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Original Research Article

Burden of smoking on the pulmonary diffusing capacity in asymptomatic smokers with chronic kidney disease in comparison to non-smokers with chronic kidney disease

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Abstract

Background: The study was aimed to assess the additional risk of smoking as a risk factor on lung function and gaseous exchange by measuring diffusion capacity of lung for carbon monoxide (D_{LCO} or T_{LCO}) in chronic kidney disease patients (CKD) on hemodialysis.

Methodology: This was a cross-sectional observational study among smokers and non-smokers with chronic kidney disease who were clinically stable in the last four weeks, without a past history of pulmonary and cardiac disorders. Spirometry and D_{LCO} tests were performed within 24 hours after hemodialysis.

Results: There were 40 CKD subjects on hemodialysis included in the study and were categorized into two groups as smokers & non-smokers. Smokers which included current smokers and forever smokers. All were males with the median age of 49.47 years and mean body mass index of 22.85 ± 2.29 kg/m^2 and with a mean hemoglobin level of 9.59 ± 1.58 g/dl among Non-smokers and 8.63 ± 1.51 g/dl among smokers. The mean of D_{LCO} among non-smokers with CKD was 49.35% of LLN of the normal value of D_{LCO} which is mild to moderate degree of reduction and 25.48% among smokers with CKD which is of a severe degree of reduction. There was a significant relation between D_{LCO} reduction with smoking history and also with CKD with a p-value of <0.001.

Conclusion: Reduction of diffusion capacity of the lung is common in chronic kidney disease patients even though not symptomatic. Risk factors for D_{LCO} reduction like smoking further increase the disease burden adding to further morbidity with more decrease in D_{LCO}.

Introduction

Chronic Kidney Disease (CKD) describes the gradual loss of kidney function. Altered lung function in chronic kidney disease cases was found to be well-established [1-5]. Chronic kidney disease affects the lung in many ways, Infections, Pleural effusions, and ARDS and fibrosis, calcification of the lung parenchyma and finally respiratory impairment. Anemia and gas diffusion defects, fluid overload and premature airway closure, hypoxemia due to centrally driven hypoventilation, uremic respiratory muscle dysfunction, ventilation-perfusion mismatching were reported in these patients. Several pulmonary functional abnormalities, including restriction, obstruction, and impaired diffusion capacity have also been described [6]. The latter seems to be the most serious respiratory defect adding to the morbidity and is probably the result of pulmonary fibrosis which is not evident on X-ray and is consequent to chronic or recurrent pulmonary edema, uremic pneumonitis and or pulmonary microcalcification [7-9].

Tobacco smoking is a common habit prevalent in our country. Cigarette smoking is one of the major contributorsto the rise of burden in various chronic diseases worldwide. Cigarette smoking is one of the major contributorsto the rise of burden in various chronic diseases worldwide [11-15]. Jha *et al*., have estimated that around 1 million deaths a year in India will be attributable to smoking by the early 2010 [10]. The estimates of the Global Adult Tobacco Survey (GATS) conducted among persons 15 years of age or older during 2009–10 indicate that 34.6% of the adults (47.9% males and 20.3% females) are current tobacco users. Fourteen percent of the adults smoke (24.3% males and 2.9% females) and 25.9% use smokeless tobacco (32.9% males and 18.4% females) [11]. In order to identify the progression of kidney disease apart from various pathological conditions and risk factors, cigarette smoking can be considered as a triggering factor for the decline in D_{LCO} in CKD. This could account for some of the reversible changes observed in ex-cigarette smokers [12]. The decrease in the diffusing capacity in smokers is shown to be due to alteration in the blood volume in the capillaries [13].

This study assessed the association of pulmonary function considering smoking as a significant factor in 40 chronic kidney failure patients. Also, the study was outlined to evaluate the impact of smoking on lung diffusion and to correlate the effect of smoking with various other comorbid conditions associated with chronic kidney disease.

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Materials and Methods

The present study was a cross sectional study conducted during June to July 2018. We had enrolled 40 subjects after fulfilling iclusion and exclusion criteria who underwent a physical examination, spirometry and D_{LCO} tests upon receiving informed consent. Inclusion criteria included; Male subjects greater than 18 years with a clear diagnosis of CKD undergoing hemodialysis with the history of smoking and without smoking. All the patients who were recruited were on maintenance hemodialysis done twice a week and are stable for the last 4 weeks. Exclusion criteria includes subjects with a prior history of pulmonary and cardiac disorders which was done by asking history, physical examination, a base line chest X-ray ECG and 2D Echo. Hemodynamically unstable patients were excluded who could not perform the tests and are unable to breathe hold for 10 seconds.

All the procedures and complications were explained to the subjects before the commencement of the study related tests and have obtained informed consent.

D_{LCO} Test by Single Breath Method done. The D_{LCO} estimates the diffusion capacity of the lungs by transferring the gas containing carbonmonoxide from the inhaled air to the red blood cells in pulmonary capillaries. During the test, the subject was instructed to inspire the carbon monoxide gas and one or more tracer gases and later to hold breath for ten seconds.

Statistical analysis

All the data obtained through the study were statistically analyzed using the Statistical Package for Social Science (SPSS, version 22). The data were represented as mean and standard deviation (SD) of the variables which were obtained from the descriptive programs. The Independent t-test was performed in order to evaluate the statistically significant different variables and Levine's test for equality of variances. Probability (p) value of less than or equal to 0.05 was taken as statistically significant.

Results

There were 40 subjects who met our study inclusion criteria and had undergone Hemodialysis.

Table 1: Demographic and pulmonary diffusion data of 40 smokers and non-smokers with chronic kidney disease

	Non-Smokers	Smokers	P-value
Age	46.85± 7.25	52.10 ± 10.74	0.79
BMI	22.85 ± 2.29	22.16 ± 2.74	0.394
CKD Duration [years]	2.5100 ± 1.78706	2.6750 ± 2.23203	0.798
Underlying disease			
DM	16(80%)	15(75%)	
HTN	4(20%)	6(25%)	
Hb%	9.5900 ± 1.58443	8.6300± 1.51279	0.057
V_A	69.80 ± 11.06	44.40 ± 6.68	<0.0001
K_{CO}	70.95 ± 11.96	58.40 ± 11.33	0.002
DL_{CO}	49.35 ± 11.72	25.48 ± 6.06	<0.0001

BMI: Bodu mass index, DM: diabetes mellitus, Hb: Hemoglobin, VA: alveolar volume, K_{CO}: carbon monoxide transfer coefficient, DL_{CO}: diffusing capacity of lung for carbon monoxide.

There was no difference with respect to the demographic data Age, BMI, underlying history of chronic kidney disease and hemoglobin between smokers and non-smokers. V_A, K_{CO} of D_{LCO} which shows a strong statistically significantly evidence in smokers.

Table 2: Associative relationship between the hemoglobin levels (severity of anemia) and diffusion lung capacity for carbonmonoxide in both smokers and non-smokers

	Mean $D_{LCO\%}$
No Anemia (>11 gm/dl)	56.4
Mild Anemia(9 - 10.9 gm/dl)	41.9
Moderate Anemia(7 - 8.9 gm/dl)	40.38
Severe Anemia (4 - 6.9 gm/dl)	37.25
Very Severe Anemia(<4gm/dl)	0

There was a significant reduction in the D_{LCO} levels with respect to Hb concentrations in the patients of severe and very severe anemia. This defines anemia as a independent factor for decrease in D_{LCO}.

Table 3: Comparison of the severity of smoking with D_{LCO}

	D_{LCO}% (corrected to Hb)
Non-smokers	49.35 ± 11.72
<10 pack years	36.4 ± 1.84
10-19 pack years	31.66 ± 15.30
>20 pack years	22.4 ± 47.04

The carbon monoxide that usually accompanies nicotine, restricts the amount of oxygen that the blood can carry. D_{LCO} is significantly reduced with increased years. Table 3 shows that there was a significant difference when compared with various degrees of smokers. (p-value<0.001)

Spirometry:

Of all subjects including smokers and non-smokers, 66.67% had restrictive pattern and 7.5% obstructive pattern by spirometry.

Table 4: Spirometry

		N	%
FVC(ml)	2303 ± 722		
FVC(prediction)	59.09%		
Normal		11	27.5
Mild Restriction		6	15
Moderate Restriction		12	35
Severe Restriction		7	17.5
Mild Obstruction		0	0
Moderate Obstruction		3	5
Severe Obstruction		1	2.5
Total		40	

FVC: Forced vital capacity.

Patients with end-stage renal disease on maintenance hemodialysis may have acute effects on lung microcirculation, which may result in pulmonary fibrosis and diffusion defects in long-standing dialysis.

Table 5: Relationship between spirometry and D_{LCO} reduction

Spirometry findings	D_{LCO} reduced		D_{LCO} normal	
	Smokers	Non smokers	Smokers	Non smokers
Restriction	15	10	0	3
Obstruction	02	0	1	1
Normal	02	02	0	04
Total	19	12	1	08
%	47.5	30	2.5	20

Patients who were found to have restrictive pattern in spirometry were found to have more D_{LCO} reduction than obstuctive pattern on spirometry.

Discussion

The mean age of our study patients was 49.47 and in that 62% were of less than 50 years, thus signifying that chronic kidney disease has emerged as an early complication in various disease pathologies. Only males were included in our study as most of the CKD patients attending to our hospital were males and etiologies of female CKD patients are varied if at all present. This is also in support of publishing evidence of more prevalence rate in the males. Neugarten et al., have found that men with chronic kidney disease of numerous etiologies show a more rapid failure in the renal function with time than do women. Gender difference of males to females among CKD may also be attributed to the lack of access of female patients [14].

The mean BMI of the study group was 22.85 ± 2.29 kg/m^2 and in that 20% had < 18.5 kg/m^2, which was found to be normal. In spite of chronic illness, most of the patients were shown with normal BMI due to various reasons like water retention and edema.

Our study showed anemia with mean Hb levels of 9.59 ± 1.58g/dl among non-smokers and 8.63 ± 1.51g/dl among smokers. The underlying mechanism may be due to higher levels of renal dysfunction and poor nutritional status, which indirectly reflects both the inflammatory state and poor nutritional status. Slight more decrease among smokers remains unexplained.

In accordance with the theory by Roughton and Forster et al., hemoglobin level may also affect the D_{LCO} value [15].

Hypertension remains to be the most common underlying disease in patients with or without smoking. Of course, more accountability with smoking based on the evidence of published literature.

The spirometry results in our study showed that there is a decreased FVC, restrictive pattern is seen in 66.7% of subjects and reduced airflow or obstructive pattern is seen in 7.5% of subjects irrespective of smoking etiology. Chronic subclinical pulmonary edema due to increased capillary permeability and hypoalbuminemia were considered to be the cause for the decreased FVC and the airway edema may elucidate the obstructive pattern seen in the rest.

Our study evaluated the Mean D_{LCO} value among smokers group and non- smokers group and was found to be 49.35 ± 11.72 % and 25.48 ± 6.06 % respectively which clearly indicated a higher reduction in the smokers group. Hence, it was assessed that smoking also plays a major role in a further decline in D_{LCO} among CKD patients. Bush and Gabriel et al, did not find any correlation between D_{LCO} reduction and smoking history [16].

Among smokers, we have observed the risk of a decrease in D_{LCO} with a proportional increase in the number of pack years. The results are shown to be as D_{LCO} values of 36.4 ± 1.84 % in mild smokers, 31.66 ± 15.30 % in moderate smokers and 22.4 ± 4.04 % in heavy smokers.

This study had several limitations as we have included a small number of patients, did not include ex-smokers hence further studies would require much more subjects to acquire more descriptive data.

Conclusions

Our study demonstrates that there was a significant relation with the pulmonary diffusion capacity in chronic renal failure to the spectrum of smoking. Hence, the D_{LCO} test has to be performed in addition to the spirometry in order to evaluate the diffusion characteristics of a smoker's lungs which reflect both airway and alveolar function. This study also adds more strength to the existing studies on diffusing capacity in chronic renal failure patients and establishes a further additional burden of smoking on decreased diffusing capacity in CKD patients. It establishes the ill effects of disease burden of current smoking on chronic kidney disease. Our study also suggests a need for behavioral change for a good quality of life and to reduce disease progression in CKD patients.

Conflicts of interest: None declared.

Acknowledgment

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