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# To study the level of Nitric Oxide and Ceruloplasmin in Chronic Obstructive Pulmonary Disease

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**Abstract**

Chronic obstructive pulmonary disease is a multicomponent condition, characterized by airflow obstruction that is not fully reversible and is a major global cause of morbidity and mortality. Worldwide COPD ranked as the 6$^{th}$ leading cause of death in 1990. It is projected to be the 4$^{th}$ leading cause of death worldwide by 2030 due to increase in smoking rates and demographic changes in many countries. With this view, we planned to assess the inflammation marker by determining the level of nitric oxide and ceruloplasmin in chronic obstructive pulmonary disease. The aim of this study is 1) to determine the level of ceruloplasmin and nitric oxide in COPD patients and healthy controls. 2) to find the correlation between these parameters in COPD patients. 70 clinically diagnosed COPD patients in the age group 51-70 years and 70 healthy controls in the same age group were included in this study. Serum nitric oxide levels and serum ceruloplasmin levels were significantly increased ($P< 0.001$) in COPD patients as compared to control group. An ubiquitous messenger molecule NO can diffuse rapidly from point of synthesis and interact with ROS to form other RNS which may be involved in progression of pathophysiology of COPD. Ceruloplasmin is major extracellular antioxidants may play a role in preventing lung injury of COPD patients. Thus ceruloplasmin can be considered as a potential biomarker of COPD.

**Keywords:** Chronic Obstructive Pulmonary Disease (COPD), Nitric oxide (NO), Ceruloplasmin ( Cp), Reactive Oxygen Species (ROS), Reactive Nitrogen Species (RNS).

## INTRODUCTION

Chronic obstructive pulmonary disease is a multicomponent condition, characterized by airflow obstruction that is not fully reversible and is a major global cause of morbidity and mortality. The pathological hallmarks of chronic obstructive pulmonary disease (COPD) are inflammation of the small airways (bronchiolitis) and destruction of lung parenchyma and enlargement of alveoli (emphysema). The functional consequence of these abnormalities is airflow limitation [1]. People with COPD have trouble breathing in and out due to long term damage to the lungs, usually because of smoking.

Worldwide COPD ranked as the 6$^{th}$ leading cause of death in 1990. It is projected to be the 4$^{th}$ leading cause of death worldwide by 2030 due to increase in smoking rates and demographic changes in many countries [2]. Studies in many countries have found that people who live in large cities have a higher rate of COPD compared to people who live in rural areas [3].

Oxidative stress plays an important role in development of exacerbations and progressing of COPD but the underlying mechanism are not clear [4]. An important process causing lung damage in COPD may be cytokine release due to inflammation as the body responds to irritant particles such as tobacco smoke in the airway [3].

Nitric oxide may be a marker of disease activity in variety of lung disease [5]. In COPD Nitric Oxide (NO) levels are related to smoking habits and disease severity, showing a positive relationship with respiratory fractional parameters. More ever NO is increased in patients with COPD exacerbation compared to stable ones [6]. Reactive Oxygen Species (ROS), Reactive Nitrogen Species (RNS) formed from nitric oxide derived from its isoform is able to modulate bronchomoter tone and seems to be proinflammatory mediator with immunomodulatory effects [7].

Ceruloplasmin the major serum inhibitor of lipid peroxidation has been documented as a main extracellular antioxidant, in serum. It may play a role in preventing lung injury and could be involved in pathogenesis of COPD [8]

We therefore decided to study certain biochemical parameters which are relevant to systemic inflammation and also related to oxidant, in result as both these processes may be involved in exacerbations of COPD.

With a view of obtaining more information, regarding the pathogenesis of COPD the study was designed to measure these parameters i.e. nitric oxide and ceruloplasmin in COPD patients.

## MATERIALS AND METHODS

Present study was conducted in the Department of Biochemistry, Government Medical College and Hospital Miraj.

The Institutional Ethical Committee approved the study and informed consent was obtained from each participant in the study.

Study group included 70 clinically diagnosed COPD patients in the age group 51-70 years. Diagnosis is confirmed on the basis of clinical history, physical examination, chronic cough and chest X-ray. Control group consisted of 70 healthy controls without any respiratory disease and matching in same age and sex group were included in this study.

Feasibility criteria- patients, who were co-operative and willing to participate after explaining them the nature of study, were included in this study.

Exclusion criteria- The patients having disease such as connective tissue disorder, RA, SLE, malignancy, etc. were excluded from this study feasibility.

Blood samples were collected from study group and from control group under aseptic conditions. Serum was separated and analyzed for estimation of nitric oxide [as nitrite] by Najwa K. Cortas and Nabid W. Waked method (colorimetric) [9] and ceruloplasmin by turbidometric immunoassay [10].

All data were expressed as mean ± SD. Statistical analysis was done by using "t" test.

**Table 1:** Comparison of biochemical parameters between COPD patients and control group.

| **Sr No.** | **Biochemical markers** | **Controls** (without any respiratory disease) **n = 70 Mean ± SD** | **COPD Patients n= 70 Mean ± SD** |
|---|---|---|---|
| 1) | Nitric oxide µmol/L | 17.56 ± 6.7 | 85.07 ± 19.08* |
| 2) | Ceruloplasmin ( mg/g creatinine ) | 34.10 ± 9.9 | 88.06 ± 11.02* |

Statistical method used to compare data was "t" test.

* $P < 0.001$ Highly significant

## RESULTS AND DISCUSSION

Mean level of serum nitric oxide was found to be significantly elevated in COPD patients when compared with control ($P < 0.001$, Table 1).

Nitric oxide (NO) plays an important role as an inflammatory mediator in the airways, since chronic obstructive pulmonary disease (COPD) is characterized by airway inflammation.

One of the most important pathogenetic mechanisms of COPD is oxidative stress associated with inflammatory cellular infiltration (macrophages, neutrophils, and lymphocytes CD8) that in conjunction with an altered release of endogenous nitric oxide (NO) may provoke the formation of "nitrative stress" [11].

Oxidative stress generates superoxide anions and in combination with NO may result in the formation of the highly reactive species peroxynitrite, which is increased in exhaled breath condensate and airway mucosa of COPD patients [12–13] . In COPD when airways cells are exposed to oxidative stress elicited by environmental pollutants, or inflammatory reactions, increased levels of ROS and RNS can have a variety of deleterious effects within the airways including damage to DNA, lipids, proteins, carbohydrates and impairment of cellular functions. This may amplify the inflammatory reactions and induce the pathogenesis of COPD.

Highly significant increase in the mean levels of ceruloplasmin was found in COPD patients as compared to control group ($P < 0.001$, Table 1).

COPD is characterized by the presence of progressive obstruction of the airways that is not completely reversible and associated with an abnormal inflammatory response of the lungs and the airways to harmful particles and gases. Due to inflammation and oxidative stress, synthesis of ceruloplasmin an acute phase protein increases leading to its higher concentration in plasma. Our study is supported by Begum et.al (2014) [14].

Ceruloplasmin is a major extracellular antioxidant in serum. It inhibits ferrous ion stimulated lipid peroxidation and plays a role in preventing lung injury of COPD patients. Our study demonstrates an association between both the biochemical parameter with COPD. Although nitric oxide and ceruloplasmin are found to be raised, but no significant correlation was observed between these two parameters.

## CONCLUSION

Oxidative stress is an important factor in the pathogenesis of chronic obstructive pulmonary disease (COPD). The measurement of serum nitric oxide is helpful to examine the oxidative stress in disease condition. Thus Nitric oxide is used as marker for oxidative stress and in other inflammatory diseases. Ceruloplasmin is a major extracellular antioxidant may play a role in preventing lung injury of COPD patients. Thus serum ceruloplasmin can be considered as potential biomarker for COPD.

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