STUDY OF ASSOCIATION BETWEEN SEVERITY OF ASTHMA AND DLCO IN STABLE ASTHMATICS PRESENTING TO A TERTIARY CARE HOSPITAL IN SOUTH INDIA

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ABSTRACT

INTRODUCTION: Diffusing capacity of lungs to Carbon Monoxide (DLCO)is used to assess the lungs ability to transfer gas from inspired air to the blood. Studies of DLCO in bronchial asthma have yielded conflicting results; decreased, normal or increased values have all been reported.

MATERIALS AND METHODS: This study was a hospital based prospective cross sectional study. Patients diagnosed as Bronchial Asthma according to GINA guidelines, who were on medications and on follow up at AJ Institute of Medical Sciences, Mangalore were included in the study over a period of 18 months. Patients were classified based on severity of asthma and were subjected to DLCO. Severity do asthma and DLCO were compared and analysed statistically.

RESULTS: Total of 80 subjects were included in the study. 48(60%) were male and 32 female. Majority i.e, 42 (52.2%) subjects had mild asthma, 26(32.5%) had moderate and 12(15%) had severe asthma. There was significant difference in mean DLCO with respect to Severity of Asthma

(P value = 0.002).Among those with mild asthma, 14.3% had increased, 85.7% had normal DLCO. Among those with moderate asthma, 65.4% had increased DLCO, 34.6% had normal DLCO and among those with severe Asthma, 66.7% had increased, 8.3% had normal and 25% had reduced. There was significant association between Severity of asthma and DLCO (p=<0.001).

CONCLUSION: There is a statistically significant association between severity of asthma and DLCO. Most of the DLCO abnormalities were seen with increasing severity of asthma. DLCO was increased in majority of moderate and severe asthmatics. Reduced DLCO was seen only in severe asthma.

Key words: DLCO, Asthma, PFT, severity of asthma, types of asthma

INTRODUCTION

Asthma is defined as a chronic inflammatory disorder of the airways which manifests itself as recurrent episodes of wheezing, breathlessness, chest tightness and cough. Bronchial hyper-responsiveness and fluctuating airflow restriction are common symptoms, which are generally reversible either naturally or with therapy. In India, asthma affects roughly 2% of the population, and it is the leading cause of illness. In India, the projected annual cost of asthma treatment in 2015 was estimated to be over 139.45 billion Indian rupees.

Diffusing capacity of lungs to Carbon Monoxide (DLCO) is used to assess the lungs ability to transfer gas from inspired air to the blood.[1]Measurement of DLCO helps to distinguish between Emphysema and other causes of chronic airway obstruction. Emphysema lowers the DLCO.[2]Studies of DLCO in bronchial asthma have yielded conflicting results; decreased, normal or increased values have all been reported.[3]The DLCO in patients with asthma depends on several factors. In asthmatic patients with preserved lung function, the DLCO is typically normal.[4]Since there are no much published studies in India regarding DLCO and its association with severity of asthma. Hence, we attempted to study the association between DLCO values with respect to severity of asthma.

MATERIALS AND METHODS:

This study was a hospital based prospective cross sectional study. Patients diagnosed as Bronchial Asthma according to GINA guidelines[5], who were on medications and on follow up at AJ Institute of Medical Sciences, Mangalore,

which is tertiary care teaching hospital were included in the study over a period of 18 months. Purposive sampling technique was used.

Sample size was estimated using the StatCalc mode on the software Epi-InfoTM version 7.2.3.1 using the following formula

$$n = [Z_{1-\alpha}]^2 \, SD^2/d^2$$

Z= normal variate [at 5%type 1 error(p<0.005) it is 1.96], SD = Standard deviation of variable, d= absolute error or precision

Taking the study Phillipe Collard et al[3] as a reference point, which calculated a standard deviation of 17, and assigning the error of 3.75 at 95% confidence Interval, the minimum sample size was calculated as 79. The final number in our study was 80.

INCLUSION CRITERIA:

- Age above 18years
- Diagnosed cases of Bronchial Asthma
- Patient who present to OPD in stable condition
- Who was able to perform spirometry

EXCLUSION CRITERIA:

- Smoker
- Respiratory tract infections in the last 2 months

- Acute exacerbation of bronchial asthma in the last 4 weeks
- Asthma COPD overlap
- Co-existing chronic lung disease
- Prior Lung resection surgeries
- Pulmonary vascular disease
- Coexisting heart disease
- History of pulmonary tuberculosis

After taking Informed consent of the patients demographic data was collected. Chest radiography was taken for all patients. Patients who were satisfying the inclusion criteria as mentioned above were subjected to perform spirometry and Diffusion lung capacity for carbon monoxide (DLCO) so as to see the association between the severity of asthma and its values. Severity of Asthma was assessed as per GINA 2018 guidelines[5] as follows

- Mild: Asthma well controlled by step1 or step 2 treatment
- Moderate: Asthma that is well controlled by step 3 treatment
- Severe: Requires step 4 or 5 treatment

DLCO was performed in our institute using Easy One Pro^TM LAB machine with Easy One Pro DLCO valve tube under the supervision of PFT technician.

Statistical analysis:

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software. Categorical data was represented in the form of frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. ANOVA (Analysis of Variance)was the test of significance to identify the mean difference between more than two groups. p value of <0.05 was considered as statistically significant .SPSS version 22 was used to analyze data.

RESULTS

Total of 80 subjects were included in our study. 48(60%) were men and 32 women. In this study , majority of subjects were in the age of 31 to 40 years (28), 30% (24) were in the age group <30 years, 25% were in the age group 41 to 50 years and 10% were in the age group >50 years

Table 1 : Age distribution

		Count	%
	<30 years	24	30
	31 to 40 years	28	35
Age	41 to 50 years	20	25
	>50 years	8	10
	Total	80	100

Severity of Asthma

52.2% subjects had mild asthma, 32.5%had moderate and 15% had severe asthma.

Table 2: Gender distribution

		Count	%
	Female	48	60.0%
Gender	Male	32	40.0%
	Total	80	100.0%

Table 3: Severity of Asthma

		Count	%
Severity	Mild	42	52.5%
of	Moderate	26	32.5%
Asthma	Severe	12	15.0%

Mean DLCO comparison with Severity of Asthma

In our study mean DLCO among those with Mild Asthma was 101.64 ± 14.51, among moderate asthma was 117.12 ± 17.03 and among severe asthma was 110.50 ± 25.58. Hence mean DLCO value was 109.75+/- 19.04. There was significant difference in mean DLCO with respect to Severity of Asthma (P value = 0.002) (Table-4).

Association between DLCO with Severity of Asthma

In our study among those with mild asthma, 14.3% had increased, 85.7% had normal DLCO. Among those with moderate asthma, 65.4% had increased DLCO, 34.6% had normal DLCO and among those with severe Asthma, 66.7% had increased, 8.3% had normal and 25% had reduced. There was significant association between Severity of asthma and DLCO (p=<0.001) (Table-5).

Table 4: Mean DLCO with severity of Asthma

		DLCO					P value
		Mean	SD	Minimum	Median	Maximum	
Severity of Asthma	Mild	101.64	14.51	84	97	134	0.002*
	Moderate	117.12	17.03	86	125	136	
	Severe	110.50	25.58	69	125	132	

Table 5: DLCO and severity of asthma

		Severity of Asthma							
		Mild		Moderate		Severe		Total	
		Count	%	Count	%	Count	%	Count	%
Results	Increased	6	14.3%	17	65.4%	8	66.7%	31	38.8%
	Normal	36	85.7%	9	34.6%	1	8.3%	46	57.5%
	Reduced	0	0.0%	0	0.0%	3	25.0%	3	3.8%
	Total	42	100.0%	26	100.0%	12	100.0%	80	100.0%

$\chi 2 =43.8$, df =4, p <0.001*

Discussion

In our study majority of subjects were in the age group 31 to 40 years (35%), 30% were in the age group <30 years, 25% were in the age group 41 to 50 years and 10% were in the age group >50 years. An Indian study done by S K Jindal et al on epidemiology of bronchial asthma, it was found that 49% of asthmatics were <35 years of age.[6] Another study conducted in mangalore, 55% of asthmatics were below 40 years and 19% were above 55 years[7]. As per the CARAS survey, mean age group among asthmatics was found to be 40.5+/- 17.5(8).In this study 60% were females and 40% were males. Sex distribution of asthmatics in male and female were 53% and 47% respectively in a study conducted by S K Jindal et al.[6] In a study done at a tertiary care centre in mangalore, it was noted that sex distribution among male(49%) and female(51%) was almost equal.[7] Conflicting results by various studies in gender distribution may be due to regional and genetic differences.[8,9]

In our study 52.5% had mild, 32.5% had moderate and 15% had severe asthma. A study conducted by Jaggi V et al across ten cities in India including 1161 asthma patients. The mean age was 40.41 years.

Southern regions of India had highest prevalence of 80%. This study concluded that 33.7% had mild, 52.4 % had moderate and 13.9% had severe asthma. [8] Another study done on Prevalence and management of severe asthma (PACEHR) noted that increased risk of exacerbations and mortality was found in patients with severe and uncontrolled asthma. This study was carried out across 36 primary health centres in Sweden which included 18724 asthmatics of which 62.8% were women and mean age was 49 years. This study showed 95.8% had mild to moderate asthma & 4.2% had severe asthma with more frequent exacerbations. Furthermore disease burden increased in poorly controlled asthmatics that comprised 28.2% of mild to moderate asthma and 53.6% with severe asthma.[9]

In our study mean DLCO among those with Mild Asthma was 101.64 ± 14.51, among moderate asthma was 117.12 ± 17.03 and among severe asthma was 110.50 ± 25.58. Hence mean DLCO value was 109.75+/- 19.04. There was significant difference in mean DLCO with respect to Severity of Asthma. Mean DLCO value was 102.8 among asthmatics as noted in a study done by Shimizu et al.[10] Among non-smoking asthmatics, 107.5 was obtained as the mean DLCO value.[11]

In our study among those with mild asthma, 14.3% had increased, 85.7% had normal DLCO. Among those with moderate asthma, 65.4% had increased DLCO, 34.6% had normal DLCO and among those with severe Asthma, 66.7% had increased, 8.3% had normal and 25% had reduced. There was significant association between Severity of asthma and DLCO (p =<0.001). Philippe Collard et al conducted a study to determine the factors influencing DLCO in asthmatics. DLCO of 80 non smoker stable asthmatics were studied and lung perfusion of 10 asthmatics and 10 controls was determined by [133]Xe Radionuclide scan. The mean value of DLCO was increased to 117% of predicted value. Asthmatics as compared with controls were found to have better perfusion in the upper zones of the lungs. A strong positive correlation between DLCO and apex to base perfusion ratio was also noted in them. As a conclusion of his study, high or normal DLCO was found in stable asthmatics. This elevated DLCO may be ascribed to a better lung perfusion at the apices which could possibly be explained by two mechanisms i.e highly negative pleural pressure during inspiration as a result of bronchial narrowing and/or elevated pulmonary arterial pressure. Thus the value of DLCO above normal limits is highly

suggestive of asthma in the absence of obvious indicators pointing to other cause.[3]In moderate to severe asthma the DLCO is usually elevated and will also increase with bronchodilator treatment. The high DLCO values have been explained by hyperinflation, increased intrathoracic pressure, and a more likely cause, increases in pulmonary capillary blood volume or extravasation of red blood cells into the alveolus.[4]

In order to investigate the respiratory physiology, Yoshiaki K et al subjected 27 asthmatic patients with airflow limitation to high-resolution computed tomography (HRCT) and pulmonary function tests. Bronchial wall thickening on HRCT, elevated FEV1 & PEFR values, decreased residual volume and DLCO was significantly high.[12]An Indian study was conducted by Vishvdeep saini et al to evaluate the role of DLCO in differentiation of various obstructive lung diseases. Total of 46 patients who were diagnosed with obstructive lung diseases were subjected to DLCO .Majority of the subjects in the study were males (65.2%) as compared to females (34.8%) with the age group of 31-50 years. Bronchial asthma had the highest mean DLCO percentage predicted value of 102.20 +/- 14.36.[13] Saydain G et al conducted a

study to identify clinical significance of elevated diffusing lung capacity. Two groups including 245 patients with high DLCO and 245 patients with normal DLCO were compared for the demographic features, clinical diagnoses and pulmonary function tests. It was found that high DLCO group consisted of patients with higher body mass index, larger mean total lung capacity with more common clinical diagnoses of asthma and obesity. Thus elevated DLCO is frequently associated with obesity, asthma and large lung volumes.[14]

In our study 25% of severe asthmatics had reduced DLCO. Conversely in another study published in European Respiratory Journal, a total of 54 patients were studied out of which 31 had severe asthma and 23 had non severe asthma. On comparing the two study group it was found that vital capacity was lower in severe asthmatics. Among 77% patients with severe asthma and 43% with non severe asthma had non reversible airway obstruction. Thus the study concluded that there is decrease in DLCO in severe asthma group. This has been attributed to presence of airway remodelling and presence of prominent air trapping in this group of patients.[15]DLCO measurements have value in severe asthma patients to get an assessment about the response to therapy. Clinically this group of asthmatics who tend to behave like COPD due to permanent pathological changes will be difficult to treat.[16]

Conclusion

There is a statistically significant association between severity of asthma and DLCO. Most of the DLCO abnormalities were seen with increasing severity of asthma. DLCO was increased in majority of moderate and severe asthmatics. Reduced DLCO was seen only in severe asthma.

Limitations:

Small sample size

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