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**Title:** Role of pulmonary bio-markers in systemic inflammation in chronic obstructive pulmonary disease: A one year follow up study

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**Body:** Background & Aim: Elevated circulating levels of inflammatory biomarkers have been found to play an important role in Patients of COPD. We measured TNF alpha, IL6, and CRP levels in COPD patients and assessed their relationship with smoking status, inflammation and disease. Methods: we assessed three blood biomarkers in 202 COPD patients, 50 current smokers with normal lung function and 30 non smokers. Subjects were evaluated with medical history, Spirometry, 6-minute walk test, BODE index. Biomarkers repeatability was assessed using baseline and 1- year follow up samples. Results: Serum TNF Alpha Level was higher in COPD patients than smokers controls and Non smokers controls at the base line and at 1 year interval (p value- 0.001]. CRP and IL6 were also significantly higher in COPD patients compared to smoker and non smoker controls. TNF Alpha showed moderate repeatability and was found to be least variable bio-marker over 1- year period with a high degree of statistical significance and multiple regression analysis for CRP, IL-6 confirmed only their association with disease and not smoking status.

Repeatability of Biomarkers over one year Interval

Biomarkers		Baseline			one year interval		p value
	COPD Subjects	smoker controls	Non Smoker Controls	COPD Subjects	Smoker control	Non Smoker Controls	
<b>TNF Alpha(pg/ml)</b>	4.2 (4.9)	3.8 (4.2)	2.9 (3.7)	3.9 (4.8)	3.6 (4.4)	2.6 (3.8)	< 0.001
<b>IL6 (pg/ml)</b>	0.9 (1.8)	0.38 (1.4)	0.27 (1.8)	0.6 (2.6)	0.42 (1.8)	0.23 (1.6)	0.002
<b>CRP (pg/l)</b>	6.2 (8.2)	3.8 (6.4)	2.8 (4.24)	5.7 (8.2)	3.2 (6.82)	2.4 (5.2)	< 0.001

Conclusions: Smoking is associated with higher levels of TNF- alpha mediated systemic inflammation with or without COPD.