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STUDY OF SERUM MAGNESIUM LEVELS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Objective: The aim of this study is to assess the serum magnesium levels in chronic obstructive pulmonary disease (COPD) patients during stable and exacerbating clinical conditions. **Patients and Methods:** Case- Control Study conducted for the period one year(April 2019-April2020) at Tishreen University Hospital in Lattakia-Syria. 160 patients(109 male, 51 female) diagnosed as COPD, divided into group I(50): stable COPD and group II (110):exacerbated COPD. Group III consists of 60 healthy smoker persons(51 male, 9 female) as a control group. **Results:** Mean serum magnesium level for exacerbated COPD(1.73±0.1 mEq/L) was significantly lower than in stable COPD patients group(2.02±0.1 mEq/L) and control group(2.23±0.1 mEq/L). Pearson's correlation analysis revealed significant positive correlation between serum magnesium level and FEV1 (r =0.69, P=0.0001) and FEV1/FVC(r: 0.52, p:0.0001). In addition to, magnesium level showed negative correlation with number of exacerbations in year(r: -0.79, P=0.0001) and cigarette pack per year(r:-0.67, p:0.0001). **Conclusion:** Serum magnesium levels might be as a useful biomarker in assessing severity of COPD, in which frequency of acute exacerbations correlate with severity of hypomagnesemia.

KEYWORDS: Chronic obstructive pulmonary disease (COPD), acute exacerbation, serum magnesium.

INTRODUCTION

Chronic obstructive pulmonary disease(COPD) is a common preventable and treatable disease, characterized by persistent airflow limitation.[1] It is the third leading cause of death, and patients have a two-to three fold higher risk developing cardiovascular diseases.[2] The exact prevalence of COPD worldwide is largely unknown, but estimates have varied from 7-19%.[3]

The most important cause of COPD is exposure to tobacco smoke, as well as smoke from other sources and air pollution.[4] Patients with COPD present with a range of respiratory symptoms. The most common symptoms include dyspnea, cough and/or sputum production.[5]

Diagnosis of COPD is frequently made at a late stage, as many patients ignore early symptoms of cough and exertional dyspnea. Establishing a correct diagnosis of COPD is crucial because appropriate management can decrease frequency and severity of exacerbations, and prolong survival.[6]

Risk factors for COPD exacerbations include low forced expiratory volume in 1s(FEV1), current smoking, bacterial and viral infections, bronchiectasis, and history of previous exacerbations.[7] Most patients with exacerbation of COPD have comorbidities such as low serum magnesium.

Magnesium is the second most common intracellular cation in the body, found principally in bone, muscle and soft tissues. Less than 1% is present in the blood.[8] Magnesium has several actions on bronchial airway including relaxation of airway smooth muscle, bronchodilation, anticholinergic effects, and stabilization of mast cells. Many clinical trials had shown that hypomagnesemia is associated with diminished respiratory muscle power.[9] Therefore, the objectives of the study were to: 1- determine whether serum magnesium levels in COPD patients during acute

exacerbation differ from those of a stable COPD and control group, 2- evaluate the correlation of serum magnesium with lung function and frequency of exacerbations.

Patients and Methods This is Case-Control Study of a group of COPD patients who attending Department of Pulmonology at Tishreen University Hospital in Lattakia-Syria during a one year period (April 2019-April 2020). Patients that presented with the diagnosis of stable COPD were assigned to Group I and patients who presented with COPD exacerbation were assigned to Group II. Diagnosis of COPD and severity of disease were identified based on clinical manifestations and spirometry. Control group (Group III) included healthy smoker persons. The exclusion criteria were: diabetes mellitus (DM), pregnancy, chronic renal failure, gastrointestinal diseases that cause hypomagnesemia such as: Crohn's disease, ulcerative colitis, patient receiving Mg- Ca- vit D containing drugs, and diuretic therapy. The following data were recorded: demographic data (age, sex), number of exacerbations, and cigarette pack per year. Serum magnesium levels were determined by Auto chemistry analyzer, and FEV1, FEV1/FVC values were evaluated by Spirolab III. **Ethical consideration:** All patients were provided a complete and clear informed consent after discussion about this study. This study was performed in accordance with the Declaration of Helsinki.

DefinitionsNormal range of serum magnesium: 1.64-2.52 mEq/L[10] Modified global initiative for chronic lung disease(GOLD) criteria:

Mild COPD (GOLD I, FEV1 ≤ 80%), moderate COPD(GOLD II, 50% ≥ FEV1<80%), Severe COPD (GOLD III,30% ≥ FEV1<50%), very severe COPD (GOLD IV,FEV1<30%).[11]

Statistical Analysis Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations (SD),median ,Frequency and percentages. Independent t student test was used to compare 2 independent groups. One way Anova to compare between the three groups. Pearson's correlation coefficient was used to measure the association between quantitative variables. P value <0.05 was considered as statistically significant.

RESULTS

As shown in Table(1) males constitute 72 % of the stable group, 66.4% of exacerbation group and 85 % of the control group with no statistically significant difference between groups regarding sex. There were no significant differences between groups regarding age(p:0.09).

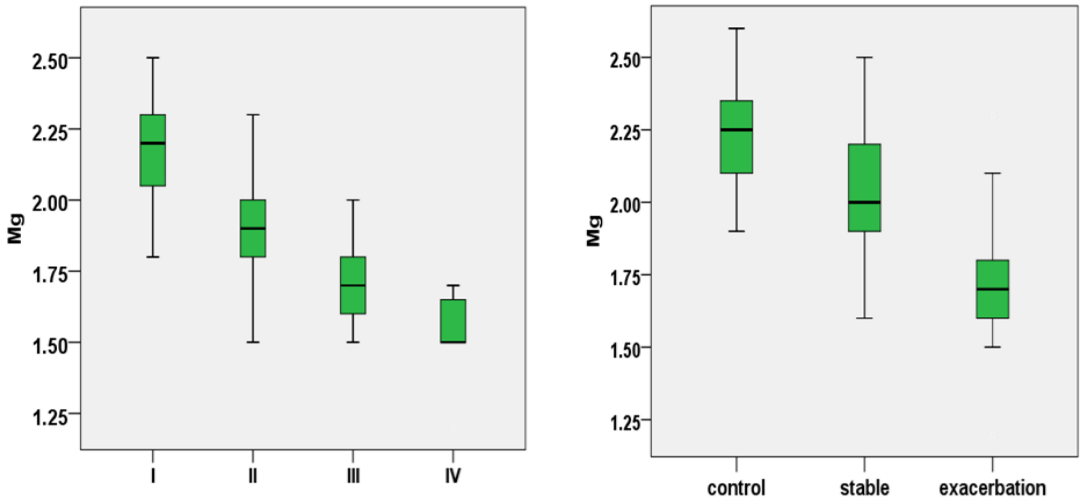
FEV1 values were significantly lower in exacerbation group (50.4±15.6) compared to stable group (62.7±15.5) and control group(91.06±3.7), p:0.0001.

FEV1/FVC ratio was statistically lower in exacerbation group (64.9±4.7) compared to stable patients (69.2±6.6) and control group (92.2±4.06), p:0.0001.

COPD staging was performed on the basis of these results. It was noted that most of the patients were at stage II(41.88%)and stage III(38.12%). Other patients were in stage I(12.5%) and stage IV(7.5%). The mean number of exacerbations in year was 1.02±0.9 in stable group compared to 3.46±1.1 in exacerbation group,p:0.001. The mean values of serum Mg^{+2} were in decreasing with increasing the degree of COPD as follow:2.15±0.1, 1.87±0.1, 1.71±0.1, and 1.51±0.1 in the Grade I, II, III, and IV respectively,p:0.0001.Serum Mg^{+2} levels were significantly lower in exacerbation group(1.73±0.1),compared to stable patients(2.02±0.1) and control(2.23±0.1),p:0.0001, Figure1.

Table 1: Demographic characteristics of the study population with COPD.

Variable	Group IStable group (50)	Group IIExacerbation group(110)	Group III Control(60)	p-value
Age(years)	53.5±9.3	58.6±10.6	47.1±6.1	0.09
Sex Male Female	 36(72%) 14(28%)	 73(66.4%) 37(33.6%)	 51(85%) 9(15%)	0.06
FEV1(L)	62.7±15.5	50.4±15.6	91.06±3.7	0.0001
FEV1/FVC	69.2±6.6	64.9±4.7	92.2±4.06	0.0001
Exacerbation(n/year)	1.02±0.9	3.46±1.1		0.0001
Serum magnesium(Mg^{+2})mEq/L	2.02±0.1	1.73±0.1	2.23±0.1	0.0001



(a) **(b)**

Figure (1): Mean values of serum Mg^{+2} according to the (a) classification of COPD, (b) comparisonbetween stable, exacerbation, and control groups

Serum Mg^{+2} showed positive correlation with FEV1 (r = 0.69, p:0.0001), in which reduction in serumMg^{+2} levels was correlated with decreased in FEV1.

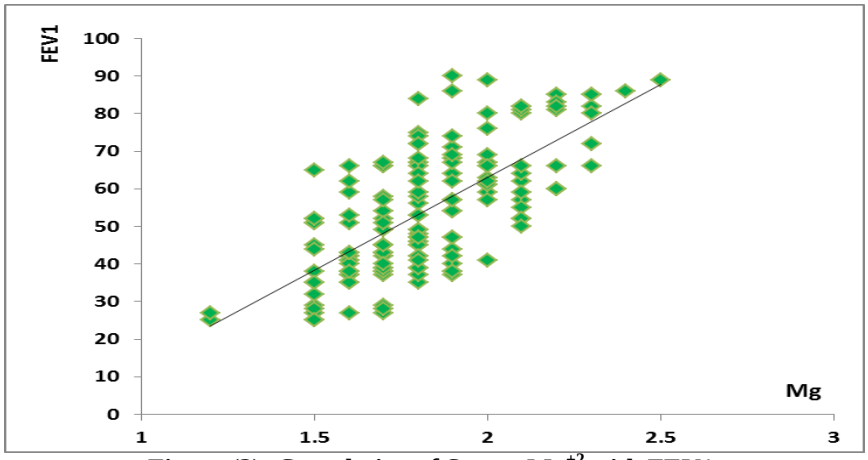


Figure (2): Correlation of Serum Mg^{+2} with FEV1.

Serum Mg^{+2} also showed positive correlation with FEV1/FVC(r = 0.52, p:0.0001), in which reduction in serum Mg^{+2} levels was correlated with decreased in FEV1/FVC.

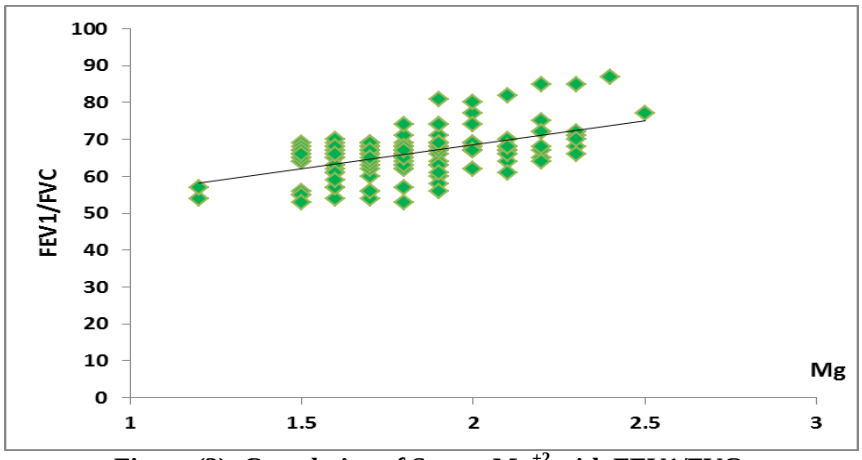


Figure (3): Correlation of Serum Mg^{+2} with FEV1/FVC.

Serum Mg^{+2} showed negative correlation with number of exacerbations in year (r = -0.79, p:0.0001), in which reduction in serum Mg^{+2} levels was correlated with increasing number of exacerbations in year.

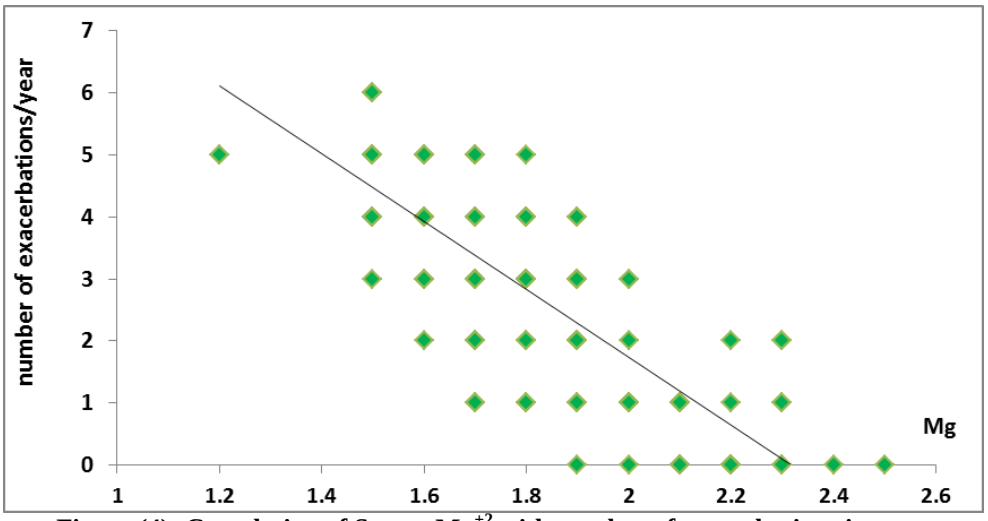
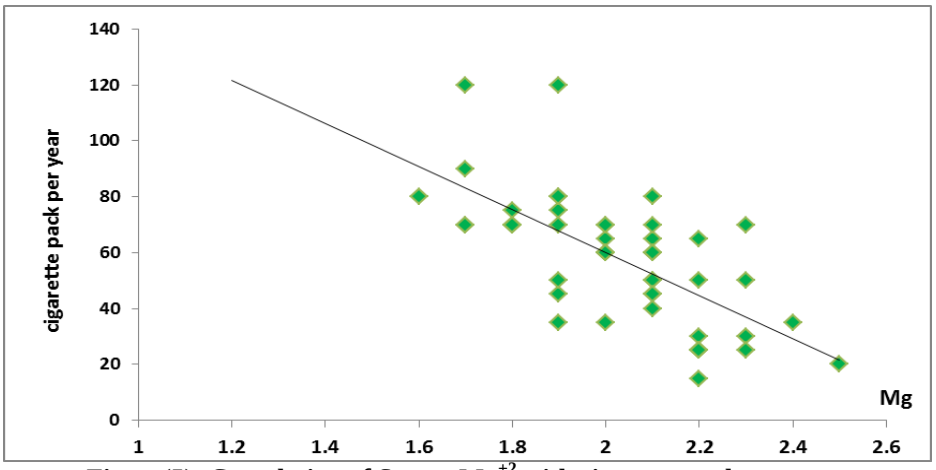


Figure (4): Correlation of Serum Mg^{+2} with number of exacerbations in year.

Serum Mg^{+2} also showed negative correlation with cigarette pack per year (r = -0.67 p:0.0001), in which increasing in cigarette pack per year was correlated with reduction in serum Mg^{+2} levels.



Figure(5): Correlation of Serum Mg^{+2} with cigarette pack per year.

DISCUSSION

The current study showed a significant reduction in FEV1and FEV1/FVC ratio in patients with an exacerbation of COPD than in stable and control group. Most patients were classified into the subgroup II,III. This reduction is due to severe obstruction of air escaping from the lungs during the exacerbation. The results were in agreement with Sanowara *et al*(2018).[12] who found that FEV1 and FVC values were lower in exacerbated status than stable;(25.5% vs. 42.8%,p:0.1), (43.43±19.92 vs. 46.95±16.74,p:0.5) respectively. Aziz *et al*(2014).[13] also found that most patients were in the stage II, III (75%).

Our study demonstrated that serum Mg+2 levels were significantly decreased in patients with exacerbation of COPD than in stable patients and control group. This result was in agreement with studies done by Hany *et al*(2005).[14] Sanowara *et al*(2018),[12] and Kumar *et al*(2017).[15]

Hany *et al*(2005) found that serum Mg+2 level in patients with exacerbation was lower than stable patients(0.77±0.10 vs. 0.91±0.10, p:0.0001).

Sanowara *et al*(2018) also showed that serum Mg+2 levels were lower in exacerbated status(1.6±0.26) vs. stable patients(2.09±0.11),p:0.0001 Kumar *et al*(2017) demonstrated that mean serum Mg+2 value in the stable group was 2.33 mg/dL vs.1.69 mg/dL in acute exacerbation.

In addition to, reduction in serum Mg+2 levels was correlated with decreased in FEV1/FVC, FVC, and increased number of exacerbation in year with statistical significance. Increased packs of cigarettes per year was correlated with reduction in serum Mg+2 levels. The

exact mechanism responsible for biochemical and physiologic processes of magnesium in pulmonary structure and function is not fully understood, and there are many supposed mechanisms for the effects of hypomagnesemia in patients with COPD. Magnesium deficiency causes increased airway hyperreactivity, alteration in airway smooth muscle function, immune function and oxidative stress.[16] This result was in agreement with the studies done by Bency *et al*(2017).[17] and Aziz *et al*(2014). Bency *et al*(2017) demonstrated a positive correlation between serum Mg+2 levels and FEV1(r:0.43,p:0.0001) and FVC(r:0.32,p:0.01). Aziz *et al*(2014) found that serum magnesium level correlated with frequency exacerbation. In summary, serum Mg+2 levels have a direct correlation with the clinical status of COPD patients (stable, exacerbation). Maintaining serum Mg+2 levels in normal range might reduce exacerbations which is the major objective in treatment COPD.

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