

Occurrence of COPD in Patients with Respiratory Allergy: A Clinico-Spirometric Evaluation in a Tertiary Hospital, Kolkata

SUJOY MUKHERJEE¹, GOUTAM BANERJEE², DEBAJYOTI DAS³, ANIL BARAN SINGHA MAHAPATRA⁴

ABSTRACT

Introduction: Smoking is established as the most important causative factor responsible for Chronic Obstructive Pulmonary Disease (COPD). Occurrence of allergy in COPD patients causes acute exacerbation of this disease, but role of allergy is not established in aetiopathogenesis of COPD.

Aim: The present study was aimed at evaluation of occurrence of COPD in patients having symptoms suggestive of respiratory allergy.

Materials and Methods: An observational cross-sectional study was conducted to evaluate occurrence of COPD in patients having respiratory allergic symptoms by routine spirometric screening. Five hundred and fifty urban patients aged 18-60 years (both gender) ailing from chronic respiratory symptoms like cough, wheeze and Shortness Of Breath (SOB), who were referred from OPDs of RGKMCH, Kolkata, were included in this study. After obtaining detailed clinical profile, patients were

divided into two groups: subjects having additional clinical symptoms suggestive of respiratory allergy (n=260) like nasal catarrh, nasal stuffiness and sneezing and subjects with no symptoms suggestive of respiratory allergy (n=290). Thereafter, routine spirometry was carried out following recommendations of ATS/ERS (2005). Patients were then categorized based on FVC, FEV₁, FEV₁/FVC, FEF₂₅₋₇₅ and PEF percent predicted values.

Results: Study revealed that 18.97% of non-allergic population was suffering from COPD whereas only 7.69% of allergic subjects had COPD. This difference was statistically highly significant (p=0.0001). Although there was no significant difference in prevalence of respiratory symptoms between these two groups.

Conclusion: Present study concludes that patients with respiratory allergy may have coexistent COPD but occurrence of COPD is much less than that in patients with no respiratory allergy.

Keywords: Acute exacerbation, Pandemic, Spirometry

INTRODUCTION

Chronic lung disease is a rapidly emerging pandemic. Volcano is a more appropriate word to depict the situation rather than the traditional iceberg phenomenon [1]. Intergovernmental Panel on Climate Change (IPCC) and WHO concluded that overall incidences of obstructive lung diseases, upper respiratory tract allergy and respiratory tract infection are rapidly rising as a result of global warming.

Till date smoking is the most important causative factor for COPD. Dyspnoea, wheeze & wet cough are the major symptoms [2,3]. Sinonasal inflammation in COPD may be produced as a result of inflammation, pathological neurogenic reflexes or directly by products of smoking [4]. Allergens, dust, microbes and nonspecific respiratory irritants typically narrow the airways by excessive mucus production thereby exacerbating COPD symptoms [5,6]. On the other hand, till recently American Thoracic Society did not include strategies for the management of respiratory allergies in routine treatment protocol of COPD [6]. The principal focus of the present study was to evaluate the coexistence of COPD with respiratory allergy so that the treatment of respiratory allergy may accelerate the recovery from acute exacerbation of COPD. The combination of clinical examination followed by spirometry can significantly increase the sensitivity of detection of lung diseases [7]. Reversibility testing with bronchodilators reduces the overall prevalence of airway obstruction significantly and post bronchodilatation obstruction is more specific for COPD [8].

The aim of the present study was to evaluate the occurrence of COPD in respiratory allergy among subjects presenting with chronic respiratory symptoms.

MATERIALS AND METHODS

An observational cross-sectional study was conducted between November 2015 and April 2016. Male and female subjects aged 18 to 60 years presenting with chronic respiratory symptoms like cough, wheeze and SOB for more than three months duration were included in the study. All patients were Bengali speaking and belonged to urban areas of North 24-Parganas district, West Bengal, India. They were referred from different outpatient departments of a tertiary hospital, Kolkata for routine spirometric screening at the spirometry laboratory in Department of Physiology.

Asymptomatic patients coming for pre-anaesthetic checkup, Paediatric and Geriatric patients, patients suffering from acute illness and debilitation of any origin, patients with third trimester pregnancy, active haemoptysis, tuberculosis, sub diaphragmatic and known cardiovascular diseases associated with SOB were summarily excluded from the present study. On an average in our department we perform routine spirometry in 160 patients per month. In six months from about 950 patients we selected 550 patients maintaining appropriate inclusion and exclusion criteria. The sampling technique was complete enumeration. Ethical permission was obtained from Institutional Ethics Committee, prior to study and written consent was taken from each of the subject prior to examination.

At first all patients were asked to respond to a standardized respiratory symptoms questionnaire (ATS/DLD-78 A questionnaire) [9]. After obtaining detailed clinical profile, patients with respiratory symptoms were divided in two groups: subjects suffering from clinical symptoms suggestive of respiratory allergy (n=260) like nasal catarrh, nasal stuffiness and sneezing all together as written on OPD card and subjects with no symptoms suggestive of respiratory allergy (n=290).

We did not perform any laboratory test for allergy as clinical symptomatology is established as the most reliable factor in detection of allergy [10,11]. Smoking history was obtained and subjects were categorized as per US Centers for Disease Control and Prevention definition of “Never Smokers” – adults who have never smoked a cigarette or who smoked fewer than 100 cigarettes in their entire lifetime. Rest of the subjects was marked as smokers. All the patients had received one or more bronchodilators and anti-inflammatory agents for treatment of their respiratory symptoms.

As all the data was collected at a point of time (cross-sectional data) with no known confounding variable so unpaired t-test was applied to compare these two populations. After calibration, spirometry was carried out by using a non-heated spirometer (RMS HELIOS 702) following current guidelines of the American Thoracic Society [12]. The largest observed values of FEV₁ and FVC available from among at least three acceptable and reproducible tests were taken as the key parameters for interpretation. Then, the subject was asked to inhale short acting bronchodilator in the pre-prescribed doses. After ten minutes of taking the inhaler the subject was asked to perform the spirometry once again and thus the reversibility test done [12]. The highest values of FVC and FEV₁ were selected. Periodic calibrations were done as per protocol.

In absence of normative spirometric data of Indian population the data obtained was interpreted as per directions furnished in the user manual of RMS HELIOS 702 along with given ethnic correction [13]. As the study populace seemed to be ethnically homogenous predictive equation was not obtained.

We categorized all the patients as per pre-set criteria: i) Normal Spirometric Finding; ii) Small Airway Obstruction (SAO); iii) COPD; iv) Mixed Ventilatory Defect; & v) Restrictive Pattern [13].

STATISTICAL ANALYSIS

Descriptive analyses were performed using Fisher’s-Exact Test (for categorical variables) and two-sided unpaired t-tests (for continuous variables). All spirometric variables were expressed in percent predicted (%) form. Statistical analyses was done by using Microsoft excel sheet and GraphPad Quickcalcs Software, California, USA. A p-value of <0.05 was considered significant.

RESULTS

Non allergic patients were significantly more likely to be older (mean age was 44 years), percentage of smokers were also higher in the older population. There was no significant difference regarding prevalence of respiratory symptoms like SOB, dry cough, wet cough between allergic and non-allergic populations except wheeze which was more significant finding in allergic population. Furthermore, bronchodilator reversibility (BDR) data had shown that mean values of FEV₁/FVC, FEF₂₅₋₇₅ and PEFR were significantly lower in non-allergic subjects as compared to allergic group [Table/Fig-1].

Occurrence of COPD in BDR analysis was significantly more in non-allergic group rather than allergic population [Table/Fig-2].

Non allergic patients with spirometry diagnosed COPD were significantly more likely to be older (mean age was 52 years). More than half of the non-allergic patients had smoking history. Non-allergic patients had a lesser mean body weight. Persistence of lower respiratory symptom like wet cough was more in the non-allergic population compared to allergic population. Furthermore mean values of FEV₁ & FEV₁/FVC were significantly less in non allergic COPD population compared to allergic patients [Table/Fig-3].

DISCUSSION

In the present study, we divided the whole population based only on prior clinical diagnosis and allergy testing was not performed. As drug/treatment history of patients was not supposed to alter our study outcome so we had not included drug history as a study variable. As the present study was of observational and cross-

Variables	Allergic Patients (N=260)	Non-Allergic Patients (N=290)	p-value
Gender {N (%)}	Male: 110 (42.30) Female:150 (57.70)	Male: 145 (50.00) Female:145 (50.00)	0.0729
Age (Years) (Mean ±SD)	35.07±13.02	43.89±11.33	<0.0001*
Weight (Kg) (Mean ±SD)	55.34±13.05	54.89±11.47	0.6671
Height (Cm) (Mean ±SD)	155.88±9.23	156.53±8.78	0.3979
BMI (Kg/M ²) (Mean ±SD)	22.92±5.01	22.45±4.4	0.242
Smoking Status ^a {N (%)}	Ever Smoker: 40 (15.38) Never Smoker: 220 (84.62)	Ever Smoker: 100 (34.48) Never Smoker: 190 (65.52)	<0.0001*
SOB ^b {N (%)}	Yes: 260 (100.00) No: 00 (0.00)	Yes: 290 (100.00) No: 00 (0.00)	1.000
Dry Cough ^c {N (%)}	Yes: 100 (38.46) No: 160 (61.54)	Yes: 105 (36.20) No: 185 (63.80)	0.5972
Wet Cough ^c {N (%)}	Yes: 70 (26.92) No: 190 (73.08)	Yes: 75 (25.86) No:215 (74.14)	0.8464
Wheeze {N (%)}	Yes: 40 (15.38) No: 220 (84.62)	Yes: 00 (0.00) No: 290 (100.00)	<0.0001*
FVC ^d (Mean ±SD)	112.75±26.42	113.2±37.19	0.8715
FEV ₁ ^e (Mean ±SD)	99.05±44.58	96.01±53.78	0.4737
FEV ₁ /FVC (Mean ±SD)	92.63±29.18	81.51±30.14	<0.0001*
FEF ₂₅₋₇₅ ^f (Mean ±SD)	72.88±34.61	66.62±37.58	0.0434*
PEFR ^g (Mean ±SD)	69.61±32.49	63.27±35.43	0.0298*

[Table/Fig-1]: Overall profile of the study population. (SD: Standard Deviation, BMI: Body Mass Index; a. Smoking status defined as ever/never smoker of cigarette, beerie or hugga; b. Shortness of breath: to evaluate SOB NYHA standard guidelines were followed*; c. Dry and wet cough defined as cough on most days of month, for three consecutive months or more in a year; d. (FVC) Forced Vital Capacity. e. (FEV) Forced Expiratory Volume in one second; f. (FEF) Forced Expiratory Flow 25-75%; g. (PEFR) Peak Expiratory Flow Rate.) (*All of the patients belonged to NYHA Class I or Class II grade of dyspnoea.)

Spirometric Finding	Allergic patients (n=260)	Non-Allergic patients (n=290)	p-value
Normal Pattern ^h {n (%)}	Yes: 150 (57.69) No: 110 (42.31)	Yes: 145 (50.00) No: 145 (50.00)	0.0729
Small airways obstruction ⁱ {n (%)}	Yes: 75 (28.85) No:185 (71.15)	Yes: 65 (22.41) No:225 (77.59)	0.0956
COPD ^j {n(%)}	Yes: 20 (7.69) No: 240 (92.31)	Yes: 55 (18.97) No: 235 (81.03)	0.0001*
Mixed Ventilatory Defect ^k {n(%)}	Yes: 15 (5.77) No: 245 (94.23)	Yes: 20 (6.90) No:270 (93.10)	0.6052
Restrictive Pattern ^l {n(%)}	Yes: 00 (0.00) No: 260 (100.00)	Yes: 5 (1.72) No: 285 (98.28)	0.0632

[Table/Fig-2]: Categorization of BDR test results. (h.FVC:80%-120%pred; FEV1: 80%-120% pred.; FEV1/FVC:70%-85%; FEF₂₅₋₇₅ : Values ranging from 50%-60% & up to 130% of the average, PEFR : >60% pred. value. i. FEF₂₅₋₇₅<50% pred. mainly. j. FEV1/FVC <70% & FEV1 value <100% pred.: Mild COPD or higher. k. FEV1/FVC <0.7 and FVC <80% of predicted. l. FVC <80%, FEV1 ≤ 80% (normal /decreased) & FEV1/FVC ≥0.7.)

sectional nature so no confounding variable like age and smoking could be ascertained. However, these were important variables which influenced the overall outcome. Therefore, we categorized the study subjects based on these parameters and compared the different groups to deduce the study results.

In the present study, we did not categorize patients based on grade of SOB as all of the patients fell in NYHA grade I or grade II. This is most probably because spirometry is very difficult or rather impracticable in the management of NYHA grade III or grade IV SOB.

In this study we found that respiratory allergic group was significantly younger and had lesser percentage of smokers compared to nonallergic group. This finding was in accordance with the study

Parameter	Allergic Patients having COPD (n=20)	Non-Allergic Patients having COPD (n=55)	p-value
Age (Years) {Mean ±SD}	40.25±11.24	51.63±9.60	<0.0001*
Weight (Kg) {Mean ±SD}	57.75±8.47	50.09±10.45	0.0044*
Smoking Status {N (%)}	Ever Smoker: 00 (00.00) Never Smoker: 20 (100.00)	Ever Smoker: 35 (63.63) Never Smoker: 20 (36.37)	<0.0001*
Wet Cough {N (%)}	Yes:00 (00.00) No:20 (100.00)	Yes:20 (36.37) No: 35 (63.63)	0.0008*
FEV ₁ {Mean ±SD}	79.5±21.15	44.00±22.39	<0.0001*
FEV ₁ /FVC {Mean ±SD}	57.75±3.99	45.54±12.97	<0.0001*

[Table/Fig-3]: Comparison of COPD Patients with and without Allergy.

result of Eder W et al., [14]. They also documented that allergic hypersensitivity due to plant pollens was more commonly found in younger age group and in older people, the cause was almost always hypersensitivity to nonallergenic types of irritants in the air, such as irritants in smog.

The present study had shown that post BDR parameters were significantly lower in non allergic patients compared to allergic patients and smokers were at a significantly higher number in non allergic group. Detection of COPD by spirometry screening was much higher in the same group. Similarly Sichletidis L et al., found that prevalence of COPD was not significantly high among individuals having respiratory allergy [11]. As smoking causes COPD which showed poor BDR response in this study, the hypothesis that can be drawn from the constellation of these findings was that presence of respiratory allergy might refrain the affected subjects from smoking. This was in accordance with the findings of Shargorodsky J et al., that the relationship between tobacco smoke exposure and sinonasal pathology in adults might be independent of allergic sensitization [15]. Therefore, smoking may cause symptoms of respiratory allergy. Our study further indicates that smoking was probably a stronger causative factor for development of COPD than allergy. This was in accordance with the findings of Sichletidis et al., who had shown that prevalence of COPD was not significantly high among allergic subjects [11].

The mean age was significantly higher with greater percentage of smokers and more persistence of wet cough in non-allergic COPD population compared with allergic COPD patients. This was in accordance with the findings of Eisner et al., Jarad et al., & Smith et al., [16-18]. This further asserts that smoking was much stronger aetiological factor for COPD than respiratory allergy.

There were no significant differences in BMI, chronic respiratory symptoms like SOB, dry and wet cough and also FEV₁ reversibility between these two populations again most possibly because smokers were present in both in allergic and non-allergic patients with COPD and as because of stronger aetiopathogenic effect of smoking on COPD effect of allergy on symptoms was blurred.

All the subjects were residents of urban downtown areas. High degree of air pollution might also contribute to higher prevalence of symptoms in COPD besides smoking in non-allergic populace as shown by Ko FW et al., [19].

LIMITATION

Due to cross-sectional nature of this study, it was difficult to establish causal association between impaired lung function and the chronic respiratory symptoms. Furthermore air pollution as a contributing factor cannot be quantified. These might act as important confounding variables influencing the study result.

CONCLUSION

This present study concludes that COPD may coexist with respiratory allergy but overall occurrence of COPD was significantly much more in non-allergic population presenting with chronic respiratory symptoms. However to establish this finding large scale follow up investigations should be performed in future.

ACKNOWLEDGEMENTS

The authors are thankful to all faculty members and staff of Department of Physiology of a medical college, Kolkata and also our study subjects who gave consent for the research work.

REFERENCES

- [1] Bhome AB. COPD in India: Iceberg or volcano. *J Thorac Dis.* 2012;4(3):298-309.
- [2] World Meteorological Organization, United Nations Environment Programme. Intergovernmental Panel on Climate Change. Available from: <http://www.unep.org/climatechange/>
- [3] Matthies F, Bickler G, Cardenosa Marin N, Hales S. Heat-Health Action Plans. Guidance. Copenhagen, World Health Organization Regional Office for Europe, 2008. http://www.euro.who.int/__data/assets/pdf_file/0006/95919/E91347.pdf
- [4] Hakansson K, Konge L, Thomsen SF, Backer V, Buchwald CV. Sinonasal inflammation in COPD: a systematic review. *Eur Respir J.* 2013;42:1402-11.
- [5] Jovinelly J. COPD and Allergies: Avoiding Pollutants and Allergens. Healthline. August 31, 2016. <http://www.healthline.com/health/copd/allergies#Overview1>
- [6] Hansel NN. Allergic Disease Worsens Respiratory Symptoms and Exacerbations in COPD. American Thoracic Society. May 2013 press releases. <http://www.atsjournals.org/doi/abs/10.1164/rccm.201211-2103OC>
- [7] Gavrieli N, Nissan M, Cugell DW, Rubin AHE. Respiratory health screening using pulmonary function tests and lung sound analysis. *Eur Respir J.* 1994;(7):35-42.
- [8] P'erez-padilla R, Hallal PC, V'azquez-garc'ia JC, Mu'no A, M'aque M, L'opez MV, et al. Impact of bronchodilator use on the prevalence of COPD in population-based samples. *Journal of Chronic Obstructive Pulmonary Disease.* 2007;4(2):113-20.
- [9] Ferris BG. Epidemiology standardization project (American thoracic society). *Am Rev Respir Dis.* 1978;118:1-120.
- [10] Turkeltaub PC, Gergen PJ. Prevalence of upper and lower respiratory conditions in the US population by social and environmental factors: data from the second National Health and Nutrition Examination Survey, 1976 to 1980 (NHANES II). *Ann Allergy.* 1991;67:147-54.
- [11] Sichletidis L, Tsiotsios I, Gavriilidis A, Chloros D, Kottakis I, Daskalopoulou E, et al. Prevalence of chronic obstructive pulmonary disease and rhinitis in northern Greece. *Respiration.* 2005;72:270-77.
- [12] Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates RA, et al. Standardisation of spirometry. *Eur Respir J.* 2005;26:319-38.
- [13] HELIOS 702 (Portable Spirometer) Evaluation of 51 vital parameters with interpretation. Copy writes 2010-2013 Accurate. Available from: <http://www.surgicalmall.com/product/1024>.
- [14] Eder W, Ege MJ, Von-mutius E. The asthma epidemic. *N Eng J Med.* 2006;355:2226.
- [15] Shargorodsky J, Garcia-esquinas E, Galán I, Navas-acien A, Lin SY. Allergic sensitization, rhinitis and tobacco smoke exposure in US adults. *PLoS ONE.* 2015;10(7):e0131957.
- [16] Eisner MD, Anthonisen N, Coultas D, Kuenzli N, Perez-padilla R, Postma D, et al. An official American thoracic society public policy statement: novel risk factors and the global burden of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med.* 2010;182:693-718.
- [17] Jarad N. Chronic obstructive pulmonary disease (COPD) and old age? *Chron Respir Dis.* 2011;8(2):143-51.
- [18] Smith J, Woodcock A. Cough and its importance in COPD. *Int J Chron Obstruct Pulmon Dis.* 2006;1(3):305-14.
- [19] Ko FW, Hui DS. Air pollution and chronic obstructive pulmonary disease. *Respirology.* 2012;17(3):395-401.

PARTICULARS OF CONTRIBUTORS:

1. Junior Resident, Department of Physiology, R G Kar Medical College and Hospital, Kolkata, West Bengal, India.
2. Professor, Department of Physiology, R G Kar Medical College and Hospital, Kolkata, West Bengal, India.
3. Assistant Professor, Department of Physiology, R G Kar Medical College and Hospital, Kolkata, West Bengal, India.
4. Professor and Head, Department of Physiology, R G Kar Medical College and Hospital, Kolkata, West Bengal, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Sujoy Mukherjee,
253/1, Ground Floor, Block-B, Bangur Avenue, PS-Laketown, Kolkata-700055, West Bengal, India.
E-mail: dr.sujoymukherjee@rediffmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Nov 25, 2016**
Date of Peer Review: **Jan 23, 2017**
Date of Acceptance: **Feb 23, 2017**
Date of Publishing: **May 01, 2017**