

### **Serum ceruloplasmin and serum bilirubin in chronic obstructive pulmonary disease**

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#### **Abstract**

**Introduction:** Oxidative stress has been known for having a key role in pathogenesis of many diseases. The aim of this study was to investigate the antioxidant status with chronic obstructive pulmonary disease (COPD) and healthy control subjects.

**Material and methods:** Fifty subjects having COPD and fifty healthy control participated in this study. The investigation included determination of the serum ceruloplasmin (Cp) and serum bilirubin with basal metabolic rate (BMI).

**Results:** Significantly increased sr. ceruloplasmin ferroxidase activity and sr. bilirubin levels were found in subjects with COPD than healthy normal subjects. No significant difference in BMI were found in COPD patients.

**Conclusion:** Biochemical biomarkers can be reliably utilized in the prognosis of COPD. Reduced lung function is associated with increased levels of systemic inflammatory markers which may have important

pathophysiological and therapeutic implications for subjects with stable COPD.

**Keywords:** COPD, Ceruloplasmin, bilirubin and BMI

#### **Introduction**

COPD is a major and increasing global health problem and is currently the 3<sup>rd</sup> leading causes of death by 2020<sup>1</sup> are at increased risk of CVD, atherosclerosis, osteoporosis and muscle wasting. Systemic inflammation may be involved in the pathogenesis of these disorders. The use of inflammatory markers for this study have been intimately linked with the development of ischemic heart disease and stroke, which interestingly are also with COPD.<sup>2</sup> Ceruloplasmin was the strongest single predictor of COPD.<sup>3</sup>

Chronic obstructive pulmonary disease (COPD) is characterized by persistent respiratory symptoms and airflow limitation caused by significant exposure to noxious particles or gases.<sup>4</sup> Oxidative stress is an important mechanism in the development, progression, and exacerbation of COPD. Biomarkers of oxidative

stress are elevated in the exhaled breath, sputum, and blood of patients with COPD.<sup>5</sup>

Imbalance between antioxidant and oxidative stress is a major risk factor for pathogenesis of some chronic disease such as COPD. Oxidative stress not only produces direct injurious effects in the lungs, but also activates the molecular mechanisms that initiate lung inflammation. The antioxidants are the primary defenses against reactive oxygen/ reactive nitrogen species.<sup>6</sup>

Bilirubin is known as a potential antioxidant and possesses anti-inflammatory properties. Higher concentrations have been shown to protect against oxidative stress.<sup>7</sup>

The present study was conducted with the aim of estimating the levels of serum Cp and serum bilirubin in COPD patients and normal subject and correlated their levels.

### Materials and methods

**Study design:** It was an observational study.

**Inclusion criteria:** Only COPD patients included in this study

**Exclusion criteria:** Patients with a diagnosis of asthma, coronary artery disease (CAD), diffuse parenchymal lung diseases, patients on long term oxygen therapy or unable to perform spirometry were excluded.

Fifty subjects with COPD participated in this study. These diseases was diagnosed by a respiratory physician in Noor hospital and JIU'S IIMSR medical college, warudi. Dist Jalna, Maharashtra. Fifty healthy volunteers in the age group of 40-65 yrs coming to OPD for routine checkup participated in this study as control group and had no history of lung disease.

With each subject we draw 3-4 ml of venous blood into plain tube and serum was separated. The mean age of the patients was 44.30±4.5 yr. Each group (COPD and

healthy control) subjects was estimated serum Cp activity was measured with turbidometric immunoassay method and serum total bilirubin was estimated by Erba diagnostic kit method on Erba EM200 fully autoanalyzer. The data are express as mean ±SD and statistical analysis was carried out using social science package software (SPSS) version 21

Statistical and correlation analysis were performed using analysis of variance test and Spearman correlation coefficient test. A P value <0.05 was accepted as statistically significant.

### Results

#### Comparisons of serum ceruloplasmin, serum bilirubin and BMI in COPD and control group

	Patients (n=50)	Control (n=50)	P- Value
Sr. Cp	56.76±0.72	28.52±4.64	P<0.01
Sr. Bilirubin	1.20±0.34	0.70±0.21	P<0.01
BMI	22.19±5.13	22.39±7.09	P>0.05

No significant difference in BMI was found between COPD subjects and healthy control. (Table no.1)

Significantly increased levels of serum Cp and serum bilirubin activities in COPD subjects and healthy control. We performed univariate analyses with the  $\chi^2$  test for categorical variables and Student's t-test for continuous variables. A two-sided P-value < 0.05 was considered statistically significant.

### Discussion

Increased oxidative burden plays an important role in the pathogenesis of COPD.<sup>8</sup>

Antioxidant assessment among COPD patients might be beneficial effect to prevent progression of air flow limitation in COPD patients.<sup>6</sup>

Oxygen free radicals are related to tissue damage in COPD, chronic tobacco smoking, asthma, acute

respiratory distress syndrome.<sup>9</sup> This knowledge has evolved in parallel with the study of antioxidant agents able to neutralize the effects of oxygen free radicals neutralizing agents may be included in the therapeutic arsenal against may be included the principle pulmonary diseases.<sup>10</sup>

The BMI is a prognostic factor for COPD. BMI alternations COPD with no significant difference among subjects. Furthermore, it is still unclear, if BMI alteration in COPD is associated with the severity of airflow limitations or with other factors like gender, age, ethnicity, reduction, employment, tobacco consumption, clinical symptoms and geographical variations.<sup>11</sup>

Ceruloplasmin the major serum inhibitor of lipid peroxidation<sup>12</sup> has been documented as a main extracellular antioxidant in serum<sup>13</sup> inhibiting ferrous ions in the decomposition of lipid peroxides.<sup>14</sup>Cp protects protease inhibitor from oxidative inactivation. It has been reported that Cp activity play a role in preventing lung injury and an abnormality of Cp oxidative inhibition could be involved in the pathogenesis of COPD.<sup>15</sup>

Bilirubin is one of the numerous nonenzymatic antioxidants located within skeletal muscle fibers, and it inhibits both lipid and protein oxidation<sup>16</sup> In addition, bilirubin attenuates vascular endothelial activation and dysfunction in response to proinflammatory stress.<sup>17</sup> Albumin bound bilirubin protects human ventricular myocytes against oxyradical damage.

However, the relationship of bilirubin and clinical outcomes should be cautiously assessed in various settings when other health statuses could confound the results. Brown et al. showed that higher bilirubin level was associated with lower risk of acute exacerbation of COPD.<sup>18</sup>

In patients with chronic obstructive pulmonary disease (COPD), higher serum bilirubin levels within the normal range may be associated with lower mortality and risk for exacerbations, a reduced incidence of COPD diagnoses, and improved lung function. Results of the analysis were published in the journal BMC Pulmonary Medicine.<sup>19</sup>

### **Conclusion**

Reduced lung function is associated with increased levels of systemic inflammatory markers which may have important pathophysiological and therapeutic implications for subjects with stable OPD. Oxidative stress is one of the major physio pathological hallmarks in the development of COPD.

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