Comparative Study on Soluble Urokinase-Type Plasminogen Activator Receptor (SuPAR) and C-Reactive Protein (CRP) Levels in Stable Chronic Obstructive Pulmonary Disease

D. Rekha¹, Priscilla Johnson²*, Subhasis Das¹, B. Rajagopalan³, G.R. Sathya¹ and Lavanya Sekhar²

¹Department of Physiology; Pondicherry Institute of Medical Sciences, Puducherry-605014, India.
²Department of Physiology; Sri Ramachandra Medical College & Research Institute, SRIHER, Porur, Chennai- 600116, India.
³Department of Chest & TB; Sri Ramachandra Medical College & Research Institute, SRIHER, Porur, Chennai- 600116, India.
*Corresponding Author Email: priscillajohnson@sriramachandra.edu.in

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Chronic obstructive pulmonary disease (COPD) occurs due to inflammatory lung response characterised by progressive airflow obstruction.¹,² Lung parenchymal destruction with decrease in mucociliary clearance (MCC) and phagocytic activity of alveolar macrophages occurs leading to an increased risk of exacerbation. This alteration in the lung defence mechanism and oxidative stress can lead to mortality among exposed due to COPD³-⁵.
Conventionally, the diagnosis for SCOPD was by clinical symptoms and pulmonary function test (PFT). However, there is a need for a better tool to monitor prognosis of COPD. In the ECLIPSE cohort studies for COPD, previous exacerbation, older age, increased WBC count and poor health status were associated with increased risk of future hospitalization. Various biomarkers like C-reactive protein (CRP) and fibrinogen have been assessed to know the association of disease severity and mortality risk among COPD patients. Recent systematic review has showed that CRP was consistently elevated in COPD patients compared with control groups. However, these routine non-specific markers are not reliable for assessing disease mortality and prognosis.

Recent studies have shown that suPAR is a more stable biomarker for low-grade pulmonary inflammation. The cleavage of urokinase plasminogen activator receptor (uPAR) from the inflamed respiratory epithelium into suPAR, reflects the pathogenesis (both small airway fibrosis and emphysema) of COPD through complex molecular pathways and gene expression patterns. Assessment of serum suPAR reflects lung function impairment during acute exacerbation and for monitoring treatment response. To assess and compare the serum soluble urokinase-type plasminogen activator receptor (suPAR) and C-reactive protein (CRP) levels in stable COPD.

**Aim**

To assess and compare the serum soluble urokinase-type plasminogen activator receptor (suPAR) and C-reactive protein (CRP) levels in stable COPD.

**METHODOLOGY**

After obtaining IEC clearance Institutional Ethics Committee [IEC-NI/17/JUN/60/59], this cross- sectional study was carried out in a private medical college hospital in Puducherry, South India among stable COPD study participants. SCOPD study participants (n=50) with history of dyspnoea, chronic cough and sputum production for a period of 3 months for 2 consecutive years and apparently healthy controls (n=50) aged between 35-65 years inclusive of both sexes were included in the study based on the selection criteria after getting informed consent. Subjects with history of bronchial asthma, bronchiectasis, cystic fibrosis, collagen tissue disease, cirrhosis of liver and renal failure with conditions that could affect serum suPAR and CRP levels were excluded from the study. General information such as age, gender, occupation, literacy status, smoking status and socio-economic status were collected using a standard questionnaire. Study participants were subjected to spirometry and post-bronchodilator testing and were then grouped into grades I - IV as per Global Initiative for Obstructive Lung Disease (GOLD) criteria. Blood samples were collected from the study participants and serum suPAR and CRP levels were measured using Abcam’s Human Table 1. Descriptive characteristics of the study population

<table>
<thead>
<tr>
<th>Descriptive characteristics</th>
<th>Control N(%)</th>
<th>SCOPD N(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-55</td>
<td>29(58%)</td>
<td>34(68%)</td>
</tr>
<tr>
<td>55-65</td>
<td>21(42%)</td>
<td>16(32%)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38(76%)</td>
<td>35(70%)</td>
</tr>
<tr>
<td>Female</td>
<td>12(24%)</td>
<td>15(30%)</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight/Healthy</td>
<td>39(78%)</td>
<td>37(74%)</td>
</tr>
<tr>
<td>Overweight</td>
<td>5(10%)</td>
<td>8(16%)</td>
</tr>
<tr>
<td>Obese</td>
<td>6(12%)</td>
<td>5(10%)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed/ Semi-skilled</td>
<td>45(90%)</td>
<td>44(88%)</td>
</tr>
<tr>
<td>Skilled</td>
<td>5(10%)</td>
<td>6(12%)</td>
</tr>
<tr>
<td>Education status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>44 88%</td>
<td>45(90%)</td>
</tr>
<tr>
<td>Literate</td>
<td>6(12%)</td>
<td>5(10%)</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoker/Ex-smokers</td>
<td>40(80%)</td>
<td>5(10%)</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>10(20%)</td>
<td>45(90%)</td>
</tr>
</tbody>
</table>
ELISA (Enzyme-Linked Immunosorbent Assay) kit.11

**Statistical Analysis**

Results were tabulated in EXCEL and data analysis was done by using SPSS software version 20.0. The difference between control group and different grades of SCOPD were analysed using ANOVA.

**RESULTS**

The present cross-sectional study was conducted among 50 SCOPD study participants and 50 apparently healthy controls with age group 35 to 65 years. The distribution of study participants based on age, gender, occupation, literacy status, socio-economic and smoking status is shown in Table 1.

Table 2 shows Mean ± SD for Pulmonary function parameters like Forced expiratory volume in the 1st second (FEV1% predicted), Forced Vital Capacity (FVC), FEV1/FVC ratio, peak expiratory flow rate (PEFR) for control group and mean ± SD for post-bronchodilator parameters like FEV1% predicted, FVC, FEV1/FVC ratio and for SCOPD participants.

Table 3 represents Mean ± SD values for serum suPAR and CRP level among different SCOPD grades and controls. It was observed that levels of suPAR and CRP among SCOPD were high compared to healthy control. In addition, Serum suPAR and CRP levels were high among GOLD IV and III compared to GOLD II and I, which was statistically significant (p=0.000)

**DISCUSSION**

This cross-sectional study which involved SCOPD participants (grade I to IV) and healthy controls showed that the plasma suPAR level was higher among SCOPD grade III and IV compared to grade I and II. This indicates the role of urokinase plasminogen activator system in lung parenchymal destruction and small airway fibrosis. Similar finding has been reported by Can U et al., who observed that serum suPAR was high among grade III and IV than grade I,II and control groups.

Moreover, the raised suPAR level in SCOPD participants in our study could be due to increased expression of suPAR in the small airway epithelia and pulmonary epithelial-mesenchymal transition process among SCOPD patients which lead to disease progression and it could also be due to increased expression of urokinase plasminogen activator receptor in the small airway epithelia of SCOPD patients which contributes for the airflow limitation due to activation of inflammatory immune response. Similar finding is reported by a study done by Wang et al., and Godtfredsen et al., which shows suPAR level was higher among grade IV SCOPD when compared to grade I-III and normal subjects.13,14 Besides, studies done by Prins HJ and AboEl-Magd GH have also shown that serum suPAR was high among SCOPD than normal individuals due to activation of pulmonary inflammation.15,16
In this study, it was observed that CRP levels were also elevated in SCOPD study participants when compared to the controls. Similar observation was reported in a study which indicated CRP as a promising diagnostic marker among SCOPD. Study done by Al-Aarag et al., and Zhang et al., also found a significant difference between the COPD and the control group in relation to the CRP level which was similar to our study results. Systematic review done by few researchers confirmed that CRP levels increases in patients with stable COPD among different grades with decline in lung function. Yende S et al., and Broekhuizen R et al., also observed that the CRP level was high among SCOPD than normal individuals and the difference was statistically significant. In a study done by Sever ZK et al., it was reported that serum CRP and suPAR levels were high among COPD patients which suggested that they have significant roles in systemic inflammation associated with worse prognosis and severity.

Similarly, meta-analysis has shown that serum suPAR was high among grade IV compared to grade I and the level of suPAR correlated with diseases severity hence suPAR was suggested to be used clinically to monitor COPD patients on treatment and their prognosis. In addition suPAR is a very stable biomarker when compared to CRP, less affected by the exacerbation and directly related to disease severity which favours its high prognostic value for COPD.

**Limitation of the Study**

Drug intervention with novel anti-inflammatory therapy and follow up for lung function decline was not done to rule out ongoing pulmonary inflammation among stable COPD patients.

**CONCLUSION**

The study results support that suPAR and CRP can be used as surrogate biomarker to predict the inflammatory changes among COPD patients. suPAR seems to be independent, stable biomarker when compared to CRP, less affected by the exacerbation and is better than CRP in discriminating adverse outcome and severity progression. Further, prospective studies need to be conducted to explore whether suPAR can be used as a novel biomarker in predicting the severity of SCOPD in the early stages of disease.

**ACKNOWLEDGMENT**

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**Conflict of Interest**

None.

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**REFERENCES**


