Vol 11| Issue 2| 2021 | 68-71.

e-ISSN 2248 – 9142
print-ISSN 2248 – 9134

International Journal of
Current Pharmaceutical & Clinical Research

www.ijcpcr.com

URIC ACID LEVELS IN CHRONIC OBSTRUCTIVE LUNG DISEASE PATIENTS IN SOUTH INDIA

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ABSTRACT
Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide and results in an economic and social burden that is both substantial and increasing This study was done to measure serum uric acid levels in chronic obstructive pulmonary disease patients. Serum uric acid, the final product of purine degradation, has been shown to be increased in the hypoxic state as well as in systemic inflammation including patients with chronic obstructive pulmonary disease (COPD). elevated serum uric acid level may be a noninvasive indicator for COPD severity and hypoxemia in stable COPD patients. Therefore, it is suggested to assess serum UA as an important and additional parameter for COPD patients.

Key words: COPD, Uric Acid, hypoxia, Spirometry.

INTRODUCTION

Serum uric acid is increased in respiratory disease, especially in the presence of hypoxia and systemic inflammation. We evaluated serum uric acid as a biomarker for prediction of mortality and future acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality with increasing prevalence worldwide [1]. An acute exacerbation of COPD (AECOPD) is characterised by a significant change in symptoms that is acute in onset and may warrant a change in regular medication [1].Some COPD patients are particularly susceptible to exacerbations, and this has a negative impact on survival [2]. Serum uric acid is the final product of purine degradation [3], which increases significantly during hypoxia [4]. Elevated uric acid levels have been associated with the presence of systemic inflammation [5] and increased cardiovascular risk [6]. In this context, increased levels of uric acid have been shown in respiratory disorders, including obstructive sleep apnoea [7] and pulmonary hypertension [8]. In COPD, cigarette smoke induces oxidative stress and lung inflammation, resulting in lung tissue damage and decline of
pulmonary function [1].

Lung functions are deranged because of damage to lung tissues induced by oxidants and inflammation. This derangement reduces oxygen intake leading to tissue hypoxia causing hyperuricemia. Hyperuricemia is defined as serum uric acid (UA) levels >7.1mg/dL in males or >6.1mg/dL in females. In comparison to normal individuals, hyperuricemics have more inflammation and oxidative stress injuries.

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Proinflammatory effect of UA is more profound in those with high serum UA levels. Our study aim is to assess whether the presence of higher values of serum UA is associated with changes in clinical and functional characteristics in patients with chronic obstructive pulmonary disease (COPD).

MATERIAL AND METHODS

The study was conducted after having obtained permission from the Institutional Ethics committee, SLIMS.110 stable COPD patients in the age group 35-70 years (mean age 51.5yrs) who attended the General Medicine ,SLIMS, Pondicherry were included in this study.

Spirometric parameters like FVC and FEV were measured using 1 standard techniques with Spirometer Easy. Spirometry was done without the administration of any bronchodilator.The highest value out of three FVC maneuvers by each subject was used in the analysis. Percent predicted values for spirometric parameters are presented as FEV % predicted and FVC 1 % predicted. Subjects with FEV /FVC <70% were identified as having 1 airflow limitation (COPD).According to the Global initiative for Chronic Obstructive Lung Disease (GOLD) criteria, subjects with airflow limitation and FEV1 %predicted ≥80 were identified as having mild air flow limitation, those with FEV %predicted between 50 and 1 <80 were defined as having moderate air flow limitation, and those with FEV %predicted <50 were defined as having severe airflow 1 .2 limitation Of the total 110 cases ,52 were mild,42 were moderate and 16 were severe COPD patients.74 age and sex matched subjects were included as controls (mean age 48.7yrs). Clinical assessment included detailed physical examination, information regarding moking history, biomass exposure and accompanying diseases were elicited from both cases and control groups.

Exclusion criteria for the present study includes patients with history of pulmonary tuberculosis, asthma, coronary artery disease, renal disease, liver disease, diabetes mellitus, cancer and patients on chemotherapy and radiotherapy.Venous blood samples were drawn from controls and COPD patients. Renal function tests, liver function tests, uric acid and electrolytes and serum uric acid was analysed by using Siemens fully automated analyser.

STATISTICAL ANALYSIS

Clinical characteristics of the study population were compared using Chi square test and Student's t-test. p - Value of < 0.05 were considered statistically significant. Comparison of serum uric acid levels between patients with COPD and controls were done using Student's
Unpaired t-test. Comparison of serum uric acid levels between various stages of patients with COPD was performed using ANOVA.

RESULTS AND DISCUSSION:

Uric acid levels have been previously associated with clinical and functional characteristics in patients with COPD in cross-sectional studies [9, 10] UA is the end-product of purine degradation. Excessive intake of foods containing purine bases, alcohol consumption , renal dysfunction and genetic disorders of purine metabolism, such as hypoxanthine-guanine phosphoribosyl transferase deficiency (Lesch-Nyhan syndrome) and adenine phosphoribosyl transferase deficiency, result in elevation of serum UA levels.[11-14] In addition, other demographic and clinical factors, such as gender, BMI, smoking index, and serum glucose levels, are known to be associated with increased serum levels of UA.[15] Therefore, careful consideration of these factors is required when assessing the relationship between pulmonary function and UA levels. Tissue hypoxia has been reported to induce the degradation of adenosine.[16] This results in the release of purine intermediates and end products of purine catabolism, such as uric acid (UA).[17] Elevation of serum UA (sUA) levels has been observed in hypoxic subjects, including patients with COPD.[18]

Tissue hypoxia has been reported to induce the degradation of [19] adenosine . This results in the release of purine intermediates and [20] end products of purine catabolism, such as uric acid (UA) .Elevation of serum UA (sUA) levels has been observed in hypoxic subjects,[21] including patients with COPD .UA is a biomarker of xanthine oxidase activity, which is known to be an important source of reactive oxygen species.[22] Several investigators have reported that elevated UA levels were associated with worsening of cardiovascular disease, heart failure and COPD.[23]

As a routine laboratory index, serum uric acid is frequently used to evaluate the renal function of patients and it has also been shown to be the main contributor to the antioxidant capacity. Previous studies demonstrated that uric acid could be an independent biomarker of impaired prognosis for some extrapulmonary diseases (such as congestive heart failure and metabolic syndrome), which may be associated with impaired oxidative metabolism.[24-26] Furthermore, the association between the levels of serum uric acid and the severity of pulmonary disease has also drawn more and more attention.[27-29]

Our findings suggest that systemic UA levels are associated with oxidative stress and inflammation in vivo. UA [30] activates leukocytes through the NALP3 inflammasome . Activated leukocytes express selectins and adhere to endothelial cells, where they secrete various pro-inflammatory cytokines and chemical mediators, resulting in vessel wall damage and atherosclerosis. These findings suggest that systemic UA levels are associated with oxidative stress and inflammation in vivo. UA activates leukocytes through the NALP3 inflammasome.16 Activated leukocytes express selectins and adhere to

endothelial cells, where they secrete various pro-inflammatory cytokines and chemical mediators, resulting in vessel wall damage and atherosclerosis. Possible explanations for the association between elevated s UA levels and pulmonary function includes 1) hypoxia due to impaired pulmonary function leading to purine catabolism, 2) impaired pulmonary function inducing pulmonary hypertension and resulting in the elevation of sUA levels, 3) Toxins in cigarette smoke causes oxidative stress in the alveolar spaces of the lungs. This oxidative stress induces lung inflammation contributing to the pathogenesis of chronic respiratory diseases, such as COPD and pulmonary fibrosis.[31] While assessing the relationship between pulmonary function and UA levels, certain factors should be considered carefully. It is a known fact that UA is the end-product of purine degradation. Alcohol consumption, excessive intake of foods containing purine bases, renal dysfunction and genetic disorders of purine metabolism, such as hypoxanthine-guanine phosphoribosyl transferase deficiency (Lesch-Nyhan syndrome) and adenine phosphoribosyl transferase deficiency are the factors which increases serum UA levels[31]. The association between serum uric acid levels and COPD. This current meta-analysis demonstrated that serum uric acid levels were significantly higher in stable COPD patients than healthy control subjects, and there was a relationship between the levels of serum uric acid and the severity of the airflow limitation in stable COPD patients.

CONCLUSION:

Serum uric acid is a widely and rapidly available, easy to interpret, low-cost. This low-cost biomarker may be useful in the identification of high-risk chronic obstructive pulmonary disease patients that could benefit from intensive management. elevated serum uric acid level may serve as a noninvasive indicator for COPD severity and hypoxemia in stable COPD patients. There is a need to evaluate serum UA levels as an additional parameter for predicting outcome in COPD patients. Biomarker, suggest a possible role for serum uric acid in the identification of COPD patients at an increased risk of adverse outcomes who may need early intensive management.

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