A Study of Serum Magnesium Levels in Acute Exacerbation of Chronic Pulmonary Disease on Admission and at the Time of Discharge

Authors
Dr Tamizh Selvan.R¹, Prof. Dr Ramakrishna Rao. M², Prof. Dr Periyasamy S³
¹Postgraduate, Department of General Medicine, Rajah Muthiah Medical College and Hospital, Chidambaram, India, 608002
²Professor, Department of General Medicine, Rajah Muthiah Medical College and Hospital, Chidambaram, India, 608002
³Professor, Department of General Medicine, Rajah Muthiah Medical College and Hospital, Chidambaram, India, 608002
*Corresponding Author
Dr Ramakrishna Rao M
Professor, Department of General Medicine, Rajah Muthiah Medical College and Hospital, Chidambaram, India, 608002

Abstract
Background: COPD is one of the most common disease affecting the elderly population in the world. The course of the disease is characterized by frequent exacerbations. Many factors play role in exacerbation of COPD. One such factors is serum magnesium in the body. The objective of the study is to ascertain the correlation between serum magnesium levels during acute exacerbation of COPD.

Aim and Objective: Estimating serum magnesium levels in acute exacerbation of COPD. To correlate the relation of magnesium levels in patients of acute exacerbation of COPD at the time of admission and at the time of discharge.

Material and Methods: This study was done among 100 patients presented with acute exacerbation of COPD in emergency department of Rajah Muthiah Medical College and Hospital from November 2018 to June 2020. Patients detailed history, clinical examination and necessary investigation were done for the patients. Patients admitted with AECOPD above 40 years was included in the study, and patients with conditions causing hyper or hypomagnesemia were excluded.

Statistical Methods: The data was analyzed using SPSS version 23.0 and Microsoft excel 2019.

Results: Mean serum magnesium level at the time of admission was 1.287 mg/dl (SD±0.33) and the time of discharge was 2.009 mg/dl (SD± 0.2955). The association of serum magnesium level and acute exacerbation of COPD was found to be statistically significant with p value less than .05.

Conclusion: Patients presented with acute exacerbation of COPD had hypomagnesemia. So magnesium was modifiable and independent risk factor for COPD exacerbation.

Keywords: COPD, acute exacerbation, serum magnesium, asthma, Anthonisens criteria.

Introduction
The most common causes of airflow obstruction in adults are asthma and COPD. Bronchial asthma is defined as a clinical syndrome of unknown etiology which has recurrent episodes of airflow obstruction that may resolve spontaneously or by treatment. Bronchial asthma is differentiated from COPD by improvement in more than 25% FEV1 by giving bronchodilator therapy. COPD is a common term used for many conditions which
results in fixed airway disease and breathlessness on exertion. COPD is defined as disease which is characterized by persistent respiratory symptoms and airflow limitations not fully reversible and generally will progressive in nature\(^1\). COPD includes emphysema, chronic bronchitis and small airway disease. The disease is increasing every year mainly due to lifestyle changes, smoking and air pollution due to increased urbanization. In developing countries like India usage of biomass for cooking leads to increase in COPD among people's who never smoke.

COPD results in abnormal inflammatory response to noxious agents and gas. It has many modifiable as well as non-modifiable risk factors. Our aim is to identify factors which are modifiable and thereby reducing the exacerbation of the disease. Since COPD is emerging as major cause of morbidity and mortality in both developing as well as developed countries and it has become a major health concern.

Magnesium has important functions in airway smooth muscle relaxation, bronchodilation and it stabilizes mast cells and mucociliary clearance. So decrease in magnesium is associated with increased airway response and causes decrease in muscle strength. Evidences suggests magnesium deficiency leads to exacerbation of bronchial asthma and magnesium is used in reliving bronchospasm in asthmatic patients\(^2\),\(^\text{[2-4]}\).

Sajjad Rajab et al studied the relationship between acute exacerbation of COPD and serum magnesium levels. They concluded that the patients with acute exacerbation of COPD had hypomagnesemia and had increased hospital stay.\(^5\)

Navomi- obradovic I et al - evaluated magnesium levels in serum and urine of patients presented with acute exacerbation of COPD. They found out there's an increased loss of magnesium via urine may be due to urine loss.\(^6\)

**Aim of the Study**

To study the correlation between serum magnesium levels in patients presented with acute exacerbation of COPD at the time of admission and at the time of discharge.

**Materials and Methodology**

This study was done in 100 patients who were old cases of COPD and presented with acute exacerbation from November 2018 to June 2020 in Department of General Medicine, Rajah Muthiah medical College and hospital, Annamalai University, Chidambaram, Tamil Nadu, as defined by Anthonisens criteria.\(^8\)-\(^15\)

The patients who had been diagnosed earlier as a case of COPD on clinical grounds and by spirometry in Rajah Muthiah Medical College Hospital, and those patients who presented to emergency department with acute exacerbation of COPD defined by change in patients baseline dyspnea, sputum production, sputum purulence and cough warranting change in treatment were included in this study.

Patients with other respiratory diseases, Diabetes mellitus, Hypertension, Ca lung, CKD, Congestive Heart failure, Coronary artery disease, CVA, patients on drugs like Antacids, Proton pump inhibitors, Diuretics, Digoxin, H2 blockers were excluded from this study.

Serum magnesium level was measured at the time of admission and at the time of discharge (i.e. when the patient symptoms have returned to near baseline). Modified MRC scale was used to define severity of dyspnoea.\(^22\)-\(^27\)

From all the selected patients, about 3ml of venous blood were collected and centrifuged. Then the supernatant serum was separated and used as the sample. Serum magnesium was measured using xylidyl blue technique. Chem -5 plus v2 auto analyser is used for measuring serum magnesium level. This is easy, rapid and accurate method for determining magnesium levels. The integrity of the reaction was monitored using sera with known concentration (2.0mg/dl). The normal range for serum magnesium levels is 1.7 to 2.4mg/dl.\(^28\)
Results

Sex Distribution

The study population includes 95 male and 5 female.

Table 1: Sex Distribution

<table>
<thead>
<tr>
<th>Sex distribution</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>95</td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
</tr>
</tbody>
</table>

![Figure 1: Sex distribution](image1.png)

Age Composition

The age group of the study ranged from 40-84 years. The mean age was 63.64 ± 9.8 years.

Table 2: Age Composition

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 50</td>
<td>12</td>
</tr>
<tr>
<td>51-55</td>
<td>15</td>
</tr>
<tr>
<td>56-60</td>
<td>15</td>
</tr>
<tr>
<td>61-70</td>
<td>30</td>
</tr>
<tr>
<td>More than 70 years</td>
<td>28</td>
</tr>
</tbody>
</table>

![Figure 2: Age group and number of patients](image2.png)
MMRC Dyspnoea Scale Grading
Patients were graded according to MMRC dyspnoea scale as grades 0 to 4

Table 3: MMRC dyspnoea scale grading

<table>
<thead>
<tr>
<th>MMRC Dyspnoea scale</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>4</td>
<td>12</td>
</tr>
</tbody>
</table>

Serum Magnesium Level at the Time of Admission
Table 4: Serum magnesium level and number of patients

<table>
<thead>
<tr>
<th>Serum magnesium level (mg/dl)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8-2.4</td>
<td>10</td>
</tr>
<tr>
<td>1.5-1.7</td>
<td>11</td>
</tr>
<tr>
<td>1-1.4</td>
<td>59</td>
</tr>
<tr>
<td>Less than 1</td>
<td>20</td>
</tr>
</tbody>
</table>
Serum Magnesium Levels at the Time of Discharge

**Table 5:** Serum magnesium levels at the time of discharge

<table>
<thead>
<tr>
<th>Serum magnesium level (mg/dl)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8-2.4</td>
<td>83</td>
</tr>
<tr>
<td>1.5-1.7</td>
<td>13</td>
</tr>
<tr>
<td>1.1-1.4</td>
<td>4</td>
</tr>
</tbody>
</table>

**Figure 5:** Serum magnesium level and number of patients at discharge

Serum magnesium level and mMRC Score:

**Table 6:** Serum magnesium level at the time of admission and mMRC score

<table>
<thead>
<tr>
<th>Sr. Magnesium level in mg/dl</th>
<th>mMRC Score n (%)</th>
<th>Total</th>
<th>Pearson Chi-Square</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1.7</td>
<td>1</td>
<td>20(22.2)</td>
<td>43(47.8)</td>
<td>22(24.4)</td>
</tr>
<tr>
<td>1.7 to 2.4</td>
<td>2</td>
<td>6(60)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>26(26.0)</td>
<td>43(43.0)</td>
<td>22(22.0)</td>
</tr>
</tbody>
</table>

Table 6 shows a significant association of serum magnesium level and severity of dyspnoea graded using mMRC score with a p value .000 (p<.05).

**Figure 6:** Serum magnesium level at the time of admission and mMRC score

Discussion

There have been few predictors for exacerbation of COPD and one such independent indicators is serum magnesium. Magnesium is the second most abundant cation in the intracellular fluid. It plays an important role in muscular tone and
excitability\(^{(13)}\). Hypomagnesemia is associated with increased airway response and decreased muscle strength\(^{(14,15)}\).

Serum magnesium also plays a vital role in bronchodilation, airway smooth muscle relaxation, mucociliary clearance\(^{(16-19)}\). Extracellular rise in magnesium level has shown to inhibit contractile tension of smooth muscle\(^{(12)}\). Nagorni -obradovic et al observed low levels of magnesium in patients with severe respiratory infections\(^{(20)}\). Alamoudi et al showed similar results in asthma patients\(^{(19)}\).

In the current study serum magnesium levels were measured at the time of admission and at the time of discharge and both values are compared. Aziz et al studied the levels of magnesium in COPD patients with acute exacerbations, and stable copd patients. He found out serum magnesium levels was 0.77±0.10mmol/L for AECOPD patients. Stable patients of COPD had magnesium on the range of 0.91±0.10 mmol/L. He found out patients with acute exacerbation of COPD had hypomagnesemia compared to stable COPD patients.

Sajjadrabaj et al studied\(^{(5)}\) serum magnesium levels in patients presented with acute exacerbation, at the time of discharge and after one month of discharge. They reported serum magnesium levels were reduced in AECOPD patients 1.88±0.67mg/dl, to that if stable COPD patients 2.30±0.36mg/dl. They observed reduced serum magnesium levels during AECOPD.

David Holmes et al, observed that the patients with low serum magnesium levels are at increased risk of exacerbation and hospital admission in compared with stable COPD patients with normal magnesium levels\(^{(21)}\).

**Conclusion**

In our study serum magnesium levels at the time of admission was 1.287mg/dl (SD±0.33) and at the time of discharge were 2.009mg/dl (SD±0.2955), which is less than probability of occurrence of (p value of <0.05). Hence the serum magnesium levels is statistically significant. Patients has hypomagnesemia at the time of admission and at the time of discharge most patients had normal magnesium levels. Hypomagnesemia is one of the modifiable risk factor. So by routine monitoring levels of magnesium in COPD patients, we shall reduce exacerbations.

**Limitations**
Sample size is less and it's not an interventional study. By doing interventional studies we shall prove the association and subsequent use of magnesium as a therapeutic agent.

**Conflicts of Interest**
All authors declare that we don't have actual or potential financial interest or conflict of interest.

**Ethical Consideration**
The study was conducted after approval from Institutional Ethical Committee of Rajah Muthiah Medical College Hospital, Chidambaram, Tamil Nadu.

**References**
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7. Douglas seaton, Anthony Seaton, Leitch-Crofton & Douglas’s Respiratory Diseases,
21. David Holmes et al., low magnesium levels a cause for concern among COPD patients. Respir Med 2008; 11-12