



Original Research Article

Total serum IgE level in COPD exacerbations

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ABSTRACT

Background: COPD exacerbations were diagnosed based on the clinical parameters only. Till now we were unable to find out a reliable blood based biomarker. Serum IgE is one of the measurements of airway inflammation which is well established in asthma, it's role in COPD not studied adequately.

Materials and Methods: This is a cross sectional study conducted in a tertiary care center. This study included 75 COPD patients who were admitted in our hospital for exacerbations. Exacerbations defined by the GOLD report 2018. Complete history & Total serum IgE levels were obtained from all patients during admission, pulmonary function test has been done at the time of discharge and results were analyzed.

Results: In our study the mean value of serum IgE is 416.75 IU/L. Patients who had elevated serum IgE (>100 IU/L) levels were 55 (73.3%). FEV₁/FVC ratio significantly high in elevated IgE group (0.58±0.09 in elevated IgE vs 0.49±0.10 in IgE not elevated, p<0.001). Post BD change in FEV₁ was significantly more in elevated IgE group (13.7%+185ml in elevated IgE vs 6.4%+73ml in IgE not elevated, p=0.001). IgE elevated patients have seasonal variation history, Biomass exposure history. They had more Asthma COPD Overlap features than IgE not elevated group (p=0.001).

Conclusion: COPD patients can have elevated serum IgE levels during exacerbations. IgE may play an important role in pathogenesis of COPD and can be used as a biomarker for COPD Exacerbations.

Key message: Serum total IgE can be used as a biomarker in COPD exacerbations. This can be used as a new therapeutic target for the same.

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1. Introduction

An exacerbation of Chronic Obstructive Pulmonary Disease (COPD) is defined as an acute worsening of respiratory symptoms that results in additional therapy. Exacerbations negatively impacts on the health status of the patient, increases the health care utilization, and disease progression. They are mainly triggered by the viral, bacterial infections and air pollution.¹

Acute Exacerbations of COPD (AECOPD) are usually diagnosed based on the clinical judgement due to their heterogeneity and lack of diagnostic laboratory tests, so that is subjective and variable across the clinicians.

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Because of this there are so many biomarkers studied in AECOPD, in which most studied biomarkers were C-reactive protein (CRP), interleukin-6 (IL-6), and Tumor Necrosis Factor-alpha (TNF- α). Among these only CRP showed consistent elevations in AECOPD.² But CRP is a non-specific biomarker. So we are in need of specific biomarkers. In asthmatics Immunoglobulin E (IgE) triggered mechanism plays an important role in clinical expression of the disease and its exacerbations.³ Similar mechanisms also found in COPD also. Stoll et al. found that patients with COPD displayed an overexpression of the high-affinity IgE receptor on plasmacytoid dendritic cells as found in allergic asthma.⁴ This suggest that IgE may be involved in the pathogenesis/progression of some phenotypes of COPD.⁵ Some of the previous studies stated that stable COPD

patients can have elevated serum IgE levels and that may have an effect on progression of COPD or could be used as a marker to reflect the severity of disease.⁶

Hence there are so many triggers for IgE production detecting some of the common antigen specific IgE cannot reflect the condition of the patient completely. So detecting the Serum Total IgE may be a reliable marker for the airway inflammation of host. This is well established in asthma.^{7–10} But the role of serum IgE in COPD patients has not been established till now.

2. Materials and Methods

This is a single center, cross sectional study conducted in a tertiary care center in Varanasi, India from December 2018 to June 2019. The study population mainly from eastern Uttar Pradesh and Bihar. After approval from Institute Ethical Committee, 75 patients who were admitted in our hospital for COPD exacerbations were included in this study. Exacerbations were defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) report 2018.¹ This study included already diagnosed COPD patients who were on inhaled medications (non-steroid) for atleast 1 year. We excluded the patients who have history of lung cancer, who received systemic steroids in last month, not adherent to previous medications and comorbidities like pulmonary hypertension, who were unable to perform Pulmonary Function Test (PFT) properly. Patients having food allergy, parasite infections, allergic inflammation of other systems such as skin were excluded by history and clinical examination. All the study subjects gave informed written consent. Complete history of the patient obtained like age of onset of symptoms, no. of exacerbations in last year, previous inhaler use, seasonal variations, and diurnal variations etc.

Serum IgE levels were measured during admission by the Chemiluminescent immunoassay. IgE levels were considered raised if >100 IU/L based on previous studies.⁶ Serum Absolute Eosinophils Count (AEC) also measured by Autoanalyzer, at the time of admission. Pulmonary Function Test has been done at the time of discharge (performed by Vyaire, Germany). Bronchodilator reversibility response assessed after inhalation of salbutamol 400mcg.

Patients were evaluated for the Asthma COPD Overlap (ACO) features by the Syndromic approach stated by Global Initiative for Asthma (GINA) report 2018.¹¹ If patients have both Asthma symptoms and COPD symptoms they were assessed by Pulmonary Function Test. If Post Bronchodilator (BD) reversibility also present they diagnosed as ACO.

Statistical analysis were done using Statistical Package for the Social Sciences (SPSS) 20. Continuous data are expressed in means and standard deviation (SD), categorical data are expressed in percentage. Chi-squared test, *T*-test, Mann–Whitney U test (for abnormal distribution

parameters) and Spearman's correlation test was used for correlation analysis

3. Results

This study included total 75 patients of COPD exacerbation, in this Male 43% (n=32) and Female 57% (n=43). Baseline characteristics of the study subjects given in Table 1. Mean age in our study population is 64 years. Onset of symptoms mostly above 40 years (57%) of age.

In the present study the mean value of serum IgE is 416.75 IU/L. Patients who had raised serum IgE levels were 55 (73.3%). In the IgE elevated group there was no significant difference in sex [male-20 (62.5%), female-35 (81.4%), *p*=0.067]. Main results of our study given in Table 2. IgE elevated patients have seasonal variation history, Biomass exposure history (*p*<0.05).

3.1. Spirometric variables

Forced Expiratory Volume in one Second/Forced Vital Capacity (FEV₁/FVC) ratio significantly high in elevated IgE group (0.58±0.09 in elevated IgE vs 0.49±0.10 in IgE not elevated, *p*<0.001). Post Bronchodilator reversibility in FEV₁ was significantly more in elevated IgE group (13.7%+185ml in elevated IgE vs 6.4%+73ml in IgE not elevated, *p*=0.001). IgE elevated group had more Asthma COPD Overlap (ACO) features than IgE not elevated group (*p*=0.001). Correlations between variables shown in Table 3. Post BD FEV₁/FVC ratio and FEV₁ change (% and volume), Post BD reversibility, AEC have strong positive correlation to IgE (*p*<0.05). Age, Smoking history, Hyperinflation, previous exacerbation history have weak negative correlation with IgE.

4. Discussion

Serum Total IgE has a clear role in airway inflammation in Asthma,^{7–10} but this relation is not well established in COPD. Some of the previous studies showed that stable COPD patients also has raised serum IgE. In a study conducted by Božek A et al. demonstrated that raised allergen specific IgE levels were observed in 33.3% of patients with diagnosis of COPD. This was higher incidence than healthy subject group and lower than asthmatic group. But the IgE level of COPD patients were higher than non-allergic asthma phenotype.¹² To our knowledge this is the first study to document the elevated serum IgE level in COPD exacerbations. In our study the mean Total Serum IgE level in COPD exacerbation is 416.75 IU/L. In previous studies they mentioned the serum IgE level in stable COPD patients only. In a study conducted by Samaha HM et al. reported that mean serum total IgE level in COPD patients who has GOLD stage 1,2,3 was 65, 178, 237 IU/L respectively.⁶

Table 1: Baseline characteristics of study subjects

Variables	Patients with COPD (75 cases)
Age (yr)	64.19 ± 9.142
Male (yr)	65.47 ± 7.650
Female (yr)	63.23 ± 10.094
Male, n(%)	32 (42.7%)
Female, n(%)	43 (57.3%)
Seasonal variation, n(%)	34 (45.3%)
h/o previous exacerbation, n(%)	52 (69.3%)
Smokers, n(%)	38 (50.67%)
Biomass exposure, n(%)	41 (54.7%)
Hyperinflation, n(%)	53 (70.7%)
FEV ₁ /FVC ratio	0.56 ± 0.099
FEV ₁ change %	11 ± 8.69
FEV ₁ volume (ml)	155.4 ± 131.27
Post BD Reversibility, n(%)	28 (37.3%)

FEV₁- Forced Expiratory Volume in one second, FVC – Forced Vital Capacity, BD - Bronchodilator

Table 2: Comparison between groups

Parameters	Serum IgE <100 IU/L (20 cases)	Serum IgE >100 IU/L (55 cases)	P - value
Age (yrs)	64.65 ± 9.46	64.02 ± 9.1	0.793
Male n(%) Female n(%)	12 (60%) 8 (40%)	20 (36.4%) 35 (63.6%)	0.067
Seasonal variation, n(%)	2 (10%)	32 (58.2%)	<0.001
h/o Previous exacerbation, n(%)	16 (80%)	36 (65.5%)	0.227
Smokers, n(%)	12 (60%)	26 (47.3%)	0.330
Biomass exposure, n(%)	7 (35%)	34 (61.8%)	0.039
Hyperinflation, n(%)	17 (85%)	36 (65.5%)	0.100
FEV ₁ /FVC ratio	0.494 ± 0.1023	0.582 ± 0.0876	<0.001
FEV ₁ change %	6.4 ± 5.0	13.75 ± 8.9	0.001
FEV ₁ change volume (ml)	72.55 ± 76.56	185.53 ± 134.48	0.001
Post BD Reversibility, n(%)	2 (10%)	26 (47.3%)	0.003
ACO features	1 (5%)	26 (47.3%)	0.001
AEC (cells/mm ³)	117.45 ± 248.85	167.21 ± 192.06	0.363
Raised AEC (>300)	2 (10%)	8 (14.5%)	0.609

Continuous data expressed as mean (standard deviation). Categorical data expressed as number (percentage). All values are expressed as geometric mean (95% confidence interval). Statistically significant values (p<0.05) are shown in bold. FEV₁- Forced Expiratory Volume in one second, FVC – Forced Vital Capacity, BD – Bronchodilator, ACO – Asthma COPD Overlap, AEC – Absolute Eosinophil Count

Table 3: Correlation coefficient between Serum Total Ig E level and other parameters

Parameters	Correlation coefficient (r)	P - value
Age	-0.094	0.420
Seasonal variation	0.596	<0.001
h/o Previous exacerbation	-0.148	0.206
Smokers	-0.174	0.135
Biomass exposure	0.113	0.336
Hyperinflation	-0.072	0.541
FEV ₁ /FVC ratio	0.400	<0.001
FEV ₁ change %	0.443	<0.001
FEV ₁ change volume	0.516	<0.001
Post BD Reversibility	0.385	0.001
ACO features	0.429	<0.001
AEC	0.297	0.010

Statistically significant values (p<0.05) are shown in bold. FEV₁- Forced Expiratory Volume in one second, FVC – Forced Vital Capacity, BD – Bronchodilator, ACO – Asthma COPD Overlap, AEC – Absolute Eosinophil Count

In our study the prevalence of raised total Serum IgE in COPD exacerbation is 73%. In previous studies by Jamieson DB et al., Samaha HM et al., and Bafadhel M et al. were reported much lower prevalence than our study.^{6,13,14} The reason may be they measured the specific IgE and/or they measured in stable COPD patients. This suggests that serum total IgE may be more sensitive marker than specific IgE and it reflects the severity of the disease.⁵ In our study, patients who have raised serum IgE levels have Asthma COPD Overlap features [26 (47.3%)]. Similarly Sharma R et al. reported that Serum Total IgE levels were significantly higher in ACO patients in Indian population.¹⁵ In our study serum IgE levels positively correlated to seasonal variation, biomass exposure. And negatively correlated to age, h/o previous exacerbation, smoking and hyperinflation. This is similar to Samaha HM et al. study, in which they reported that serum IgE has negative correlation with age, hyperinflation.⁶ Several other studies reported that elevated serum IgE in biomass exposure and low levels in tobacco smokers.^{16,17} In our study we found that patients who have raised serum IgE have better lung function (FEV₁/FVC ratio). Similarly Lommatzsch M et al. found that patients with raised IgE have better lung function and less emphysema.¹⁸ Since COPD and asthma shares some similar pathologic characteristics¹⁹ we suggest that COPD exacerbations may also have elevated serum IgE levels as in Asthma. This may be the consequence of aeroallergens which leads to exacerbations.

5. Conclusion

IgE mediated sensitization plays a role not only in the pathogenesis of allergic asthma but also in the pathophysiology of COPD. Patients with COPD exacerbations may have raised Total Serum IgE. This supports the use of Omalizumab (anti IgE monoclonal antibody) in Acute Exacerbations of COPD.²⁰ Its response needs to be evaluated by the longitudinal studies.

Although COPD exacerbations commonly caused by infections by virus and bacteria,¹ in 1/3rd of times cause for the severe exacerbations cannot be identified. This may be due to the aeroallergens which causes exacerbations. Hence we suggest that Serum IgE levels to be monitored in COPD exacerbations also. Our study has certain limitations. Measurement of IgE before exacerbation, collection of samples prior to the initiation of therapies and at multiple longitudinal time points following an exacerbation are also necessary to avoid the possible confounding by medications and to characterize the activity of the serum IgE along the time course of disease.

6. Source of Funding

None.

7. Conflict of Interest

None.

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