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Research article

ALPHA – 1 ANTITRYPSIN IN SMOKERS AND NON SMOKERS CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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ABSTRACT

Aim: The aim of the present study is to correlate and compare alpha-1 antitrypsin level in smoker and non smoker chronic obstructive pulmonary disease patients. **Material and Methods**: A comparative study was carried out in 200 subjects, more than 40 years of age and having chronic obstructive pulmonary disease for more than 1 year with a history of smoking at least 20 cigarettes per day (Group A) and without a history of smoking (Group B). Pulmonary function tests were used to diagnose the disease as per the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification. Alpha-1 antitrypsin level was done by turbidimetry method on fully auto analyzer I-Lab 650 (Instrumentation Laboratory, USA) at Clinical Biochemistry Section, Laboratory Services Sir Takhtsinhji Hospital, Bhavnagar. Statistical analysis was done by using unpaired t-test and Pearson's correlation coefficient. **Results:** Results of present study shows that alpha-1 antitrypsin level was decreased in smoker chronic obstructive pulmonary disease patients (150.83±18.853) when compared to non smokers (183.97±29.383). There was statistically significant difference in alpha-1 antitrypsin level between the two groups with 'p' value of <0.0001. Pearson's correlation test show negative correlation between smoker and non-smoker chronic obstructive pulmonary disease patients. **Conclusion**: The values of serum alpha-1 antitrypsin levels were more significantly decreased in smokers indicating an important role of smoking in pathogenesis of chronic obstructive pulmonary disease. Alpha-1 antitrypsin can act as a predictor for future development of chronic obstructive pulmonary disease in smokers and in nonsmokers.

Keywords: Alpha-1 antitrypsin, Chronic Obstructive Pulmonary Disease (COPD), Forced Expiratory Volume (FEV), Global Initiative for Chronic Obstructive Lung Disease (GOLD)

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined as a disease state characterized by airflow limitation that is not fully reversible and it includes emphysema, an anatomically defined condition characterized by destruction and enlargement of the lung alveoli; chronic bronchitis, a clinically defined condition with chronic cough and phlegm; and small airways disease, a condition in which small bronchioles are narrowed [1]. The chronic airflow limitation is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema) [2]. In developing countries, cooking on open fire with subsequent exposure to excessive smoke in close environments, and mining-related pollution can cause the disease[3]. Chronic obstructive pulmonary disease is a major cause of health care burden worldwide and the only leading cause of death that is increasing in prevalence. The regional chronic obstructive pulmonary disease working group for 12 Asia Pacific countries and

regions used a prevalence model for this disease and estimated an overall prevalence rate of 6.3 % with a range from 3.5 to 6.7 %[4]. Prevalence of COPD in India with a median of studies (up to 1995) was 5.0% and 2.7% in men and women, respectively and in 2006 was 5.0% and 3.2% in men and women respectively[5]. Chronic obstructive pulmonary disease (COPD) is rapidly becoming a global public health crisis with smoking being recognized as its most important causative factor. There is mounting evidence that the rate of progression of chronic obstructive pulmonary disease can be reduced when patients at risk of developing the disease stop smoking, while lifelong smokers have a 50% probability of developing chronic obstructive pulmonary disease during their lifetime[6]. Cigarette smoke activates macrophages and epithelial cells to release chemotactic factors that recruit neutrophils and CD8 cells from the circulation. These cells release factors that activate fibroblasts, resulting in abnormal repair processes and bronchiolar fibrosis [7].

Alpha-1 antitrypsin deficiency is associated with a substantially increased risk for the development of chronic obstructive pulmonary disease, often by the third or fourth decade, and is also associated with risks for development of liver disease, cutaneous panniculitis, bronchiectasis, vasculitis, and Wegener's granulomatosis[8]. There are posttranslational modifications of alpha-1 antitrypsin in patients with chronic obstructive pulmonary disease, is that of oxidation, thought to be due to exposure to cigarette smoking components. Reactive oxygen and nitrogen species, which are increased in smokers, may target and modify the alpha-1 antitrypsin [9]. Alpha-1 antitrypsin deficiency is inherited as an autosomal – co dominant disorder, characterized by serum (and hence, lung) level of alpha-1 antitrypsin far below the laboratory reference range of 90 – 200 mg/dl. Normal level neutralizes the activity of neutrophil elastase, a protease that destroys elastin and other connective tissue components in the lung; however, a deficiency of alpha-1antitrypsin represents an imbalance in favour of neutrophil elastase and, therefore, increases the risk of emphysematous lung destruction [10, 11].

The present study is designed to measure and compare the changes in alpha-1 antitrypsin level in patients with chronic obstructive pulmonary disease with and without smoking.

MATERIALS AND METHODS

Study was conducted on the patients of COPD attending the Pulmonary Medicine department at Sir Takhtsinhji General Hospital, Bhavnagar during period of November 2013 to March 2014. Study included 100 patients of chronic obstructive pulmonary disease (COPD) with smoking (Group A) and 100 patients without smoking (Group B).

Inclusion criteria: Included patient age more than 40 years, both male and female with prior diagnosis of chronic obstructive pulmonary disease (COPD) by PFT (pulmonary function test). Ethical clearance was obtained from the institutional review board of Govt. Medical College, Bhavnagar. Informed consent was taken from all the subjects.

Exclusion criteria: Patient has alternative cause for their respiratory disorders e.g. asthma, lung cancer, sarcoidosis, tuberculosis, lung fibrosis, cancer or had cancer in the 5 years prior to study entry or had undergone lung surgery, patient having diabetes mellitus, renal failure, hypertension, cardiac disorders, liver disorders, hepatocellular carcinoma and bladder cancer, patient with habit of tobacco chewing along with smoking were excluded.

Venous blood was collected in plain vacutte from all the participants. Fresh serum was separated by centrifugation. Assay was performed on ILAB-650 fully auto analyzer (Instrumentation Laboratory, USA) at Biochemistry Laboratory accredited by National Accredited Board for Testing and Calibration Laboratory as per ISO 15189:2007 guideline. AAT was analyzed by serum anti-human alpha-1 antitrypsin which reacts specifically with the alpha1-antitrypsin of the sample to yield an insoluble aggregate which is measured by turbidimetry method[12] with commercially available ready to use reagent kits. The recorded parameters were compared in both the groups.

Stastical analysis: All the values were presented as Mean ± SEM. Data were checked for normal distribution using GraphPad InStat (version 3.00, GraphPad Software, California USA). In data analysis, comparison of this parameter between smokers and non-smoker COPD patients was carried out by applying unpaired t-test and their correlation was studied by applying Pearson Correlation test. Pearson's correlation coefficient test was used for correlation of serum AAT level and predicted FEV1

% in smoker and non smoker COPD patients. Interpretation was done according to p-value. *P* value <0.05 was considered as statistically significant.

RESULTS

Table 1: Comparison of serum AAT level between two groups

Statistics	Serum AAT(mg/dl)[$]	
	Group A (COPD Smoker)	Group B (COPD Non Smoker)
Mean ± SD	150.8±18.8	183.9±29.3
Minimum	116	136
Maximum	229	309
Significance	*** p < 0.0001	

*** p < 0.0001: highly significant difference between two groups by applying unpaired t-test with confidence interval. [$]Reference Interval **(90-200 mg/dl)**

Table-2: Comparison of FEV 1 % between Group A and Group B

Statistics	*FEV 1 % (Normal:≥80%)*	
	Group A (COPD Smoker)	Group B (COPD Non-Smoker)
Mean ± SD	48.84±13.6	77.17±14.7
Minimum	16	32
Maximum	88	96
Significance	*** p < 0.0001	

Unpaired t-test with confidence interval of 95%

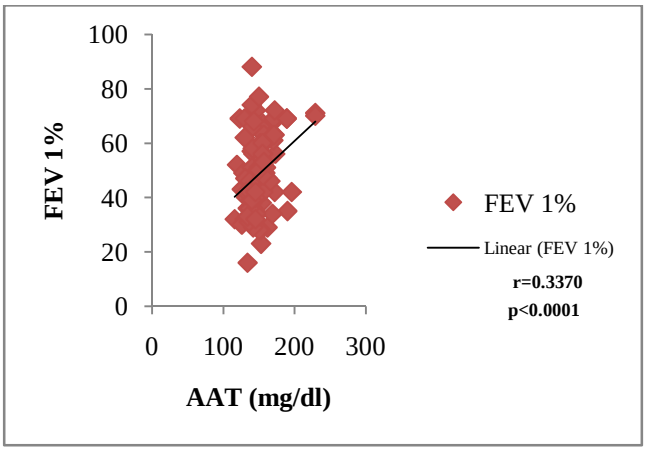

Fig 1: Correlation between serum AAT and FEV 1% in Smoker COPD Patients

In this study we measured Serum activity of AAT in both groups. There is highly significant difference observed in between group A and group B patients.

A positive correlation was observed between AAT levels and FEV 1% in smoker and non – smoker COPD patients with a Pearson correlation coefficient of 0.3370 and 0.5026 (p<0.0001) respectively. (Fig 1 and 2)

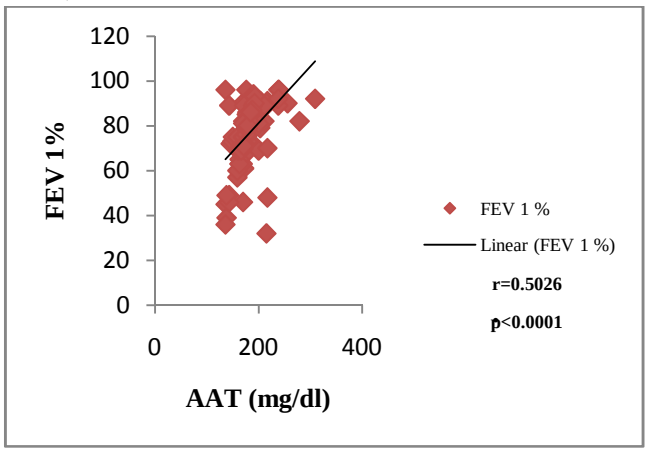

Fig 2: Correlation between serum AAT and FEV 1% in Non – Smoker COPD Patients

On analysis by using unpaired t – test the differences in AAT levels between the two groups was statistically highly significant with 'p' value of <0.0001.

DISCUSSION

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. The chronic airflow limitation is caused by a mixture of small airway disease (obstructive bronchiolitis) and parenchymal destruction (emphysema). Globally, COPD has been expected to become the 3rd most leading cause of death and the 5th leading cause of loss of 'Disability Adjusted Life Years' (DALYs) as per projection of the Global Burden of Disease Study (GBDS) [2, 13].

Tobacco use kills more than five million people a year and accounts for 10% of adult deaths worldwide. Smoking recognized as a most important causative factor for COPD. Several meta-analyses have shown that all pharmacotherapy for smoking cessation are twice as likely more efficacious than placebo with an abstinence rate in the 25-30% range at one year when pharmacological treatment and behavioural support are combined [6].

Alpha-1-antitrypsin has 394 amino acids and 3 glycosylated side chains coupled to asparagines. The

amino acid methionine is present at position 358 and it is susceptible to convert in methionine sulfoxide by oxidants from cigarette smoke, rendering it much less potent inhibitor of neutrophil elastase [14].

AAT level was lower in COPD patients with smoking as compared to COPD patients without smoking. The present study shows the significant difference in serum AAT level between the two groups ($p<0.0001$). This study supports the data of previous studies F. Ogushi et al. 1991 [15], Oliver Senn, Erich W Russi, Christian Schindler et al. 2008 [16] and Deore Deepmala et al. 2012 [2].

There are, however, some limitations to the current study most notably that, the cost of the parameter is high and the sample size is small.

Findings of the present study suggest that serum AAT levels were significantly reduced in smokers COPD in comparison to non smoker COPD patients. Therefore, AAT levels can be taken as a parameter to determine the progress of COPD and it can be used as an important tool in the management of COPD. Moreover, serum AAT and FEV 1% can also be used as a risk factor of chronic obstructive pulmonary disease along with smoking as they have significant correlation in chronic obstructive pulmonary disease.

CONCLUSION

In conclusion, serum AAT levels were significantly lower in smoker COPD patients in comparison to non-smoker COPD patients and there was a positive correlation between alpha-1 antitrypsin and FEV 1% in smoker and non-smoker COPD patients. Therefore, smoking cessation and correction of alpha-1 antitrypsin levels may be beneficial in COPD patients for better management of the disease.

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Conflict of Interest : Nil

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