INTRODUCTION

Chronic obstructive airway disease (COPD), which is an important public health challenge, is the fourth leading cause of death in the world today. It is one of the leading causes of death worldwide and becomes an economic and social burden that is substantial and rising.1,2

According to the Disability Adjusted Life Year (DALY), COPD, which was once ranking twelfth in leading cause of DALY’s lost to the world, is estimated to become the seventh leading loss by the year 2030.3,4

Pathologically, COPD can be divided into:-

1. Emphysema, where there is destruction of the gas – exchanging surfaces of the lung (alveoli) causing irreversible enlargement of airspaces and loss of lung elasticity, and
2. Chronic Bronchitis, where there is the presence of cough and sputum production for at least three months in each of the two consecutive years.5

The Global Initiative for Obstructive Lung Disease (GOLD) emphasizes on the Spirometry, which is required to make the diagnosis of COPD in a clinical context, where the presence of a post bronchodilator FEV1 / FVC is less than 0.70.6 In addition to it, there are certain key indicators that GOLD lays down especially in a patient who is above forty years of age. It should be noted that these indicators are not diagnostic themselves, but the presence of such key indicators increases the probability of COPD.

These key indicators include,

(i) dyspnea that is characteristically worse with exercise and which is persistent.
(ii) Chronic cough that is intermittent and which may be non – productive is another indicator.
(iii) Chronic sputum production.
(iv) A history of exposure to risk factors like tobacco smoke (that includes popular local preparations also) or smoke from home cooking and heating fuels or occupational dusts and chemicals.
(v) And finally whether the patient has a family history of COPD.7

The present study was to assess serum magnesium, as a biomarker in patients with COPD, to focus on the characterization of the individuals based on the severity and appropriate management of the patients.

Magnesium, which is one of the major intracellular cation, is an important co-factor for various enzymes, transporters and nucleic acids that are essential for normal cellular function, replication and energy metabolism.8

Low magnesium levels is associated with increased airway hyperreactivity and decreased muscle strength. It also plays a role in airway smooth muscle relaxation and bronchodilation, stabilization of mast cells, neurohumoral mediator release, various immune responses, muscarinic actions and mucociliary clearance.9,10

OBJECTIVES

The different objectives in this study were:-

1. To study the level of serum magnesium in patients with stable COPD, COPD exacerbations and asymptomatic smokers.
2. To compare the levels of serum magnesium with severity of airway obstruction.

REVIEW OF LITERATURE

Chronic Obstructive Pulmonary Disease (COPD) has become an important public health challenge which is in the same time preventable and treatable. A major cause of chronic morbidity and mortality throughout the world, many people suffer from COPD for years and die prematurely from it or due to its complications.

Low magnesium levels is associated with increased airway obstruction and asymptomatic smokers. The different objectives in this study were:-

1. To study the level of serum magnesium in patients with stable COPD, COPD exacerbations and asymptomatic smokers.
2. To compare the levels of serum magnesium with severity of airway obstruction.

The Global Burden of Disease Study (GBDS) had projected that COPD, which ranked sixth as a cause of death in 1990, has come up with a new estimate that it will be the fourth leading cause of death by 2030.9

By far the strongest risk factors for airflow obstruction are smoking and exposure to environmental tobacco smoke10, but many areas of the world with high mortality rates from COPD still have low consumption of tobacco11. The distribution of death from COPD in the UK is not the same as that of lung cancer, the disease most strongly associated with tobacco consumption, but is more closely associated with low social status12 and poverty13. Burney et al demonstrated that there is a high prevalence of restriction associated with poverty which could explain the high COPD mortality in poor countries.14
Magnesium is the second most abundant intracellular cation and the fourth most abundant cation in the body. It plays an essential physiological role in a number of functions of the body.

This role is achieved through two important properties of magnesium:
(i) the ability to form chelates with important intracellular anionic-ligands, especially ATP, and
(ii) its ability to compete with calcium for binding sites on proteins and membranes.10

Hypermagnesemia may result from one or more of the following mechanisms: redistribution, reduced intake, reduced intestinal absorption, increased gastrointestinal loss and increased renal loss.11,12

The exact role of magnesium in respiratory homeostasis is not clear. Hypermagnesemia is associated with increased airway hyperactivity and decreased muscle strength.13-15 It also plays a role in relaxation of smooth muscles of airways and bronchodilation, stabilization of mast cells, neurohumoral mediator release, various immune responses, muscarinic actions and mucociliary clearance.11-14 The cause of lower serum magnesium remains unclear.

While therapies for COPD such as beta agonists, steroids, and diuretics can all theoretically lower serum magnesium levels studies have shown conflicting results.

Bhatt SP and colleagues, from a study conducted in St. Luke’s Hospital, USA, observed that serum magnesium is an independent predictor of frequent readmissions for acute exacerbations of COPD.6

Jeswani G et al, concluded from a study conducted in 150 COPD patients, that serum magnesium is an independent predictor of COPD exacerbations and there exists a negative correlation between hypomagnesemia and frequency and duration of hospitalization.10

In a study conducted by JP Singh, Sahil Kohli and colleagues, they observed that hypomagnesemia in patients presenting with COPD have advanced disease, prolonged hospital stay and need mechanical ventilation more often.15

Thus, serum magnesium may have a role in assessing the disease stability in COPD patients, but the relationship between serum magnesium and COPD disease flares outcome has not been thoroughly explored. Standard guidelines have not yet recommended the implication of serum magnesium on COPD.

MATERIALS AND METHODS
The study titled, “STUDY OF SERUM MAGNESIUM IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE” was carried out in the Department of Pulmonary Medicine, Sri Manakula Vinayagar Medical College and Hospital, Puducherry.

STUDY DESIGN: Cross Sectional Study.

SAMPLE SIZE AND DURATION OF STUDY: Considering a sensitivity of 70% and specificity of 86%, with alpha error of 0.05 (freecalc software), based on a previous study16, a sample size of 126 was obtained. The study was conducted for a period of 1 year starting from the date of getting approval from the Ethics Committee.

Serum magnesium determination
After getting an informed written consent from each patient enrolled in the study, 2 ml of their venous blood was collected between 9a.m and 4p.m of each day, and serum magnesium was assessed using AGAPPE CHEMCHEK™

This kit is intended for in vitro quantitative determination of magnesium in serum or plasma. It is based on the principle that magnesium will react with xylidyl Blue, one of its reagents to form a colored compound in alkaline solution, and the intensity of the color formed will be proportional to the magnesium in the sample.

SAMPLING:
INCLUSION CRITERIA: The patients who are presented to the Chest OPD and diagnosed by spirometry were considered for the present study. Patients who were having typical symptoms of chronic cough with or without expectoration with shortness of breath on exertion were included in the study after confirming the diagnosis by FEV1 /FVC < 70% and post bronchodilator FEV1 < 70% on spirometry as per the GOLD guideline.

GOLD SPIROMETRIC CRITERIA FOR COPD SEVERITY: In patients with FEV1/FVC < 0.70:

<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Mild COPD</td>
<td>FEV1 &gt; 80 % predicted. With or without presence of chronic symptoms (cough, sputum production).</td>
</tr>
<tr>
<td>II. Moderate COPD</td>
<td>50 % ≤ FEV1 &lt; 80 % predicted. With or without presence of chronic symptoms (cough, sputum production).</td>
</tr>
<tr>
<td>III. Severe COPD</td>
<td>30 % ≤ FEV1 &lt; 50 % predicted. With or without presence of chronic symptoms (cough, sputum production).</td>
</tr>
<tr>
<td>IV. Very severe COPD</td>
<td>FEV1 &lt; 30 % predicted.</td>
</tr>
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EXCLUSION CRITERIA:
1) COPD patients with coexisting Tuberculosis.
2) Renal failure patients.
3) Heart failure patients.
4) Liver disease patients.
5) Patients who are diagnosed with any malignancy.

The subjects who satisfies the above mentioned criteria, a thorough analysis on their TLC, DLC were done to rule out any co-existing infections. Serum Urea and Creatinine levels were assessed to rule out any co-existing kidney diseases. Liver function tests were carried out to rule out liver diseases as serum magnesium is seen to be elevated in those conditions. A chest X – ray was done to further support the evidence of COPD. Sputum AFB and Grams stain was done to rule out any active Tuberculosis and other Lung infections. Finally a spirometry was performed to record and give the confirmation of COPD. Serum magnesium level was assessed finally in those subjects who satisfied the above tests.

STATISTICAL ANALYSIS:
The data was entered and analysed with epi info software version 3.4.3. Proportions were calculated and ANOVO was used to compare magnesium levels among stable COPD, COPD exacerbation and healthy asymptomatic smokers. For the statistical analysis p<0.001 was considered significant.

RESULTS:
In the present study that was conducted, of 126 subjects, all were males.

Majority of the patients were between 61 and 70 years of age (33.3%, n=42).

Figure 1. Age population in the study
Of the 126 study subjects, 33.3% (n=42) of people were stable COPD patients, 34.9% (n=44) were COPD exacerbation patients and the rest 31.7% (n=40) were asymptomatic people who smoked.

Among the 44 subjects who presented with exacerbation of COPD, 26 patients (59.1%) had their serum magnesium levels between 1.5 and 2 mg/dl.

66.7% (n=28) of the 42 stable COPD patients too had their magnesium levels ranging between 1.5 and 2 mg/dl.

Whereas 77.5% (n=31) subjects of the 40 healthy asymptomatic smokers had their serum magnesium levels between 2 to 2.5 mg/dl.
Serum magnesium has been studied to be of vital importance to indirectly observe the exacerbation event in a COPD patient. It has become one of the observed value to assess the disease stability.

Magnesium is the second most abundant intracellular cation after potassium, being essential in a great number of enzymatic and metabolic processes. It is a co-factor of all enzymatic reactions that involve ATP and found in the membranes that maintain the electrical excitability of muscular and nervous cells. The normal level of magnesium in serum is 1.8-2.6 mg/dl.

Low magnesium levels is associated with increased airway hyperreactivity and decreased muscle strength. It also plays a role in relaxation of smooth muscles of airways and bronchodilation, stabilization of mast cells, neurohumoral mediator release, various immune responses, muscarinic actions and mucociliary clearance.

The present study was conducted to determine serum magnesium levels among stable COPD, exacerbation of COPD and normal healthy asymptomatic smokers. Another aim of this study was to assess the magnesium levels with severity of airway obstruction.

It was observed from the present study that the majority of stable COPD patients and COPD exacerbation patients had their serum magnesium levels ranging from 1.5-2 mg/dl, whereas asymptomatic smokers had their serum magnesium levels in the normal range between 2 and 2.5 mg/dl.

It was also seen that their was a significant reduction in serum magnesium levels with the severity of airway obstruction.

**CONCLUSION**

From the present study it was concluded that their is a low magnesium level seen among COPD individuals compared to normal healthy smokers and a significant reduction of magnesium levels with airway obstruction severity.

It could be implicated from this study that magnesium supplements could be administered among these patients in order to reduce the risk of frequent exacerbations and comorbidities.

**ACKNOWLEDGEMENT**

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