Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com/journal/sjams/home

OPEN ACCESS

Pulmonary Medicine

Diffusing Capacity of Lung for Carbon Monoxide (DLCO) as an Additional Diagnostic Modality to Spirometry in Diagnosis of Chronic Obstructive Pulmonary Disease (COPD) and Bronchial Asthma

Dr. Adavelli Prathyusha MD[1*], Dr. P. Mahaboob Khan MD[2]

[1]Senior Resident, Department of Pulmonary Medicine, Kakatiya Medical College/ Government Chest & TB Hospital, Warangal, Telangana, India
[2]Professor and HOD, Department of Pulmonary Medicine, Osmania Medical College/ Government General & Chest Hospital, Erragadda, Hyderabad, Telangana, India

***Corresponding author:** Dr. Adavelli Prathyusha
| **Received:** 15.01.2019 | **Accepted:** 26.01.2019 | **Published:** 30.01.2019
DOI: 10.36347/sjams.2019.v07i01.055

Abstract **Original Research Article**

COPD and Bronchial asthma are global public health challenges. COPD is projected to be third leading cause of death by 2030 and asthma represents 1-18% of world's population. Both of them are underdiagnosed or misdiagnosed in primary care. Their differentiation based on clinical features and other lung function tests besides spirometry has not been well characterised. Hence there is an utmost need to find an additional method for accurate diagnosis and differentiation between the two entities as management and prevention strategies differ for both. This cross sectional observational study was conducted on 50 cases visiting the outpatient department of Government General and Chest Hospital, Erragadda, Hyderabad with an aim to compare bronchodilator reversibility using spirometry with DLCO and to evaluate whether DLCO can be used as additional diagnostic modality to spirometry in diagnosis and differentiation of COPD and asthma. Cases were categorised into objective asthma and COPD based on history, physical examination, radiology and spirometry. All of them were subjected to DLCO single breath testing. Our study group consisted of 84% (42) males,16%(8) females. Men were predominant in COPD and women among asthmatics. Most common age of presentation in COPD was 5^{th}-6^{th} decades and asthma was 3^{rd} - 4^{th} decades. Smoking was more common in COPD 95.8%(23).FEV_1 was lower in COPD than asthmatics indicating more severe obstruction in COPD. Bronchial reversibility in asthmatics was significantly higher than in COPD. Low diffusion capacity was more in COPD group (43.40± 19.14) compared to asthmatics (98.80±18.16) with increasing stage of COPD, there was more decline in DLCO with stage 1 COPD DLCO values between 52.60±12.38 and stage 4 between 32.57±17.80 indicating significant impairment with progression of disease. Few studies stressed that DLCO was the first parameter to change in early COPD even before spirometry. The results in our study suggest that integration of DLCO in the clinical workup provides a more comprehensive assessment in patients with COPD and asthma and will help plan strategies for management.

Keywords: Chronic Obstructive Pulmonary Disease, COPD, Bronchial asthma, Diffusing capacity of Lung for Carbonmonoxide,DLCO,spirometry,FEV1(Forced Expiratory Volume in one second).

INTRODUCTION

COPD and Bronchial asthma represent important public health challenges. COPD is currently the fourth leading cause of death in the world but is projected to be third leading cause of death by 2020[1]. Many people suffer from this disease for years and die prematurely from it or it's complications [1]. On the other hand, asthma is also a chronic respiratory disease affecting 1-18% of world population [2]. Both COPD and asthma are commonly under diagnosed or misdiagnosed in primary care. Their differentiation based on clinical characteristics and other lung function tests besides spirometry has not been well characterised [3].

Increasing evidence demonstrates that parameters of airflow obstruction (FEV1) do not reflect the level of lung hyperinflation and does not fully reflect upon the declining exercise capacity and exertional dyspnea in COPD [4]. By the time airflow limitation becomes obvious on spirometry, significant parenchymal and airway damage already occurs in COPD.

Management options for both these entities differ. The current recommended approach to asthma

focuses on the early use of anti-inflammatory 'controllers', principally corticosteroids, and the measurement of day to day variability in respiratory function using peak flow measurements[2].For COPD, symptomatic relief is paramount, with corticosteroids playing a more limited role [1].

Diffusing capacity of lung for carbon monoxide (DLCO) provides qualitative and quantitative assessment of gas transfer. There are only a limited number of studies evaluating the utility of DLCO. Few available studies suggest that DLCO is closely linked to impaired exercise capacity, elevated inflammatory biomarkers and arterial oxygen desaturation in patients with COPD [5-7].

Furthermore, DLCO has been found to be an independent predictor of mortality in COPD patients[8].It was also found that DLCO can be a useful predictor of decline in lung function in smokers even before clinical and radiological abnormalities become apparent. Hence, there is an utmost need to find an additional method like DLCO which when added to our routine protocol would increase the accuracy of diagnosis and differentiation of COPD and bronchial asthma.

This study was conducted from March 2016 to March 2017 in Government General & Chest Hospital, Erragadda, Hyderabad. The purpose of our study is to compare the lung function parameters obtained using spirometry and DLCO and to determine whether DLCO is useful in differentiating COPD and asthma.

Aim and objectives

1.To evaluate whether Diffusing Capacity of Lung for carbon monoxide (DLCO) can be used as an additional diagnostic modality to spirometry in diagnosis of COPD and Bronchial asthma.2.To compare bronchodilator reversibility using spirometry with DLCO in patients with clinical diagnosis of COPD and Bronchial asthma.3.To evaluate utility of DLCO in differentiating COPD and Bronchial asthma.

METHODS

A Cross sectional observational study was done in 50 outpatient cases. Patients aged between 30-70years and who had symptoms suggestive of obstructive airway disease like cough, shortness of breath, wheeze and seasonal or diurnal variation of symptoms were included in our study. Patients who are medically and hemodynamically unstable, Cor pulmonale, Asthma-COPD Overlap Syndrome, Other comorbidities like Diabetes mellitus, anemia, pregnancy, past history of pulmonary tuberculosis etc were excluded. Thorough history and physical examination was done. Routine investigations like CBP, ESR, Hb, sputum examination and specific investigations like chest xray/HRCT, spirometry was done and cases were categorised as objective asthma and COPD.COPD cases were further categorised into 4 stages according to GOLD 2017 classification. DLCO was done in all cases. Spirometry was done by '*spida 5 pc based spirometry pc software cat no. sd5000'.* DLCO single breath method was done by '*cobra (co breath analysis software) cosmed OMNI' by* micro medical ltd and the data was subjected to statistical analysis. Grading of impairment based on DLCO was done according to ATS/ERS 2017 guidelines (Elevated >140% predicted, Normal=81% to 140 %, mild = 61 to 80 %**,** moderate = 41% to 60%**,** severe < 40%).

Study was done over a period of one year from March 2016 to March 2017 after clearance from ethical committee.

RESULTS AND DATA ANALYSIS

Out of 50 cases, 84 % (42) were males and 16 % (8) were females. In the present study,40% (10) of individuals are in the age group between 31-40years (mean=45.28years) among asthmatics (n=25) and 32% (8) between 51-60years (mean = 53.60 years) among COPD (n=25).In the present study, most common presenting symptoms among asthmatics (n=25) were shortness of breath 84% (21) and chest tightness 84%(21) followed by dry cough 76%(19).Among COPD patients, most common symptom was shortness of breath 96% (24) followed by productive cough 92%(23).Most of the patients among both the groups showed seasonal variation of symptoms 100%(25) among asthmatics and 84 % (21) among COPD. Mean age of our study population was 49.44years (SD±12.00),BMI was 21.64 (SD±4.14), FEV1 was 53.16% (SD±19.05), FEV1/FVC=0.57(SD±0.12), ΔFEV1=13.72% (SD±11.14),DLCO = 70.54(SD ± 31.64),DLCO/VA = 88.94(SD±27.25). In the present study, 52 % (26) of the study group comprised of non-smokers and 48% (24) were smokers. In the present study 50% (25) of patients had X ray features consistent with bronchial asthma and 50 % (25) had features consistent with COPD. In the present study 50% (25) were asthmatics and 50% (25) were COPD and were classified into 4 stages based on GOLD 2017 criteria. Most of the COPD cases were in stage 2 i.e.,16%(8) followed by stage 4 i.e.,14%(7) of total study group and 10%(5) belonged to stage 1 and 3 indicating moderate and very severe COPD contributing to major part of our study. Most of the COPD patients had FEV_1 between 50-79 % followed by < 30% which come under stage 2 and 4 of GOLD 2017 classification of severity of COPD. Change in FEV1 of >12% in our study group was seen in 92% of asthmatics, remaining 8 %(2) had change of 12% with all the characteristics of asthma and all 100 % (25) COPD patients showed change of < 12% indicating irreversible airway obstruction. Mean value of DLCO among asthmatics (25) was 98.80 ±18.16 and among COPD, mean DLCO was 43.40 ± 19.14; stage 1 COPD was 52.60 ±12.38; stage 2 was 50.38 ± 24.41; stage 3 38.20 ± 9.20; stage 4 32.57 ± 17.80. In our study, it was found that among asthmatics

92 %(23) had normal DLCO and 8% (2) had elevated DLCO. Among COPD 20 % (5) showed mild reduction, 28 %(7) had moderate reduction and 82 %(13) had severe reduction in DLCO. Chi square value was 46.67 with p value < 0.001 indicating significant association of normal or elevated DLCO among asthmatics and for reduction in DLCO among COPD with greater decline in DLCO with increasing severity of COPD. In the present study bronchial asthma cases had mean DLCO/VA = 110 ± 18.01 and among COPD mean DLCO/VA was 65.44 ± 12.87,stage1 had values between 73.80 ± 5.22 ,stage 2 between 66.00 ±17.60 ,stage 3 between 62.40 ± 8.29 and stage 4 between 61 ± 12.17. Indicating that reduction in DLCO/VA was not proportionate to decrease in DLCO. But similar to DLCO, DLCO/VA decreases more with increase in severity of COPD. In our study, out of 50 subjects,23 out of 25 asthmatics (92 %) had normal DLCO/VA and 2 of 25 had elevated DLCO/ VA (8%) p value < 0.001 indicating significant association.

Table-1: Gender distribution of patients in entire study group (N=50)

Sex	Frequency	Percent
Female	8	16.0
Male	42	84.0
Total	50	100.0

Table-2: Age distribution of patients among COPD (n=25) and asthma (n=25)

Age	Asthma (n=25)		COPD(n=25)	
	Frequency	Percent	Frequency	Percent
21-30	2	8.0	1	4.0
31-40	10	40.0	3	12.0
41-50	3	12.0	6	24.0
51-60	8	32.0	8	32.0
61-70	1	4.0	7	28.0
71-80	1	4.0	0	0.0
Total	25	100.0	25	100.0

Table-3: Presenting symptoms among asthma (n=25) and COPD (n=25)

Symptoms	Asthma (n=25)		COPD (n=25)	
	Frequency	Percent	Frequency	Percent
Productive cough	2	8.0	23	92.0
Dry cough	19	76.0	0	0.0
SOB	21	84.0	24	96.0
Wheeze	20	80.0	0	0.0
Chest tightness	21	84.0	0	0.0
Seasonal variation	25	100.0	21	84.0
Diurnal variation	23	92.0	1	4.0

Table- 4: Distribution of patients among asthma and various stages of COPD according to gold 2017 classification (N=50)

Diagnosis	Frequency	Percent
Asthma	25	50.0
COPD(1)	5	10.0
COPD(2)	8	16.0
COPD(3)	5	10.0
COPD(4)	7	14.0

Table-5: Distribution of FEV1 among COPD patients (n=25)

FEV1 % predicted	Frequency	Percent
≥80	5	20.0
50-79	8	32.0
30-49	5	20.0
<30	7	28.0
Total	25	100.0

Table-6: Distribution of ΔFEV1 among asthma (n=25) and COPD patients (n=25)

ΔFEV1	Asthma (n=25)		COPD (n=25)	
	Frequency	Percent	Frequency	Percent
≤12	2	8.0	25	100.0
>12	23	92.0	0	0.0
Total	25	100.0	25	100.0

Table-7: Distribution of DLCO among asthma (n=25) and various stages of COPD according to Gold 2017 classification (n = 25)

Diagnosis	DLCO				
	N	Min	Max	Mean	SD
ASTHMA	25	61	141	95.24	16.67
COPD(1)	5	39	70	52.60	12.38
COPD(2)	8	14	77	50.38	24.41
COPD(3)	5	29	50	38.20	9.20
COPD(4)	7	15	70	32.57	17.80

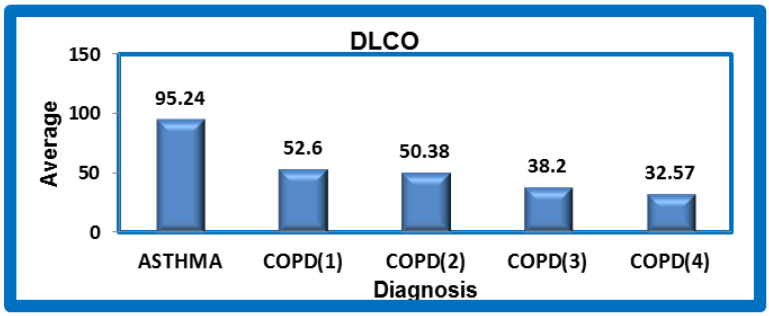

Fig-1

Table-8: Distribution of DLCO/VA among bronchial asthma (n=25) and various stages of COPD according to Gold 2017 classification (n = 25)

Diagnosis	DLCO/VA				
	N	Min	Max	Mean	SD
ASTHMA	25	80	148	109.48	19.13
COPD(1)	5	70	80	73.80	5.22
COPD(2)	8	26	78	66.00	17.60
COPD(3)	5	50	70	62.40	8.29
COPD(4)	7	45	78	61.00	12.17

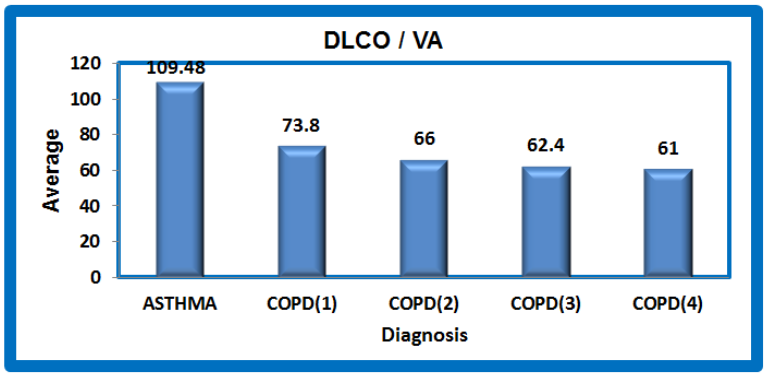

Fig-2

Table-9: Correlation of DLCO among bronchial asthma (n= 25) and COPD (n=25) according to grading of severity of DLCO

DLCO	Diagnosis		Total
	Asthma	COPD	
<40	-	13(52.0%)	13(26%)
41-60	-	7(28%)	7(14%)
61-80	-	5(20%)	5(10%)
81-140	23(92%)	-	23(46%)
>140	2(8%)	-	2(4%)
Total	25(100%)	25(100%)	50(100%)
Chi-square = 46.67		df = 4 P-value < 0.001	

DISCUSSION

Bronchial asthma and COPD are the two most common obstructive airway diseases and more recent review of literature revealed a shift in focus towards multimodality approaches in diagnosis of COPD and bronchial asthma than based on bronchodilator reversibility alone. DLCO is the least explored tool in obstructive airway diseases.

Most of the patients in our study group were men. Among both asthma and COPD patients, men were predominant and were more commonly affected by COPD. Women were more predominant among asthmatics than COPD. Most common age of presentation of COPD in our study group was 5th and 6th decade when compared to 3rd and 4th decade among bronchial asthma. COPD patients are more likely to be older. Among 50 patients in our study group 48.3 % (24) were smokers and smoking was more common in COPD i.e., 95.8 % (23).

Most common presenting complaints among asthmatics were shortness of breath and dry cough and among COPD was shortness of breath and productive cough, with majority of them showing seasonal variation of symptoms. Both the groups had almost similar BMI. Most of them were either normal weight (40%) or underweight (28%) according to Asian standards.

FEV1 was lower in COPD patients than in asthmatic patients indicating more severe obstruction. Bronchodilator reversibility in asthmatics was significantly higher than in COPD patients.

Woodruff PG, Barr RG, *et al*. [9] found that symptomatic current or former smokers with preserved pulmonary function, although they do not meet the current criteria for COPD, have exacerbations, activity limitation and evidence of airway disease.

Regan A, Lynch DA, *et al*. [10] stated that lung disease and impairments were common in smokers without spirometric COPD. Effect of chronic smoking on lungs and individual is substantially underestimated when using spirometry alone.

Hanania NA, Celli BR, *et al*. [11] found that patients with COPD were traditionally believed to have largely irreversible airway obstruction, and the acute reversibility status was often used to differentiate between COPD and asthma. However, recent studies demonstrate that many patients with COPD do indeed exhibit bronchodilator reversibility and that reversibility testing is not a reliable measure to differentiate between asthma and COPD.

Hogg JC, Timens W [12] stated that although the measurements of FEV1 and FEV1/FVC provide a reliable way of diagnosing airflow limitation and classifying COPD severity, they cannot separate the precise contribution of either small-airway obstruction or emphysematous destruction to the airflow limitation in individuals with COPD.

Low diffusion capacity was more in COPD group (43.40 ± 19.14) compared to asthmatics (98.80 ±18.16) that had either normal or elevated DLCO. With increasing stage of COPD there was more decline in DLCO with stage 1 COPD had DLCO values between 52.60 ±12.38 and stage 4 32.57 ± 17.80 between indicating significant impairment with progression of disease. In our study, it was found that among asthmatics 92 % (23) had normal DLCO and 8% (2) had elevated DLCO. Among COPD 20 % (5) showed mild reduction, 28 %(7) had moderate reduction and 82 %(13) had severe reduction in DLCO. Chi square value was 46.67 with p value < 0.001indicating significant association of normal or elevated DLCO among asthmatics and for reduction in DLCO among COPD with greater decline in DLCO with increasing severity of COPD.

In the present study bronchial asthma cases had mean DLCO/VA = 110 ± 18.01 and among COPD mean DLCO/VA was 65.44 ± 12.87, stage1 had values between 73.80 ± 5.22, stage 2 between 66.00 ±17.60 ,stage 3 between 62.40 ± 8.29 and stage 4 between 61 ± 12.17.Indicating that reduction in DLCO/VA was not proportionate to decrease in DLCO. But similar to DLCO, DLCO/VA decreases more with increase in severity of COPD.

In our study, out of 50 subjects,23 out of 25 asthmatics (92 %) had normal DLCO/VA and 2 of 25

had elevated DLCO/ VA (8%) p value < 0.001 indicating significant association.

B.A. Sin *et al*. [13], studied 51 patients above 60 years of age group and found that 27 had late onset asthma and 24 were diagnosed as COPD. Mean DLCO among asthmatics was 69.70 ± 25.43 and among COPD was 49.16 ± 22.47 and concluded that patients with COPD demonstrated significantly decreased diffusing capacity for carbon monoxide when compared to asthmatic patients (p<0.05).Mean DLCO/VA among asthmatics was 103.10 ± 17.21 and among COPD was 79.47 ± 24 and found that patients with COPD demonstrated significantly decreased diffusing capacity for carbon monoxide when compared to asthmatic patients (DLCO %: 49.16 vs 69.70, p<0.05).

In a study by D. Rosenberg *et al*. [3]. Low diffusion capacity was more likely in COPD (68% vs 8%, P <0.0001), a receiver operating characteristic (ROC) curve for discriminating between COPD and asthma was most accurate at a DLCO < 70% predicted (LR=14.7, sensitivity 63%, specificity=96%).

Treatment options for COPD and bronchial asthma differ and even within different stages of COPD. Inhaled corticosteroids (ICS) are corner stone of pharmacotherapy for asthma and, bronchodilators are fundamental for stage 1 and 2 COPD.ICS in COPD is reserved for use in combination with long acting bronchodilator in patients with stage 3 and 4 COPD.

Studies have proved that long term use of ICS increased risk of osteoporosis and their withdrawal decreased risk of pneumonia in COPD patients. A metaanalysis revealed two fold increased risk of TB in patients with COPD receiving ICS.

Based on these findings and studies done so far, it can be emphasized that early confirmation or exclusion of diagnosis of COPD or asthma based on multimodality approach may avoid needless trials of therapy or delays in intiating other investigations.

Keeping in view of limitations and factors influencing DLCO we also found that DLCO results cannot be used in isolation to "make a diagnosis" and the results should be added to other known medical or physiological parameters, which determine the pre-test probability of the disease under consideration.

CONCLUSION

DLCO is least explored tool in obstructive airway diseases. It was proved to be an additional useful tool to differentiate COPD from bronchial asthma when combined with spirometry and has also been proved to be an independent predictor of diagnosis of COPD and Bronchial asthma in the available studies. A stepwise approach to diagnosis is needed, with syndromic categorization as characteristic asthma and characteristic COPD, confirmation of chronic airflow limitation by spirometry and specialized investigations like DLCO and not only on a single tool to achieve the highest probability.

Present study also emphasizes to use spirometric criteria as a guide but not as an unimpeachable gold standard to make a diagnosis of asthma & COPD. Results in our study suggest that integration of DLCO in the clinical workup provides a more comprehensive assessment in patients with COPD and bronchial asthma and will help plan strategies for disease management.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD).Global Strategy for Diagnosis, Management and Prevention of COPD. Vancouver. USA.2019
2. Global Intiative for Asthma. Global strategy for asthma management and prevention. Updated 2018.Vancouver, USA GINA. 2018
3. Rozenberg D, Stanbrook MB. Non-Spirometric Pulmonary Function Parameters For Differentiating COPD And Asthma. InD51. COPD: DIAGNOSIS AND EVALUATION 2012 May (pp. A5894-A5894). American Thoracic Society.
4. Cooper CB. Exercise in chronic pulmonary disease: limitations and rehabilitation. Med Sci Sports Exerc. 2001; 33(7 Suppl):S643–646.
5. Owens GR, Rogers RM, Pennock BE, Levin D. The diffusing capacity as a predictor of arterial oxygen desaturation during exercise in patients with chronic obstructive pulmonary disease. N Engl J Med. 1984;310(19):1218- 21.
6. Cockayne DA, Cheng DT, Waschki B, Sridhar S, Ravindran P, Hilton H, Kourteva G, Bitter H, Pillai SG, Visvanathan S, Müller KC. Systemic biomarkers of neutrophilic inflammation, tissue injury and repair in COPD patients with differing levels of disease severity. PloS one. 2012 Jun 12;7(6):e38629.
7. Farkhooy A, Janson C, Arnardottir RH, Malinovschi A, Emtner M, Hedenstrom H. Impaired carbon monoxide diffusing capacity is the strongest predictor of exercise intolerance in COPD. COPD 2013; 10(2):180–185.
8. Farkhooy A, Janson C, Arnardóttir RH, Emtner M, Hedenström H, Malinovschi A. Impaired Carbon Monoxide Diffusing Capacity is the strongest lung function predictor of decline in 12 minute-walking distance in COPD; a 5-year follow-up study. COPD: Journal of Chronic Obstructive Pulmonary Disease. 2015 May 4;12(3):243-51.
9. Woodruff PG, Barr RG, Bleecker E, Christenson SA, Couper D, Curtis JL, Gouskova NA, Hansel NN, Hoffman EA, Kanner RE, Kleerup E. Clinical significance of symptoms in smokers with preserved pulmonary function. New England Journal of Medicine. 2016; 12;374(19):1811-21.

10. Regan EA, Lynch DA, Curran-Everett D, Curtis JL, Austin JH, Grenier PA, Kauczor HU, Bailey WC, DeMeo DL, Casaburi RH, Friedman P. Clinical and radiologic disease in smokers with normal spirometry. JAMA internal medicine. 2015 Sep 1;175(9):1539-49.
11. Hanania NA, Celli BR, Donohue JF, Martin UJ. Bronchodilator reversibility in COPD. Chest. 2011 Oct 1;140(4):1055-63.
12. Hogg JC, Timens W. The pathology of chronic obstructive pulmonary disease. Annual review of pathology. 2009; 4:435-59
13. Sin BA, Akkoca O, Saryal S, Oner F, Misirligil Z. Differences between asthma and COPD in the elderly. Journal of Investigational Allergology and Clinical Immunology. 2006 Jan 1;16(1):44.