Evaluation of HS-CRP and Lipid Profile in COPD

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ABSTRACT

Introduction: COPD is a major public health problem. More than 50 % of the patients of COPD die because of some cardiovascular event. Traditionally, the risk of CVD is assessed by the presence of dyslipidaemia. Recently, HS-CRP has emerged as a novel risk factor for the CVD assessment. In this study, we assessed the patients of COPD for CVD with HS-CRP and lipid indicators.

Material and Methods: Forty Five diagnosed patients of COPD and 45 age, sex, and BMI matched healthy controls were enrolled for the study after the institutional ethical committee's clearance was obtained. The fasting serum samples of the study subjects were evaluated for the lipid profile and HS-CRP.

Results: There was no statistical difference in the lipid profile in the two groups, while HS-CRP was significantly raised in the COPD patients. On applying kappa statistics, we found a poor agreement between the lipid parameters and HS-CRP in estimating the risk for CVD. This underlines the independent importance of HS-CRP in the CVD assessment of COPD patients.

Discussion: GOLD has described COPD as a systemic chronic inflammatory disease which involves the lung and the distant organs by the emissary of the systemic inflammation, which is also an antecedent to cardiovascular diseases. COPD is a systemic inflammatory disease which is underlined by this study. But the derangement of the lipid indicators is not statistically significant. This suggests the addition of HS-CRP in the assessment of the COPD patients for CVD. This further needs to be ascertained in a large prospective model.

Conclusion: COPD is systemic inflammatory disease, but there is hardly any derangement of the lipid indicators.

INTRODUCTION

COPD has increasingly been an important health problem worldwide, also in India. The prevalence of COPD in India is 4.1% [1]. The Global Initiative for Obstructive Lung Disease (GOLD) guidelines have defined COPD as 'a disease state which is characterized by an airflow limitation that is not fully reversible' and depending upon the predicted FEV1%, COPD is categorized into 4 stages [2] [Table/Fig-1]. The airflow limitation is usually progressive and it is associated with an abnormal inflammatory response of the lungs to noxious particles and gases, which ultimately leads to systemic inflammatory diseases. The systemic involvement manifests in the forms of musculoskeletal dysfunction, cachexia, a decreased BMI, etc. [3]. The systemic nature of the disease is also evident from the raised oxidative biomarkers, interleukins, HS-CRP, etc in the serum [4, 5]. COPD is associated with several comorbidities like hypertension, Diabetes mellitus and Cardiovascular Disease (CVD) [6-8]. Amongst these, CVD is the most prevalent cause of comorbidities and the second most common cause of mortality, next to respiratory failure [6]. More than just an association of CVD in COPD, there is a real presence of stiffened central arteries in COPD. This is shown by the accelerated pulse wave velocity which underlines the presence of the stiffness and the associated atheroma burden [9].

The antecedent presence of the systemic inflammation in COPD is the most favoured hypothesis which can explain the presence of CVD in COPD. A number of inflammatory markers have found to be elevated in COPD, like IL-6, TNF-alpha and fibrinogen [10]. The circulating CRP levels are associated with an increased mortality in COPD. CRP is found to be inversely associated with the FEV1 %, which is predicted in stable COPD [4,11]. High sensitive C-Reactive Protein (HS-CRP) is considered as a marker of systemic inflammation and this is also assessed for the primary stratification of the general population for the risk of CVD [12].

Traditionally, dyslipidaemia is considered to be one of the most important risk factors for the development of atherogenesis and to assess the cardiovascular risk. Increased LDL cholesterol levels and decreased HDL cholesterol levels are indicative of an atherogenic lipid pattern [13].

HS-CRP i.e. high sensitive C-reactive protein is an indicator of a low grade systemic inflammation. Now-a-days, it is used to stratify the general population for cardiovascular risk assessment in the mild (0-1 mg/L), moderate (1-3 mg/L) and the severe (>3 mg/L) categories. Moreover, HS-CRP is considered as independent risk factor other than dyslipidaemia [12].

So, the aim of the present study was to evaluate the levels of both HS-CRP and the lipid profile and to reveal the correlation with FEV1%, as is predicted in COPD and to assess the agreement in between these parameters in COPD.

MATERIAL AND METHODS

In this study, 45 stable COPD patients who attended the Respiratory Medicine OPD were enrolled, after obtaining the approval of the institutional ethical committee. They were devoid of any acute exacerbation. A history regarding their smoking status was obtained, which showed that 40 patients were ex-smokers who

had left the habit of smoking at least 5 years back and 5 were never smokers. The patients were categorized into the GOLD stages according to their pulmonary function tests [Table/Fig-1]. Their fasting blood samples were collected for the measurement of HS-CRP and, the lipid profile (Total cholesterol, Triglycerides, LDL, and HDL).

Methods: HS-CRP was measured by the latex immunoturbimetric method.

The lipid parameters were measured by routine enzymatic methods which are commercially available. The ratio of total cholesterol and HDL was calculated and the patients who had a ratio of TC: HDL which was > 4 were considered to be at a high risk for CVD.

Study design: Case control study

Study duration: 1 year

Study Area: A hospital based study from a tertiary care hospital

Selection of the cases: The cases of COPD were defined from the GOLD guidelines, based on the FEV 1% levels which were predicted.

Selection of the controls: Age and sex matched controls were selected from the same hospital set up from amongst the relatives who visited the patients and who did not fit in the case definition.

The case report form included information about the age, sex, BMI, a h/o of smoking in pack years and the exposure to biosmoke of the patients.

Informed consents were obtained from both the cases and the controls.

An approval was obtained from the **institutional ethical committee.**

Statistical analysis: The data was entered into Microsoft Excel and SPSS, version 17 was used. The unpaired t test and kappa statistics were used.

Gold stage	severity	Spirometry
0	At risk	Normal
1	mild	FEV1/FVC< 0.7 and FEV1<=80% predicted
2	moderate	FEV1/FVC< 0.7 and FEV1 = 50-80 % predicted
3	severe	FEV1/FVC< 0.7 and FEV1=30-50% predicted
4	Very severe	FEV1/FVC< 0.7 and FEV1 < 30% predicted or FEV1< 50% predicted with respiratory failure or signs of right heart failure.

[Table/Fig-1]: GOLD criterion to diagnose and categorize COPD patients

	Patient (mean±s.d)	Control (mean±s.d)	p-Value
Age	61±11.31	59±10	0.42
FEV1 PRED	43.27±15.5	78.33±12.8	0.20
Hs-CRP	4.6±2.8	0.9±0.2	<0.001
TCH	167±31	188±24	0.09
LDL	96.61±29.24	90.2±25.1	0.3
TG	98.8±46.46	88±36	0.09
HDL	50.6±17.06	60±14.5	0.29
TC/HDL	3.6±1.22	3.03±1.1	0.49

[Table/Fig-2]: Age, and result of PFT in the patients and controls

Lipid Parameter	HS CRP<3 mg/L	HS CRP>3 mg/L	P value
Total cholesterol	170.2 ± 7.601 N=18	164.9 ± 5.905 N=27	0.1
Triglycerides	99.33 ± 9.691 N=18	98.44 ± 9.686 N=27	0.4
HDL Cholesterol	49.28 ± 2.784 N=18	51.52 ± 3.845 N=27	0.3
LDL cholesterol	101.1 ± 7.024 N=18	93.64 ± 5.590 N=27	0.2

[Table/Fig-3]: Lipid indicators x HSCRP in COPD

	High risk for CVD by TC/HDL if ratio > 4		
High risk for CVD by HSCRP YES(>3mg/L) NO (<3mg/L)	YES	NO	Total
	4	11	15
	10	20	30
Total	14	31	45

[Table/Fig-4]: Kappa statistics for agreement between high risk for CVD by hs-CRP and TC/HDL
Kapa Value = 0.1(Indicating of poor agreement)

RESULTS AND OBSERVATIONS

[Table/Fig-1] The lipid markers and the HS-CRP were analyzed in the cases and the age and sex matched controls. The smoking habits were also controlled; the patients were ex smokers who had quit the habit of smoking at least years back and the controls were never smokers. This showed that in the patients with COPD, the HS- CRP levels were significantly higher than in the controls, while there was no significant difference in the levels of the lipid indicators between the controls and the COPD patients.

Then, we categorized the patients, based on their HS-CRP levels; an HS-CRP level of > 3.0 mg/L is taken as high risk for CVD and it was seen that the lipid indicators were still not statistically different between these 2 groups, as has been shown in [Table/Fig-2].

Further, we tried to assess the risk for CVD, based on the HS-CRP and the TC/HDL ratio, by using kappa statistics. A ratio of TC/HDL which was > 4 was considered as high risk for CVD. This exercise, as has been shown in [Table/Fig-3], showed a poor agreement (kappa= 0.1) between these two.

This concluded that the HS-CRP measurement could be more sensitive in picking up the COPD patients with a high risk for CVD, which needs to be ascertained by doing a cohort study [Table/Fig-4].

DISCUSSION

COPD is a disease, not only of the lung compartment, but it involves many other distant systems, by way of the spillage of the local inflammation into the systemic circulation. This is supported by the elevated levels of various inflammatory indicators like TNF-alpha, fibrinogen and HS-CRP and various interleukins. Meta-analytical studies have shown that more than 50% of the COPD patients die of cardiovascular diseases. In our study, we estimated the traditional lipid parameters and the novel risk indicator, HS-CRP and it was seen that there was very poor agreement between these two. This showed that both were behaving independently in the COPD patients. Clearly, the patients had more HS-CRP than the controls, but there was no statistical difference in the levels of the lipid indicators. This may be due to the fact that HS-CRP is the earlier response of the body, as it is secreted as acute phase reactants by the liver in response to IL-6. It seemed that the changes in the lipid markers had a late chronology and that so it was not easy to pick up the cases of high risk CVD. Though

it is not possible to comment on the cause and the effect relation between the raised CRP and the lipid indicators, it was learnt from the current study, that HS-CRP should be added as a laboratory indicator to assess the cardiovascular risk in COPD patients, along with the lipid profile.

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