

PREVALENCE AND SEVERITY OF HYPOPHOSPHATEMIA IN COPD PATIENTS**Dr. V. Rajesh Babu and Dr. S. Rajagopal***

Assistant Professor, Department of Medicine, Tirunelveli Medical College, Tirunelveli.

***Corresponding Author: Dr. S. Rajagopal**

Assistant Professor, Department of Medicine, Tirunelveli Medical College, Tirunelveli.

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ABSTRACT

Introduction: Chronic obstructive pulmonary diseases are a major health hazard in the recent years. Bronchial asthma is a chronic inflammatory disease of the airways characterized by variable and recurring symptoms of reversible airflow obstruction and bronchospasm. The mortality rate in patient with Bronchial asthma and COPD is still rising and is being partly attributed to the adverse effects of its treatment. Hypophosphataemia can worsen respiratory failure in severely ill asthma patients by impairing respiratory muscle performance. This study therefore intends to study the prevalence and severity of hypophosphatemia in COPD patients and also to evaluate the relationship between the type of medications taken for COPD and severity of hypophosphatemia. **Methodology:** This study was conducted in Government Rajaji Hospital, Madurai as cross sectional study, our study included 75 male patients admitted to hospital with diagnosis of COPD. Patients with COPD as primary diagnosis and also if diagnosis of COPD was made during previous hospitalization or outpatient visits based on history of smoking, clinical and radiologic findings and pulmonary function tests suggestive of COPD were included in study, All patients underwent necessary biochemical investigations. All patients were included in study after getting informed consent. Study permission was received from institutional human ethics committee. **Results:** In our study group most of the patients were in 61-70 years age group. In our study group 80 percent of patients required two medications in our study group. 12 patients (16%) had hypophosphatemia. Among these patients 2 had mild hypophosphatemia with serum phosphate levels ranging from 2-2.4 mg/dl, 8 patients had moderate hypophosphatemia (1-1.9 mg/dl) and rest 2 patients had severe hypophosphatemia with serum phosphate below 1 mg/dl. Next we analysed the related signs and symptoms of hypophosphatemia, Except Prednisolone in patients on other drugs there was significant relation between duration of intake and phosphate levels. **Conclusion:** The prevalence of hypophosphatemia was significantly higher among COPD patients taking one or more drugs commonly used for COPD due to negative renal phosphate handling. Hypophosphatemia impairs the contractile properties of the diaphragm and can even delay weaning from the ventilator and increase duration of intensive care and hospitalisation. Therefore, any acute deterioration of respiratory function in COPD patients warrants analysis of serum phosphate levels and judicious correction of depleted phosphate levels should be considered whenever necessary.

KEYWORDS: COPD, Hypophosphatemia, Serum Phosphate.**INTRODUCTION**

Chronic obstructive airway diseases are a major health hazard in the recent years. It comprises of Bronchial asthma and Chronic obstructive pulmonary disease (COPD). Bronchial asthma is a chronic inflammatory disease of the airways characterized by variable and recurring symptoms of reversible airflow obstruction and bronchospasm. Predisposing factors for asthma are atopy and obesity (recently recognized). Exposure to common allergens like dust mites and pollen trigger the symptoms. Pathogenesis includes inflammatory cell infiltration; goblet cell hyperplasia plugging the small airways with thick mucus; collagen deposition beneath the basement membrane; smooth muscle hypertrophy; airway oedema; mast cell activation and denudation of airway epithelium. This causes airway hyper-

responsiveness, airflow limitation and respiratory symptoms like recurrent episodes of wheezing, breathlessness, chest tightness and cough. Treatment aims to reduce recurrence of exacerbations. It includes short acting bronchodilator-salbutamol nebulization, anti-inflammatory systemic corticosteroids, oral and parenteral therapy in severe cases.^[1]

Prevalence of Bronchial asthma globally is more in males than in females. Approximately 300 million people suffer from Bronchial asthma globally. Prevalence of Bronchial asthma is about 10-12% in adults and about 15% in children.^[2] COPD is a clinical syndrome associated with gradually progressive narrowing of the airways due to inflammation. COPD includes Bronchitis, Emphysema and small airway

disease with common symptoms of chronic obstruction to the air flow and inflammation. Cigarette smoking is the main cause of COPD. Pathogenesis includes proteinase-antiproteinase hypothesis, immunological mechanisms, oxidant-antioxidant balance, systemic inflammation, apoptosis and ineffective repair. COPD affects people of all ages and both the sexes, mostly adult males, thirty five years and above. However the ratio of prevalence of COPD is equalizing in recent times because of increased tobacco use among women in high-income countries and the higher risk of exposure to indoor air pollution (such as biomass fuel used for cooking and heating) in low-income countries. Genetic (α 1-antitrypsin deficiency) predisposition is proven.^[1] Three common symptoms are cough, sputum production and exertional dyspnea. COPD is treated with inhaled bronchodilators, inhaled corticosteroids, oral theophylline and phosphodiesterase-4 inhibitor. Acute exacerbations are common in COPD.^[2]

There are wide variations in the prevalence of COPD across countries due to the method of diagnosis and classification of COPD. According to WHO estimates, 65 million people have moderate to severe COPD. Global prevalence of COPD in adults aged > 40 years is approximately 9-10%. Recently, Indian study of epidemiology of Asthma, Respiratory symptoms and Chronic bronchitis in adults >35 years is 3.49%.^[3] COPD is the fourth leading cause of mortality worldwide.^[2]

The mortality rate in patient with Bronchial asthma and COPD is still rising and is being partly attributed to the adverse effects of its treatment.^[5] Hypokalemia, hypomagnesaemia and hypocalcemia cause cardiac arrhythmia. Hypophosphotaemia can worsen respiratory failure in severely ill asthma patients by impairing respiratory muscle performance.^[4] Hyponatremia may cause central nervous system dysfunction^[6] and hyperglycemia will lead to diabetic ketoacidosis.

P Ravi Kumar et al^[7] performed a Study of Electrolyte disturbances in acute asthma done with samples taken at three intervals (0 min, 90 min, 180 min) found that maximum decrease of sodium level was noted at 180 min, maximum drop in potassium level was noted at 90 min, maximum drop in magnesium level was noted at 90 min and maximum fall in phosphorous level was noted at 180 min. Hence they quoted that maximum fall in electrolyte levels occurs within 2 hours of nebulization.^[5]

DaCruz^[8] and Holburn^[9] found that most of the large falls in serum potassium occurred in patients with low pre-treatment pCO_2 values-patients with less severe respiratory disease. A possible explanation for this phenomenon is that an already maximally stressed patient may be incapable of responding metabolically to the adrenaline-mediated side effects of salbutamol.^[10]

Only few studies have been done with this regard. This study therefore intends to study the prevalence and

severity of hypophosphatemia in COPD patients and also to evaluate the relationship between the type of medications taken for COPD and severity of hypophosphatemia.

MATERIALS AND METHODOLOGY

This study was conducted in Government Rajaji Hospital, Madurai as cross sectional study, our study included 75 male patients admitted to hospital with diagnosis of COPD, all patients were aged between 40-80 years. Patients with COPD as primary diagnosis and also if diagnosis of COPD was made during previous hospitalization or outpatient visits based on history of smoking, clinical and radiologic findings and pulmonary function tests suggestive of COPD were included in study, Similarly patient on oral medications for more than one month on any of one or more following drugs like methyl xanthines, corticosteroids, beta agonists and furesamide were included in study. Whereas patient with history of chronic alcoholism, chronic antacid intake, elevated urea and creatinine levels, diabetes mellitus and fever suggestive of malaria were excluded from the study. All patients underwent necessary biochemical investigations. All patients were included in study after getting informed consent. Study permission was received from institutional human ethics committee.

RESULTS

In our study group most of the patients were in 61-70 years age group, while range was between 46-76 years, the mean age of our study group was 61.8 years. In our study group we included patients who had history of smoking habit and among our patients around 88% of patients had smoking history for more than 20 years. We also analysed the number of medications taken by each patients. In our study group most of the patients required more than one medication, 80 percent of patients required two medications in our study group. In our study group patients were taking deriphylline or salbutamol for a mean duration of 4.8 yrs. While they were on furesamide for a mean duration of 5.4 months and prednisolone for a mean duration of 1.43 months.

Next we analysed presence of hypophosphatemia in our study group, 12 patients (16%) had hypophosphatemia. Among these patients 2 had mild hypophosphatemia with serum phosphate levels ranging from 2-2.4 mg/dl, 8 patients had moderate hypophosphatemia (1-1.9 mg/dl) and rest 2 patients had severe hypophosphatemia with serum phosphate below 1 mg/dl.

Table 1: Grading of serum phosphat levels.

Serum phosphate levels	No of cases	Percentage
Normal(>2.5mg/dl)	63	84%
Mild(2-2.4mg/dl)	2	2.70%
Moderate(1-1.9mg/dl)	8	10.70%
Severe(<1mg/dl)	2	2.70%

Next we analysed the related signs and symptoms of hypophosphatemia, In our study among 75 patients

11(14.7%) patients had muscle weakness, 14 (18.7%) patients had peripheral neuropathy. Whereas respiratory rate was increased (>18/min) in 9 patients and decreased (<12/min) in 4 patients. Coming to mean respiratory rate, it was 11.5 /min in patients with low phosphate levels whereas it was 16.6 in patients with normal phosphate levels. This correlation was statistically significant with P value of 0.0001. Among patients with muscle weakness 9 patients with low phosphate levels had muscle weakness while only 2 patients with normal phosphate level had muscle weakness, this was statistically significant. Similarly among patients with peripheral neuropathy 9 patients with low phosphate levels had muscle weakness while only 5 patients with normal phosphate level had muscle weakness, this was also statistically significant.

Next we analysed the relationship between duration of intake of medications with hypophosphatemia status. To start with hypophosphatemia was present in patients who had taken deriphyllin for a mean duration of 8.0 ± 2.7 years. Hypophosphatemia was absent in patients who had taken deriphyllin for mean duration of 4.25 ± 3.1 years. This correlation is statistically significant with P value of 0.0011. Similarly hypophosphatemia was present in patients who had taken salbutamol for a mean duration of 8.0 ± 2.7 years. Hypophosphatemia was absent in patients who had taken salbutamol for mean duration of 4.27 ± 3.08 years. This correlation is statistically significant with P value of 0.0011.

Table 2: Hypophosphatemia and duration of medication.

Hypophosphatemia status	Duration of intake(mean±sd)			
	Deriphyllin (yrs)	Salbutamol (yrs)	Prednisolone (months)	Furesamide (months)
Positive	8.0 ± 2.7	8.0 ± 2.7	1.67 ± 0.88	4.14 ± 0.8
Negative	4.25 ± 3.1	4.27 ± 3.08	0.92 ± 0.66	1.16 ± 0.6
P value	0.0011	0.0011	0.1386	0.0072
	Significant	Significant	Non significant	Significant

Next we analysed in patients on prednisolone, hypophosphatemia was present in patients who had taken prednisolone for a mean duration of 1.67 ± 0.66 months. Hypophosphatemia was absent in patients who had taken prednisolone for mean duration of 0.92 ± 0.66 months. This correlation was not statistically significant with P value of 0.1386. Finally we analysed hypophosphatemia in patients on frusamide which was present in patients who had taken frusemide for a mean duration of 4.14 ± 0.8 months. Hypophosphatemia was absent in patients who had taken frusemide for mean duration of 1.16 ± 0.6 months. This correlation is statistically significant with P value of 0.0072.

We also analysed the relation between number of drugs taken and serum phosphate levels where mean number of drugs taken in patients with hypophosphatemia was 2.82 in comparison 2.06 in patients who have normal phosphate levels. This was statistically significant with P value of 0.0001.

DISCUSSION

In this study 75 COPD patients who were taking medications were selected according to inclusion and exclusion criteria. Serum phosphate levels and symptomatology of hypophosphatemia were analysed in these patients. In our study among 75 patients, 4 patients were less than 50 years age group, 28 patients in 51-60 age group, 31 patients in 61-70 age group and rest were more than 70 years. Sirkku Vikman et al in his study of found that among 110316 hospital treated patients about 34.2% patients were in 65-75 years age group and 30.2% patients in 75-85 years age group. In another study done by Nikolaos Tzanakis et al^[11] 40% of individuals were in

40 -60 year age group. These findings were similar to our study.

In our study among 75 patients around 66 persons had history of smoking for more than 20 years to 40 years. We also analysed the number of medications taken by each patients. In our study group most of the patients required more than one medication, 80 percent of patients required two medications in our study group. In our study group patients were taking deriphylline or salbutamol for a mean duration of 4.8 yrs. While they were on furesamide for a mean duration of 5.4 months and prednisolone for a mean duration of 1.43 months.

Coming to hypophosphatemia 12(16%) patients had low phosphate status in our study group, Ficcadori et al^[12] in his study of 150 patients had prevalence of hypophosphatemia of 21.5%, In another study done by Sukran Atickan et al the prevalence was 20%. Litchman et al^[13] did a study in patients with respiratory illness which had prevalence of hypophosphatemia of 25%. In our it less than all above studies.

In our study hypophosphatemia was present when a mean of 2.82 drugs were taken against absence of hypophosphatemia when mean of 2.06 drugs were taken, this difference was statistically significant. Among our study group 2(2.66%) had mild hypophosphatemia with serum phosphate levels ranging from 2-2.4 mg/dl, 8(10.66%) patients had moderate hypophosphatemia (1-1.9 mg/dl) and rest 2(2.66%) patients had severe hypophosphatemia with serum phosphate below 1 mg/dl. In study done by Ficcadori et al^[12] 12.5% patients had

mild hypophosphatemia and 9% had moderate hypophosphatemia similar to our study.

Coming to muscle weakness 11(14.7%) of patients manifested the symptom, among which 9 patients with low phosphate levels had muscle weakness while only 2 patients with normal phosphate level had muscle weakness, this was statistically significant. Thomas R Gravelyn *et al*^[14] studied hypophosphatemia associated respiratory muscle weakness and found around 70% of patients with hypophosphatemia had muscle weakness. In our study too there was such weakness in form of reduced respiratory rate in 5.3% of patients. There was difference in mean respiratory rate with a mean RR of 11.5/min in patients with hypophosphatemia and 16.6/min in patients without hypophosphatemia.

Finally we analysed the relationship between duration of intake of medications with hypophosphatemia status. To start with hypophosphatemia was present in patients who had taken deriphyllin for a mean duration of 8.0 ± 2.7 years. Hypophosphatemia was absent in patients who had taken deriphyllin for mean duration of 4.25 ± 3.1 years. This correlation is statistically significant with P value of 0.0011. Similarly hypophosphatemia was present in patients who had taken salbutamol for a mean duration of 8.0 ± 2.7 years. Hypophosphatemia was absent in patients who had taken salbutamol for mean duration of 4.27 ± 3.08 years. This correlation is statistically significant with P value of 0.0011.

Next we analysed in patients on prednisolone, hypophosphatemia was present in patients who had taken prednisolone for a mean duration of 1.67 ± 0.66 months. Hypophosphatemia was absent in patients who had taken prednisolone for mean duration of 0.92 ± 0.66 months. This correlation was not statistically significant with P value of 0.1386. Finally we analysed hypophosphatemia in patients on frusemide which was present in patients who had taken frusemide for a mean duration of 4.14 ± 0.8 months. Hypophosphatemia was absent in patients who had taken frusemide for mean duration of 1.16 ± 0.6 months. This correlation is statistically significant with P value of 0.0072.

CONCLUSION

The prevalence of hypophosphatemia was significantly higher among COPD patients taking one or more drugs commonly used for COPD due to negative renal phosphate handling. Hypophosphatemia impairs the contractile properties of the diaphragm and can even delay weaning from the ventilator and increase duration of intensive care and hospitalisation. Therefore, any acute deterioration of respiratory function in COPD patients warrants analysis of serum phosphate levels and judicious correction of depleted phosphate levels should be considered whenever necessary.

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