sup> The possible mechanisms of action of magnesium on airways include inhibition of vascular and bronchial smooth muscle contraction, inhibition of acetylcholine release from cholinergic nerves, promotion of nitric oxide and prostacyclin generation, and stabilization of smooth muscle.<sup>14,15</sup>

Several studies<sup>16, 2</sup> have proved beyond doubt that hypomagnesemia in asthma is associated with increased incidence of wheeze, impairment of lung function, and more significantly increased bronchial hyper-reactivity (BHR). These findings are similar to our study which has shown high prevalence of hypomagnesemia and the significant association of hypomagnesemia with severe asthma (P<0.04).

Two patients out of 50 showed clinical manifestations of hypomagnesemia. Multiple logistic regression analysis showed that severe asthma was associated significantly with hypomagnesaemia (p value=0.04). Present study is consistent with study done by Bodenhamer et al.<sup>17</sup>

Therefore, in patients with acute exacerbation of asthma, care should be taken during management to avoid the adverse effects of bronchodilator therapy. If there is Hypomagnesemia during admission the use of such treatment may further decrease the existing magnesium levels. Consequently, this may pose potential cardiac and respiratory hazards in the form of myocardial

# ORIGINAL ARTICLE

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depression, ventricular arrhythmia, and respiratory muscle fatigue, which finally may increase the incidence of fatal asthma.

**CONCLUSION:** Hypomagnesaemia showed clinically and statistically significant association with severe asthma attack. Checking Magnesium level during admission and after 2 hours of nebulization is needed. However, further studies are needed to confirm our findings and to clarify these speculations using large number of patients, and measurement of Mg ++ level in RBC, WBC, or muscle cell in addition to serum Mg ++ would give better insight.

## REFERENCES:

1. Marino PL, Krasner J, O 'Moore P. Fluid and electrolyte expert. Philadelphia: WB Saunders, 1987.
2. Alamoudi OSB. Electrolyte disturbances in patients with chronic stable asthma: effect of therapy, Chest; August 2001; 120(2):431-436.
3. Alamoudi OSB. Hypomagnesemia in chronic stable asthmatics: prevalence, correlation with severity and hospitalization. European Respiratory Journal; 2000: 16,427-431.
4. Rolla G, Bucca C. Hypomagnesemia and bronchial hyper-reactivity: a case report. Allergy; 1989: 44,519-521.
5. Iseri LT, Freed, J, Bures AR. Magnesium deficiency and cardiac disorders: American Journal of Medicine; 1975:85,837-844.
6. Haffner CA, Kendall MJ. Metabolic effects of  $\beta_2$ -agonists Clinical Pharmacology and Therapeutics; 1992:17,155-164.
7. Britton J, Pavord I, Richards K, et al. Dietary magnesium, lung function, wheezing, and airway hyper-reactivity in a random adult population sample. Lancet; 1994:344,357-362.
8. Hill J, Micklewright A, Lewis, S, et al. Investigation of the effect of short term change in dietary magnesium intake in asthma. European Respiratory Journal; 1997: 10, 2225-2229.
9. Gustafson, T, Boman K, Rosenhall L, et al. skeletal muscle magnesium and potassium in asthmatics treated with oral  $\beta_2$ -agonists. European Respiratory Journal; 1996: 9,237-240.
10. Bos WJW, Postma DS, Doormaal JV. Magnesiuric and calciuric effects of terbutaline in man. Clinical Science; 1988:4,595- 597.
11. Benatar SR. Fatal asthma. New England Journal of Medicine. 1986; 314,423-429.
12. Crane J, Pearce N and Flatt A et al. Prescribed fenoterol and death from asthma in New Zealand, 1981-1983: case-control study. Lancet; 1989; 1: 917-922.
13. Bateman ED, Hurd SS, Barnes PJ, Bousquet J, Drazen JM, Fitz Gerald M, et al. Global strategy for asthma management and prevention. GINA executive summary. Eur Respir J 2008; 31:143-78.
14. Spivey WH, Skobeloff EM, Levin RM. Effect of Mg Chloride on rabbit bronchial smooth muscle. Ann Emerg Med 1990; 19:1107-12.
15. Bois P. Effect of Magnesium deficiency on mast cells and urinary histamine in rats. Br J Exp Pathol 1963; 44:151-5.
16. Tan KL, Rauff S and Cheng SF et al. electrolyte disturbances in acute asthma; Chest meeting, October, 2004.

## ORIGINAL ARTICLE

17. Bodenhamer J, Bergstrom R, Brown D, ET al. frequently nebulised  $\beta$ -agonists for asthma: effects on serum electrolytes. *Annals of Emergency Medicine*; 1992: 21, 1337-1342.

Time interval	Proportion of hypomagnesemia
0-min	15(30%)
90-min	22(44%)
180-min	16(32%)
24-hours	7(14%)

**Table 1: Proportion of hypomagnesemia at various intervals**

	0 Hour	90 Minutes	180 Minutes	24 Hour
N	50	50	50	50
Mean	1.970	1.808	1.906	2.052
Std. Deviation	0.3598	0.3349	0.3644	0.2950
Minimum	1.2	1.0	1.0	1.4
Maximum	2.6	2.4	2.7	2.5

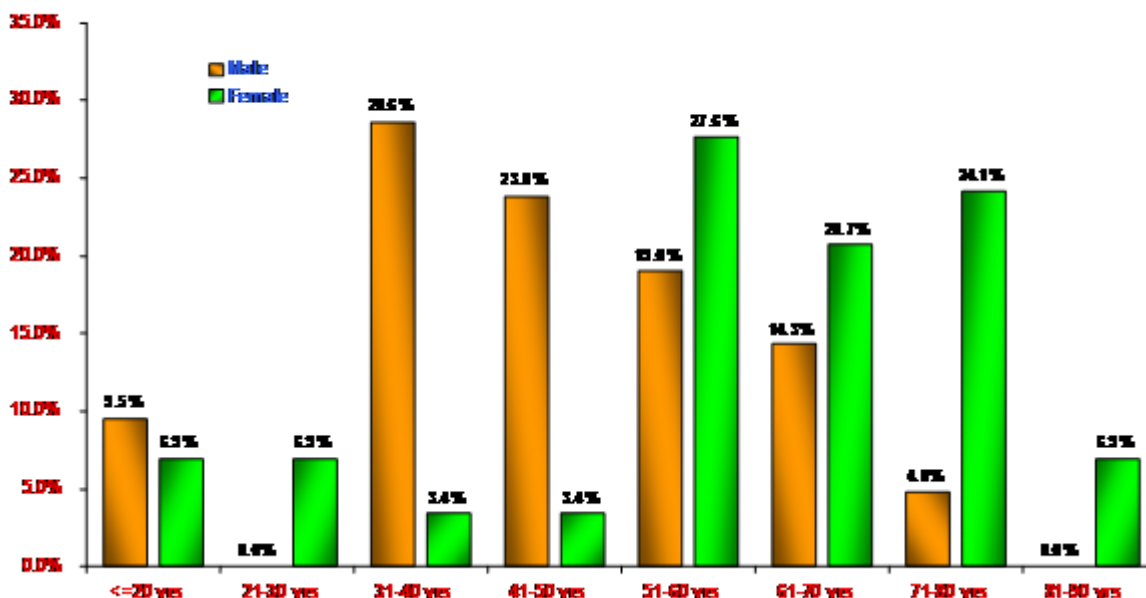
**Table 2: Changes in Magnesium levels at various intervals with nebulization**

Mean magnesium concentration was 1.970 mg/dl at 0 min which was dropped by 0.162 at 90 min, 0.064 at 180 min and increased to 2.052 mg/dl at 24 hours.

Severity	No. of cases	Mean Hospital Stay (Days)	Std. Deviation	Minimum	Maximum
Mild	14	2.71	.611	2	4
Moderate	28	3.29	.600	2	4
Severe	8	6.00	1.852	4	10

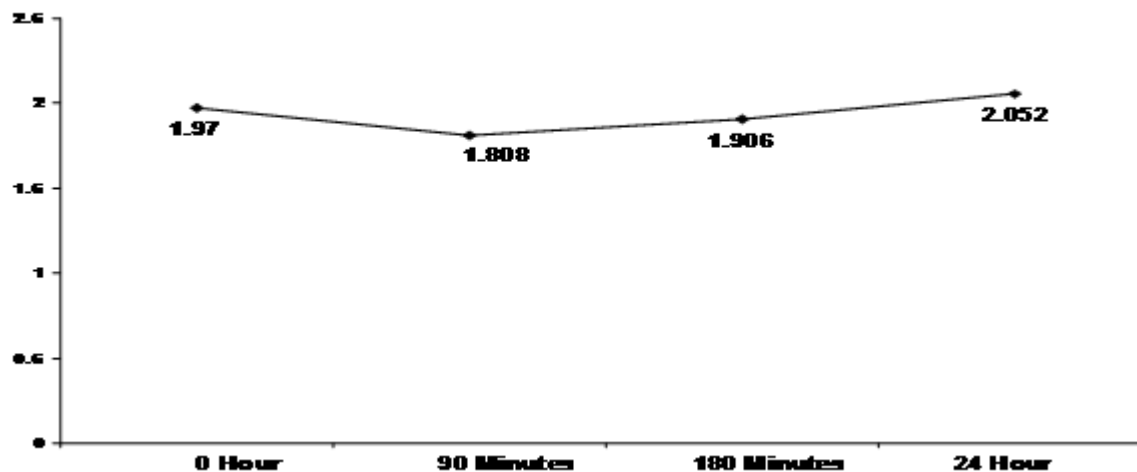
**Table 3: Comparison of Mean Hospital Stay according to Severity\***

\*'P' value <0.001



**Fig I: Age and gender distribution of study population**

**FIGURE LEGEND:** In the present study out of 50 cases 29 (58%) were females, with female to male ratio of 3:1. Among the males studied 13 out of 21 were below 40 yrs and among females 23 out of 29 were above 40 yrs.



**Fig II Mean Magnesium Concentration after Nebulization**

**FIGURE LEGEND:** Mean magnesium concentration was 1.970 mg/dl at 0 min which was dropped by 0.162(1.808) mg/dl at 90 min, 0.064(1.906) mg/dl at 180 min and increased to 2.052 mg/dl after 24 hours of starting nebulization.

# ORIGINAL ARTICLE

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