Relationship between respiratory symptoms and FEV₁ in COPD and Bronchial asthma in RIMS Medical College & Hospital, Kadapa, Andhra Pradesh, India.

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Abstract: Background : Chronic obstructive pulmonary disease (COPD) and Bronchial Asthma are the major causes of pulmonary disability. Both are chronic inflammatory lung diseases characterized by airway obstruction. Chronic Obstructive Pulmonary Disease (COPD), is the fourth leading cause of death in the world, represents an important public health challenge that is both preventable and treatable. COPD is a major cause of chronic morbidity and mortality throughout the world. Asthma is a common, chronic respiratory disease affecting 1-18% of the population in different countries. Asthma is characterized by variable symptoms and expiratory airflow limitation. COPD and Bronchial asthma are diagnosed based on clinical criteria and spirometry. Dyspnea is one of the major symptoms that impact the quality of life. FEV_1 is an objective index and the level of dyspnea is a subjective index in assessing patients with obstructive lung diseases. Recently there has been an increased emphasis on objective measurements of pulmonary function in the management of COPD and Bronchial asthma. There is a variable relationship between clinical parameters and pulmonary function.⁽⁷⁾ The most commonly used way to express disease severity is by assessing the FEV_1 as a measure for airway obstruction. The FEV_1 is a reproducible and objective measurement. Serial measurements of FEV_1 may provide evidence of disease progression. The purpose of this study is to compare clinical symptoms with the actual values of FEV_1 in patients with COPD and Bronchial asthma. This study also determines the best clinical predictors of COPD and Bronchial asthma to define the incremental changes in the ability to diagnose disease severity, when the symptoms and FEV_1 are combined together. This would help in optimizing the management of patients COPD and Bronchial asthma and to decrease the disease progression.

Material and methods: Out of 155 adults studied 96 patients were included. 47 out of 96 were COPD patients and the rest were Bronchial asthma patients. Sample was taken from patients who attended the outpatient department or admitted in the wards of Rajive Gandhi Institute Of Medical Sciences Hospital & College Kadapa. From July 2017 to June 2018.Patients were examined and data collected on a pretested proforma.STUDY TYPE: Cross sectional study of patients with diagnosis of COPD and Bronchial asthma.

Conclusion: In conclusion, the patients in both Bronchial asthma and COPD subgroups, the statistical significance of correlating clinical symptoms with objective measurement of airway obstruction (by FEV_1) is not exact. Therefore both groups of patients are better managed with a combination of objective assessment of pulmonary function and symptom scores. In Bronchial asthma patients, severity of symptoms does not statistically correlate with FEV_1 measurements. Subjective wheeze is the individual symptom best approaching correlation with FEV_1 . COPD patients have better inverse correlation between symptoms and FEV_1 though not achieving statistical significance in present study. mMRC grade of dyspnea is best individual symptom in this group of individuals, correlating with measured FEV_1 values.Present study emphasizes the importance of using objective assessment of lung function in both Bronchial asthma and COPD patients prior to implementation of medical treatment strategies.

Keywords:, copd, asthma, dyspnea, spirometry, FEV_1 .

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I. Introduction

Chronic obstructive pulmonary disease (COPD) and Bronchial Asthma are the major causes of pulmonary disability. Both are chronic inflammatory lung diseases characterized by airway obstruction. In both conditions, inflammation is associated with structural alterations at large and small airway levels. However, there are many differences between these two diseases with respect to their pathophysiology, pathogenesis, response to therapy and prognosis. Chronic Obstructive Pulmonary Disease (COPD), the fourth leading cause of death in the world, represents an important public health challenge that is both preventable and treatable. COPD

is a major cause of chronic morbidity and mortality throughout the world. Globally, the COPD burden is projected to increase in coming decades because of continued exposure to COPD risk factors and aging of the population.Asthma is a common, chronic respiratory disease affecting 1-18% of the population in different countries. Asthma is characterized by variable symptoms and expiratory airflow limitation. These variations are often triggered by factors such as allergen or irritant exposure, exercise, change in weather, or viral respiratory infections COPD and Bronchial asthma are diagnosed based on clinical criteria and spirometry. Over the past 20 years, major strides have been made in understanding the pathophysiology of these two diseases, although there are still gaps in our knowledge. The relation between respiratory symptoms and lung function has not been extensively investigated. The main respiratory symptoms are cough, dyspnea, wheeze, tightness of chest and nocturnal symptoms. Clinicians should be aware of the predictive value of these respiratory symptoms because therapeutic intervention may modify the associated decline in lung function. Dyspnea is one of the major symptoms that impact the quality of life. FEV_1 is an objective index and the level of dyspnea is a subjective index in assessing patients with obstructive lung diseases. Recently there has been an increased emphasis on objective measurements of pulmonary function in the management of COPD and Bronchial asthma. There is a variable relationship between clinical parameters and pulmonary function. The most commonly used way to express disease severity is by assessing the FEV1 as a measure for airway obstruction. The FEV1 is a reproducible and objective measurement. Serial measurements of FEV1 may provide evidence of disease progression. The purpose of this study is to compare clinical symptoms with the actual values of FEV_1 in patients with COPD and Bronchial asthma. This study also determines the best clinical predictors of COPD and Bronchial asthma to define the incremental changes in the ability to diagnose disease severity, when the symptoms and FEV_1 are combined together. This would help in optimizing the management of patients with COPD and Bronchial asthma and to decrease the disease progression.

II. Materials and Methods

Out of 155 adults studied 96 patients were included. 47 out of 96 were COPD patients and the rest were Bronchial asthma patients. Sample was taken from patients who attended the outpatient department or admitted in the wards of Rajive Gandhi institute of medical sciences and college kadapa .From July 2017 to June 2018. Patients were examined and data collected on a pretested proforma. A detailed history was taken and a thorough clinical examination was done in all patients. Five symptoms 1.cough, 2.dyspnea 3.wheeze 4.tightness of chest and 5.nocturnal symptoms were recorded on a two point scale.Zero point was given for absence of symptom and one point for presence of symptom. A cumulative symptom score was calculated with a maximum score of five. Dyspnea was also graded according to modified Medical Research council (mMRC) grading of dyspnea. FEV₁ was measured by spirometer (True flow by ndd Medical Technologies 2700-1-01EOPC), meeting the standard criteria of American Thoracic Society. Spirometry was obtained with the patient seated and wearing nose clips. The best of three reproducible measurements was taken for analysis. The post bronchodilator FEV₁ was assessed at 15-20 minutes after the inhalation of 400µg salbutamol using a metered dose inhaler with a spacer device. The symptom score was correlated with FEV₁.

III. Results

The records of 94 individual patients were reviewed. Among them 47 were Bronchial asthma and 47 were COPD patients. In Bronchial asthma there was no statistically significant relation between any individual symptom and FEV₁ although there was a trend towards significance between subjective wheeze and FEV₁. Similarly there was no statistically significant relation between total symptom score and FEV₁. When total symptom score and post bronchodilator FEV₁ were compared, again no statistically significant relation was found between them. In COPD, correlating the individual symptoms and FEV₁, the single symptom approaching significant correlation was dyspnea. The mMRC grade of dyspnea was an even better yardstick, the higher mMRC grades had the lowest values of FEV₁. Similarly, the relation between total symptom score and FEV₁ did not reach statistical significance although there was (compared to Bronchial asthma) better clinical estimation of severity as evidenced by the fact that there were no over estimators in this group. The same finding hold true statistically for total symptom score and post bronchodilator FEV₁.

IV. Discussion

Chronic obstructive pulmonary disease (COPD) and bronchial asthma are pulmonary disorders characterized by various degrees of airflow limitation, inflammation, and tissue remodelling. Bronchial asthma, an allergic disease that usually develops in childhood, is physiologically characterized by reversible airflow obstruction. It has an episodic course and a generally have favourable prognosis, as it responds well to anti-inflammatory treatment.⁽¹⁾ In contrast, COPD mostly caused by tobacco smoke, develops in mid-life or later, characterized by progressive decline in lung function and can lead to premature death.⁽²⁾ COPD is a leading cause of morbidity and mortality worldwide and results in an economic and social burden that is both

substantial and increasing.^(3,4) The chronic airflow limitation characteristic of COPD is caused by a mixture of small airways disease (obstructive bronchiolitis) and parenchymal destruction (emphysema), leads to air flow limitation. Airflow limitation is best measured by spirometry, as this is the most widely available and reproducible test of lung function.⁽⁵⁾ Asthma is characterized by chronic airway inflammation and history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. Diagnosis of asthma should be based on the history of characteristic symptom patterns and evidence of variable airflow limitation. Variable airflow limitation should be documented from bronchodilator reversibility testing (increase in FEV1 of >12% and >200 ml from baseline, 10–15 minutes after 200-400 mcg albuterol or 400 mcg of salbutamol)⁽²⁾ as shown in table 2. There is a variable relationship between clinical parameters and pulmonary function ⁽⁷⁾. Dyspnea is one of the major symptoms that impact the quality of life. FEV_1 is an objective index and the level of dyspnea is a subjective index in assessing patients with obstructive lung diseases. The most commonly used way to express disease severity is by assessing the FEV_1 as a measure of airway obstruction. ⁽⁸⁾ The FEV_1 is volume of air exhaled in first second of FVC manoeuvre. FEV1 is a reproducible and objective measurement. Serial measurements of FEV1 may provide evidence of disease progression. (9). Present study population includes 47 Bronchial asthma patients and 47 COPD patients. In present study, in Bronchial asthma group 27 were male and 20 were female, with mean age of 33.3± 14.1.In present study, Bronchial asthma group have male to female ratio 1:0.74 as shown in table 1. This is comparable to John, Eugene et al (10) whose study group have male to female ratio is 1:0.65, Sherman, speizer et al⁽¹¹⁾ whose study group have male to female ratio of 1:1.24, Fabio Savatore et al ⁽¹²⁾ whose study group has male to female ratio is 1:1.5 and Liam, Goh et al^{13} whose male to female ratio is 1:0.73. In present study, COPD group consists of 41 males and 6 females, aged between 54 and 78 as shown in table 5. This study is comparable to Sherrill and Khudson et al⁽¹⁴⁾ whose age group is >55 yrs. In present study, in COPD group, there are 26 current smokers, 15 former smokers and 6 never smokers as shown in table 5. Majority of patients in this group are smokers (both former plus current) indicating the fact that "tobacco smoking is an important risk factor for developing COPD".⁽¹⁵⁾ In bronchial asthma group, there are 13 current smokers, 7 former smokers and 27 never smokers as shown in table 1. Even though there are 20 smokers in this group, they showed variability in symptom pattern, seasonal variation of symptoms and bronchodilator reversibility (\geq 12% and 200ml) according to GINA 2016, so included in bronchial asthma group. In present study, five symptoms, cough, dyspnea, wheeze, tightness of chest, nocturnal symptoms were recorded on a two point scale ⁽¹⁶⁾. Zero point was given for absence of symptom and one point for presence of symptom. A cumulative symptom score was calculated with a maximum score of five. This is comparable to John, Eugene et al⁽¹⁰⁾ in which patients were asked to quantify each of six current asthma symptoms, including cough, dyspnea, chest tightness, wheezing, sputum production, and nocturnal awakening on a 0 (none) to 4 (constant) whole integer scale. Total asthma scores ranging from 0 to 24 by utilizing this scale. Further our study is comparable to *Sherman and Speizer et al*⁽¹¹⁾ whose subjects were categorized based on the presence or absence of self reported respiratory symptoms (persistent wheeze, chronic cough, chronic phlegm, or shortness of breath) at the initial visit. Symptom score of COPD group in present study is comparable to Sherrill and Khudson et al⁽¹⁴⁾ in which subjects were classified at each survey as having chronic cough, exertional dyspnea or wheeze. Present study, showed the relationship between Clinical symptoms (symptom score) and Forced Expiratory Volume in first second (FEV_1) in patients of Chronic obstructive pulmonary disease as shown in table 7, and Bronchial asthma as shown in table 4, which resembles the study of Gupta, D P Bhadoriaet al ⁽¹⁶⁾, who studied the relationship between total symptom score and FEV_1 in Bronchial asthma and COPD demonstrating the inverse correlation of symptom score with FEV1. John and Eugene et al (10) studied the relationship between symptoms and the degree of airway obstruction as determined by the FEV_1 in adult asthmatics. In this study, asthma symptoms including cough, dyspnea, wheeze, chest tightness, sputum production and nocturnal awakening was rated by patients on a 0 to 4 scale. Spirometry was measured at the clinical visit. This study demonstrated that asthma symptoms did not correlate with the degree of airway obstruction as determined by the FEV_1 . Subjective wheezing was the best individual predictor of the level of airway obstruction in this group of patients. Present study yielded similar results showing that subjective wheezing was the only symptom which had a trend towards statistical significance (p=0.07). Together with these studies, the present study results suggest that wheezing is the asthma symptom most predictive of the level of airway obstruction. Other common asthma symptoms such as cough and dyspnea may be more reflective of the state of bronchial hyper responsiveness and lung hyperinflation respectively. Present study showed that asthmatics tend to overestimate their level of airway obstruction more frequently and some tend to underestimate it. This further emphasizes the importance of using objective measures of lung function in the assessment of asthma patients. Subjective wheezing was the best predictor of airway obstruction in asthmatics. Asthmatics more frequently identify wheezing as a characteristic of their exertional breathing difficulty than patients with other forms of cardiorespiratory disease. Present study found that approximately 13 percent of patients who were believed to have clinical improvement in Bronchial asthma did not demonstrate any

improvement in post bronchodilator FEV_1 . This was similar to Kelsen et al⁽¹⁷⁾ study where 10% of patients who are believed to have clinical improvement did not demonstrate any improvement in post bronchodilator FEV₁. In present study, in asthma group, potentially 43% (under estimators + over estimators as shown in figure 1) of patients initially evaluated would have been treated improperly if assessed solely on the basis of their symptoms. Under estimators had relatively asymptomatic airway obstruction. However, this subgroup of patients should be treated with a level of therapy commensurate with their degree of airway obstruction for the following reason. The airway obstruction that occurs in asthma is thought to be a manifestation of airway inflammation and airway wall remodelling leading to fixed airway obstruction as a potential complication of chronic airway inflammation, which can be seen even in patients with clinically mild disease. In present study, in COPD group the average FEV1 (in litres) for mMRC grade II, III, IV and V are 1.25, 1.21, 1.03 and 0.96 respectively as shown in table 7. As the mMRC grade increases the average FEV1 declines. This is comparable to JC Bestall et al (18) demonstrated that MRC dyspnea grading scale is a simple and valid method of categorizing patients with COPD. FEV₁ was lowest with the highest MRC grade, though it was not statistically significant (p=0.2). Among bronchial asthma group, average FEV1 (in litres) for mMRC grade I, II, III and IV are 2.24, 2.12, 1.86 and 1.74 respectively as shown in table 2. For an equal mMRC grade the average FEV1 is low in COPD group, when compared to bronchial asthma group. In present study, among COPD group, none of the patients over estimated severity of symptoms, the FEV_1 was always correspondingly low in patients with high total symptom score. However, there were a significant number of under estimators as shown in figure 2 (21%) leading to the discrepancy in establishing a statistical correlation between total symptom score and FEV₁ in this subset of patients, just like the asthma subgroups. There may be a couple of valid reasons for this. First, the FEV_1 is not perfectly reliable and can vary by as much as 5% when tested on the same patient during same day. Second, dyspnea is not just a function of spirometric flows, but is also influenced by other clinical factors such as lung volumes, airway resistance and respiratory muscle strength. Other symptoms showed no relativity. Among the individual symptoms, dyspnea was the most predictive of severity, but it was mMRC grade of dyspnea rather than just dyspnea alone which was significant.

Characteristics	Number (%among asthma group)		
Age (18 - 71 years)/	47		
Average (33.3± 14.1)	-7		
Sex			
male (19 - 71 years)	27 (57%)		
female (18 - 55 years)	20 (43%)		
Smoking			
Current	13(28%)		
Former Smoker	7 (15%)		
Never Smoker 27 (57%)			
Symptoms			
Cough	27 (57.5%)		
Dyspnoea	27(57.5%)		

IV. Figures and Tables

Wheeze	24(51.1%)
Chest tightness	28 (59.6%)
Nocturnal symptoms	26 (55.3%)

Table 1: Patient characteristics – Bronchial Asthma

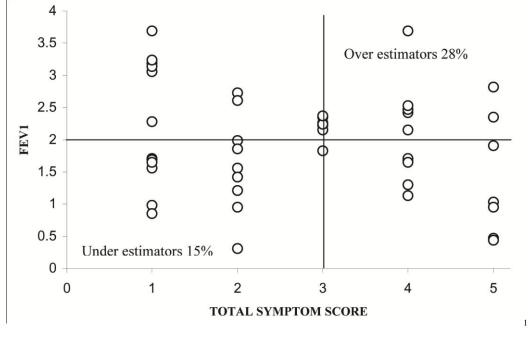
mMRC grade of dyspnea	Average FEV ₁ volume in litre
0	2.24
I.	2.12
II.	1.86
III.	1.74
IV.	No patients in this category

Table 2: MMRC grade and average FEV₁ – Bronchial asthma

FEV ₁ Test	Average value in litre
FEV ₁ prebronchodilator	1.97 ± 0.82
FEV ₁ postbronchodilator	2.54 ± 0.86

 Table 3: Spirometry – Bronchial Asthma

Figure 1 : Scatter diagram showing relationship between total symptom score & FEV



Symptoms	FEV ₁ pre	FEV_1 post
Cough	r =0.053, p =0.723	r = 0.051,p =0.662
Dyspnea	r = -0.192,p =0.196	r= -0.221, p=0.149
Wheeze	r = 0.265,p =0.071	r =0.238,p =0.094
Chest Tightness	r = -0.092,p = 0.548	r= -0.071,p= 0.582
Nocturnal Symptoms	r = -0.056,p = 0.707	r = -0.06,p =0.629
Total	r = -0.194,p = 0.191	r= -0.18 ,p =0.231

 Table 4: Relationship between individual symptoms & total symptom score with FEV1 in Broncheal asthma

Chronic Obstructive Pulmonary Disease (COPD)

Characteristics	Number		
Age $(54 - 78 \text{ years})$	47		
Average (64±6.5) Sex			
Male (54 – 78 years)	41 (87%)		
Female(62 – 68 years)	6 (13%)		
Smokii	ng		
Current smoker	26 (55%)		
Former Smoker	15(32%)		
Never Smoker	6 (13%)		
Symptoms			
Cough	39 (83%)		
Dyspnea	44 (93.6%)		
Wheeze	28 (59.6%)		

Chest tightness	24 (51.06%)
nocturnal symptoms	21 (44.7%)

Та	able 5:	Patient	characteristics	s - COPD

mMRC grade of dyspnea	Average FEV ₁ volume in litre
0	No patients in this category
I.	1.25
П.	1.21
III	1.03
IV	0.96

Table 6: mMRC grade and average FEV1 – COPD Page 500 - 2

FEV ₁ test	Average value in litre
FEV ₁ Prebronchodilator	1.15 ± 0.47
FEV ₁ Postbronchodilator	1.24 ± 0.47

Table 7: Spirometry – COPD

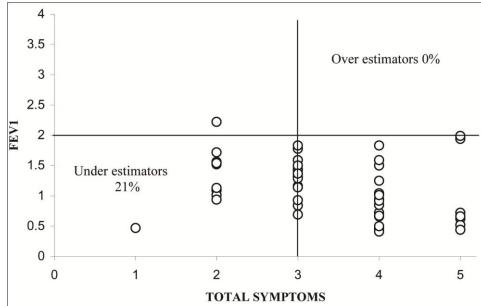


Figure 2 : Scatter diagram showing relationship between total symptom score & FEV_1 in COPD

FEV_1 pre	FEV ₁ post	
r =-0.231, p = 0.129	r =-0.219, p =0.138	
r =-0.268, p =0.088	r=-0.248, p = 0.093	
r =-0.137, p =0.381	r=-0.232, p= 0.117	
r =-0.058, p = 0.66	r=-0.264, p =0.863	
r =0.072, p =0.589	r=0.028, p= 0.892	
r =-0.231, p =0.126	r=-0.249, p= 0.122	
r =-0.271, p =0.072	r =0212, p = 0.161	
	r =-0.231, p = 0.129 r =-0.268, p =0.088 r =-0.137, p =0.381 r =-0.058, p = 0.66 r =0.072, p =0.589 r =-0.231, p =0.126	



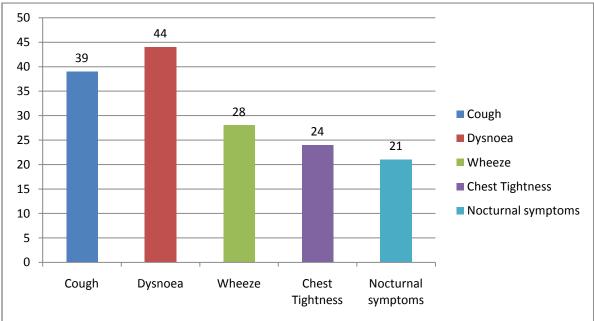


Figure 3: Symptoms in bronchial asthma

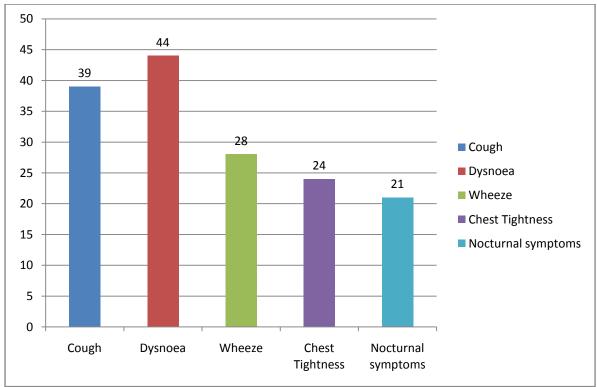


Figure 4: Symptoms in COPD

V. Conclusion

In conclusion, the patients in both Bronchial asthma and COPD subgroups, the statistical significance of correlating clinical symptoms with objective measurement of airway obstruction (by FEV_1) is not exact. Therefore both groups of patients are better managed with a combination of objective assessment of pulmonary function and symptom scores. In Bronchial asthma patients, severity of symptoms does not statistically correlate with FEV_1 measurements. Subjective wheeze is the individual symptom best approaching correlation with FEV_1 . COPD patients have better inverse correlation between symptoms and FEV_1 though not achieving statistical significance in present study. mMRC grade of dyspnea is best individual symptom in this group of individuals, correlating with measured FEV_1 values. Present study emphasizes the importance of using objective assessment of lung function in both Bronchial asthma and COPD patients prior to implementation of medical treatment strategies.

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