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"A Study on Effects of Smoking on Spirometry, Thoracic Gas Volume And Residual Volume in Apparently Asymptomatic Smokers"

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Abstract: *Smoking is one of the most important etiological risk factor in Chronic Obstructive Pulmonary Disease (COPD) and leads to progressive deterioration in lung function. The aim of our study was to detect lung function changes in asymptomatic smokers which may detect pre clinical deterioration which may convince the subject to stop smoking. Asymptomatic subjects between 18 and 40 years of age, who have smoked tobacco for at least 6 months, were selected for the study. Similar asymptomatic subjects who have never smoked or used tobacco in any form were taken as controls. A complete clinical history and examination of the subjects was done. They were also subjected to 6 minute walk test, Spirometry. In few subjects, diffusion study, thoracic gas volume and residual volume were also done by plethysmography.*

The values of FVC, FEV1/FVC% and PEFR averaged more than 94% in non smokers (n = 55, mean age 29.81 years), while 75- 85% of predicted in smokers (n = 47, mean age 27.91 years). The static volumes such as TGV, RV were increased in smokers compared to non smokers. Though the lung diffusion values in smokers as compared to non smokers were within normal range, there was a significant change for worse in smokers. 14 out of 47 subjects who initially were smokers stopped smoking after getting the test and knowing the results.

I. Introduction

Smoking is one of the most important etiological risk factor in Chronic Obstructive Pulmonary Disease (COPD) and significantly increases progressive deterioration of the lung function. Smoking also affects the growth of lungs in adolescents and is found to be associated with mild airway obstruction. The mean rate of decline in lung functions among smokers is approximately double and results in airflow obstruction around the eighth decade. However, 15 to 20% of smokers are more susceptible to develop symptomatic airway obstruction in late middle-age.

Classification Criteria As Suggested By WHO (1998).

- **Smoker**: Someone who, at the time of the study, smokes any tobacco product either daily or occasionally.
- **Non-smoker**: Someone who, at the time of the study, does not smoke at all.
- **Ex-smoker**: Someone who was formerly a daily or occasional smoker but currently does not smoke at all.

The prevalence of undetected persistent airflow obstruction in middle-aged smokers is high. Earlier detection of airflow obstruction and smoking cessation may result in significant health gain. Smoking cessation reduces the accelerated rate of decline of forced expiratory volume in one second (FEV1) found in smokers compared to non-smokers.Patients with COPD are usually diagnosed when about half of their lung function has been lost and specialists agree that early diagnosis is important for these patients in order to improve their management. The aim of early diagnosis is to improve the prognosis by effective treatment, but it is clear that non-smoking or quitting smoking is the most important measure for prevention of smoking-related diseases. Even in teenagers who have smoked only a few years, maximum expiratory flow-volume curves demonstrate decreases in flow rates at small lung volumes, yet another expression of small airway obstruction.

Spirometry is routinely used to diagnose COPD. Additional pulmonary function test methods such as body plethysmography, which measures lung volumes and airway conductance, and impulse oscillometry (IOS) which measures pulmonary resistance and compliance, provide valuable additional information on pulmonary dynamics.

II. Material And Methods

The term TGV or VTG refers to the measurement of intra thoracic gas at the time of airflow by Plethysmography. The volume is the compressible gas within the thoracic gas measured when airflow occlusion occurs at FRC.

The three most commonly used methods of measuring FRC (from which the RV is obtained) are nitrogen washout, inert gas dilution, and plethysmography.

Plethysmography measurements are based on Boyle's Law, which states that, under isothermal conditions, when a constant mass of gas is compressed or decompressed, the gas volume decreases or increases and gas pressure changes such that the product of volume and pressure at any given moment is constant.

An attractive feature of this technique is that several measurements of RV and TLC can be obtained quickly. This is not possible with the washout and dilution methods because the alveolar gas composition must be brought back to the control state before these tests can be repeated, a process that often takes 10 to 20 minutes in patients with COPD. The plethysmography method measures essentially all the gas in the lung, including that in poorly ventilated areas. Thus, in COPD, the FRC, RV, and TLC obtained with this method are usually larger

The reference values for the PFT have a wide range of normal as the lung size varies considerably in the normal subjects.

These values depend on certain variables:

– Gender (Men have bigger lungs than women)

– Age (The values drop with age)

– Height (Tall people have bigger lungs). If it is difficult to measure the height, as in kyphoscoliosis, then, the arm span can be measured instead.

A fourth important variable is race (Caucasians have bigger lungs than Africans and Asians), related to differing body proportion (legs to torso).

• Spirometry measurements from a group of healthy subjects with given gender, age, height, and race usually exhibit a normal distribution curve;

The 5th percentile is, then, used to define the lower limit of the reference range for that given gender, age, height and race.

III. Methodology

The study was conducted in the Department of Tuberculosis and Respiratory Diseases, SSIMS & RC, Davangere. The study duration was from December 2015 to October 2016. The subjects were taken from college students, young office goers and from nearby colonies, attendants of the patients visiting our medical college hospital were considered.

Asymptomatic persons between 18 and 40 years of age, who have smoked tobacco for at least 6 months, were selected for the study. Similar asymptomatic subjects who have never smoked or used tobacco in any form were taken as controls.

The statistical analysis was done by applying appropriate statistical tests. Logistic regression analysis was used with the help of statistical software SPSS.

A complete clinical history and examination of the subjects was done. They were subjected to clinical history especially to know whether they have features of any disease. They were also subjected to a general examination and systemic examination and 6 minute walk test. They were then tested for Spirometry, diffusion study, thoracic gas volume and residual volume by using a body box (plethysmograph). Diffusion studies were also carried out by single breath method, first defined by Krogh M (1914).

Pulmonary function tests were carried out with the help of computerized body box. Satisfactory demonstrations were given to the subjects about the procedure for recording the forced expiratory lung volume parameters like forced vital capacity (FVC) , forced expiratory volume in one second (FEV1), peak expiratory flow rate (PEFR) and static volumes like thoracic gas volume (TGV), residual volume (RV) and total lung capacity (TLC) and also regarding diffusion prior to the test.

The subjects were allowed to relax and familiarize the procedure. They were asked to hold the mouth piece with their lips tightly so as to prevent leakage of air during the procedure. The noses were clipped to allow airflow only through the mouthpiece. The subjects were asked to take deep inspiration and exhale forcefully and completely into the mouth piece. A minimum of three forced expiratory maneuvers were performed and the best of the three readings was selected/ accepted for analysis.

The acceptable criteria's were,

1. Full inhalation before the start of the test.
2. Satisfactory start of exhalation: maximal effort exerted with no hesitation.
3. No cough during the maneuver.
4. No early termination of exhalation.

IV. Results And Discussion

In our prospective study, the effects of smoking on lung function test parameters like FVC, FEV1, FEV1/FVC, PEFR, MEF25, TGV, RV, TLC and DLCO were assessed in asymptomatic smokers (study group) using a computerized plethysmograph (body box) and the data was compared with non smokers (control group) of similar age, height, weight and BMI.

Out of 102 subjects, 47 were asymptomatic smokers and 55 were non smokers. The subjects were in the age group of 18-40 years. Most of the study population (35.29%) belonged to the age group of 26-30 years. 36.17% of the asymptomatic smokers were in the age group of 26-30 years, whereas 34.55% of non smokers were of 26-30 years age group. The mean age of asymptomatic smokers was 29.62±5.69 years and that of non smokers was 29.45±4.95 years. In a similar study conducted by **Khan A et al (2010),** average age for both asymptomatic smokers and non smokers was 35.08±4.73 years. In another study done by **Raj JB et al (2013),** the average age for both the study group (asymptomatic smokers) and control group (non smokers) was 23.3 ± 7 years. In our study, majority of the study subjects (75.49%) were males. Males comprised 63.64% (35 out of 55) of non smokers, whereas 91.24% (42 out of 47) of the asymptomatic smokers were males, an expected observation considering that smoking is a socially unacceptable behavior among females in India. This difference in the proportion of smoking among males and females was also found by **Chhabra SK et al (2001)** when they studied patterns of smoking in New Delhi.

The asymptomatic smokers and non smokers were of similar weight, height and BMI. The mean weight of asymptomatic smokers was 66.96±8.16 kg and that of non smokers was 65.84±8.49 kg. The mean height of asymptomatic smokers was 1.68±0.09 meters and that of non smokers was 1.67±0.08 meters. The mean BMI of asymptomatic smokers was 23.64±2.29 kg/m^2 and that of non smokers was 23.68±2.07 kg/m^2. In the study conducted by **Raj JB et al (2013),** the mean weight for study and control group was 78 ± 12.2 kg and 79 ± 9.3 kg respectively. The mean height for the study group was 174 ± 5.2 cm and for the control group 174 ± 5 cm. The BMI for asymptomatic smokers and non smokers were 25.5 ± 4.2 and 22.1 ± 3.2 respectively.

In our study, asymptomatic smokers who had smoked for at least 6 months were taken as cases. The duration of smoking was 2 -5 years in 31.91% of the asymptomatic smokers. The mean amount of smoking amongst the study group was 5.2 ± 2.27 pack years. In a similar study done by **Khan A et al (2010),** asymptomatic smokers had 07 to 10 pack years of smoking with a mean of 8.51 pack years. The pack years were lowest in 18-25 years age group and highest in the age group of 36-40 years. As expected, the pack years increased with the increase in the age of the subjects. Similar observation was made in the study conducted by **Bano R et al (2009)**.

Amongst asymptomatic smokers, there were subjects who smoked cigarettes alone, others smoked bidis and also subjects who smoked both cigarettes and bidis. None of individuals smoked tobacco in any form other than bidis or cigarettes. Majority of the asymptomatic smokers, 24 out of 47 (51%) smoked cigarettes alone. 10 out of 47(21%) smoked beedis only whereas 13 out of 47(28%) smoked both cigarettes and beedis. In the study done by **Bano R et al (2009)**, most of the smokers smoked only bidi (62%) followed by both cigarette and bidi mixed (24%) and only cigarettes (14%). This could be probably because of the fact that **Bano R et al (2009)** carried out their study in a rural area, whereas our study, the subjects were from urban background such as college students, young office goers.

In our study, it was observed that among asymptomatic smokers, 12.77% (5 out of 47) were ex smokers, who were formerly daily or occasional smokers, but currently not smoking at all. In the study done by **Mohammed NH (2010),** it was found that **2**6.92% of the asymptomatic smokers (14 out of 52) were ex smokers. In our study, all the subjects, asymptomatic smokers and non smokers were subjected to a six minute walk test. The mean distance covered in asymptomatic smokers after six minute walk test was 528.30±24.90 meters and that in non smokers was 550.04±32.14 meters. The difference between the two groups was statistically significant by unpaired t test, (t=3.77, p=0.001). **Koubaa A et al (2013)** studied Cardio pulmonary adaptation following a training period of 16 weeks. Six minute walk test and the assessment of exercise responses in sedentary adult smokers. In their study, they observed that six minute walk distance improved by +51.2±36.3 meters in non smokers, whereas it improved by +26.7±17 meters in asymptomatic smokers, and the difference was statistically significant.

It was also found that all the lung function parameters were poorer in asymptomatic smokers compared to non smokers. Although the mean value of the lung functions in asymptomatic smokers were within the normal range, there was a clear trend towards decline in the lung functions of the asymptomatic smokers. Most of the non smokers (94.55%) had normal PFT results. In a similar study done by **Bano R et al (2009),** 96% of non smokers had normal PFT results.

The forced expiratory lung volumes like FVC, FEV1, FEV1/FVC, PEFR, MEF 25, MEF 50 and MEF 75 were decreased in asymptomatic smokers compared to non smokers. The values of Lung diffusing capacity for carbon monoxide (DLco/L) were lower in asymptomatic smokers than in non smokers. It was also found that Static lung volumes like thoracic gas volume (TGV), residual volume (RV) and total lung capacity (TLC) were increased in asymptomatic smokers compared to non smokers.

Although the values of lung function parameters in most of the subjects were within the normal range, there were subjects whose values were below /above the cut off values. The cut off value that we took for FEV1/FVC was less than 70. For FVC, FEV1, PEFR, MEF25, MEF50, MEF 75 and DLco/L, the cut off was less than 80%. And, for TGV, RV and TLC, the cut off was taken as more than 110%. In the subjects, whose PFT parameters were impaired as per the cut off values, the proportion of asymptomatic smokers was much higher than the non smokers. The association of impaired PFTs in asymptomatic smokers was found to be statistically significant in all parameters except PEFR, TGV and RV by applying logistic regression analysis.

The changes in the lung function test parameters are discussed below.

In our study, we found that mean FVC in non smokers was 3.98±0.86 L, and in asymptomatic smokers, it was found to be 3.70±0.84 L.

Although the values of FVC in most of the subjects were within the normal range, there were subjects whose values were below the cut off value of 80%. 5 out of 47(10.64%) asymptomatic smokers had FVC value less than 80%, whereas 2 out of 55(3.63%) non smokers had reduced FVC(less than 80%), which was statistically highly significant($p < 0.001$).

The mean FEV1 in non smokers was found to be 3.37±0.77 L, and in asymptomatic smokers, it was 3.11±0.81 L. 44.68% (21 out of 47) of the asymptomatic smokers had FEV1 < 80% and only 3 out of 55 (5.45%) non smokers had FEV1 < 80%, which was statistically highly significant ($p < 0.001$).

The mean FEV1/FVC in non smokers was found to be 82.40±5.24, and in asymptomatic smokers, it was 72.33 ±7.97. 68% (21 out of 47) of the asymptomatic smokers had FEV1/FVC < 70 and only 3 out of 55(5.45%) non smokers had FEV1/FVC < 70, which was statistically highly significant ($p < 0.001$).

Similar results were observed in the study conducted by **Burrows et al (1977), Prieto F et al (1978)**, **Gosavi GR et al (1981), Pandya KD et al (1984)** , **Gupta P et al(1984), Bano R et al (2009), Bajantri AL et al (2003), Khan A et al (2010), Raj JB et al (2013)** and **Wisnivesky J (2014) ,** who observed that the forced expiratory lung volumes like FVC, FEV1 and FEV1/FVC were reduced significantly in asymptomatic smokers when compared to nonsmokers.

Several researchers like **Sackner MA et al (1982), Angelo MT et al (1973)**, **Malo JL et al (1975) Gupta S et al (1977)** observed that there was no change in FVC in asymptomatic smokers and nonsmokers.

We observed that the mean PEFR in non smokers was found to be 8.06±1.49 L, and in asymptomatic smokers, it was 7.63± 1.70, which was statistically not significant ($p= 0.99$). This could be probably because of the reason that PEFR is largely the function of the calibre of larger and medium airways. More over it is highly effort dependent and the same results are difficult to reproduce in subjects and patients. It is also possible that the tobacco smoking predominantly affects smaller airways which are not represented by PEFR. The same observation was also made by **Sackner MA et al (1982), Bosken CH et al (1990)**, **Polatly M et al (2000)**, **Raj JB et al (2013),** who found that PEFR values were reduced in asymptomatic smokers, but not as much to the extent of other forced expiratory lung volumes.

However, **Bajantri AL et al (2003), Khan A et al (2010)** and **Boskabady MH et al (2011)** found that the reduction in PEFR among smoker subjects was significantly more than other values of PFTs which may indicate that in smoker subjects, medium and larger airways are more affected by smoking than small airways.

The mean MEF 25 in non smokers was 2.60±0.31 L/s, whereas in asymptomatic smokers, it was 7.63± 1.70 L/s. 46.81% (22 out of 47) asymptomatic smokers had MEF25 less than 80% and only 3 out of 55 (5.45%) non smokers had MEF 25 less than 80%, which was statistically highly significant($p<0.001$).The mean MEF 50 in non smokers was 5.67±0.62 L/s, whereas in asymptomatic smokers, it was 5.44± 0.58 L/s. In our study, 46.81% (22 out of 47) asymptomatic smokers had MEF50 less than 80%, whereas only 3 out of 55 (5.45%) non smokers had MEF 50 less than 80%, which was statistically highly significant($p<0.001$).

We observed that the mean MEF 75 in non smokers was 7.92±1.32 L/s, and in asymptomatic smokers, it was 7.44± 1.31 L/s, which was statistically not significant ($p=0.998$)

Sackner MA et al (1982) did an assessment of time and flow volume components of FVC with spirometry, body plethysmography and respiratory inductive plethysmography in non smokers and smokers and found that non smokers had a significantly higher MEF 25, whereas there was no major difference between non smokers and smokers in the parameters MEF 50 and MEF 75. **Boskabady MH et al** found that the reduction in MEF 75 among smoker subjects was significantly more compared to non smokers.

In our study, the mean Lung diffusing capacity for carbon monoxide (DLco/L) in non smokers was found to be 4.94±0.36 and in asymptomatic smokers, it was 4.64±0.35. Among asymptomatic smokers, 22 out of 47(46.81%) had DLCO/L <80% and only 2 out of 55 non smokers(3.63%) had DLco/L less than 80% , which was statistically highly significant ($p<0.001$).

Polatly M et al (2000) studied the early effect on smoking and transfer factor in asymptomatic smokers and found that TLCO (transfer capacity of the lung for carbon monoxide) was significantly lower in asymptomatic smokers than in non-smokers. **Andre S et al (2003)** studied the effect of smoking on pulmonary diffusion capacity in asymptomatic smokers and found that a higher number of reduced values of DLCO

comparing with small airways flow obstruction was found, which seems to mean that DLCO is a more sensitive and earliest functional test in smokers evaluation. **Aydin O et al (2008)** studied the correlation of functional and radiological findings in asymptomatic smokers and found that 54% of the asymptomatic smokers had reduced DLCO and DLCO values were significantly lower in subjects with a history of parental smoking than the subjects without parental smoking history. **Mohammed NH (2010)** studied the Lung Diffusing Capacity for Carbon Monoxide: the Influence of Cigarette Smoking and found that (DLco/VA) were lower in smokers than in never smokers. However, in the study done by **Yasunaga K et al (2013),** there were no significant differences were found in the mean values of DLCO in asymptomatic smokers.

In our study, the mean TGV in non smokers was 2.97±0.29 L, and in asymptomatic smokers, it was 3.16± 0.19 L, the values of thoracic gas volume were found to be normal in all non smokers, whereas 14.89% (7 out of 47) of asymptomatic smokers had increased TGV (>110%), which was statistically not significant (p= 0.99).In our study, the mean RV in non smokers was 1.45±0.12 L, and in asymptomatic smokers, it was 1.45± 0.08 L, the values of RV were found to be normal in all non smokers, whereas 23.4% (11 out of 47) of asymptomatic smokers had increased RV (>110%), which was statistically not significant(p=0.99)

York, Jones (1981) studied lung functions in young adults and found that there was no significant difference in overall lung function between non smokers and smokers (mean age=23.8 years), but residual volume was significantly higher in the lower-lung regions of the smokers. **Yasunaga K et al (2013)** did a study on emphysema in asymptomatic smokers, quantitative CT evaluation in correlation with PFTs and found that emphysematous changes were present in asymptomatic smokers and asymptomatic smokers with emphysematous changes had significantly higher mean values of FRC/TGV (p=0.0012),RV (<0.0001) and TLC (p=0.0157), but no significant differences were found in the mean values of TLCO.

The mean TLC in non smokers was 5.44±0.87 L, and in asymptomatic smokers, it was 6.10± 0.64 L, 1 out of 55(1.82%) non smokers had TLC >110%, whereas 44.68% (21 out of 47) of the asymptomatic smokers had TLC >110%, which was statistically highly significant (p= 0.004). **Sackner MA et al (1982)** also found that TLC was higher in asymptomatic smokers. However, in the study done by **Mohammed NH (2010),** the values of TLC had not changed with smoking.

In our study, the values of forced expiratory volumes like FVC, FEV1, FEV1/FVC, MEF25 and MEF50 were lower in bidi smokers compared to cigarette smokers and those who smoked both cigarettes and bidis whereas static lung volumes like RV, TGV and TLC were higher in bidi smokers. The values of forced expiratory volumes like PEFR and MEF75 were also lower in bidi smokers compared to cigarette smokers and those who smoked both cigarettes and bidis, though it was not as much to the extent of other forced expiratory parameters.

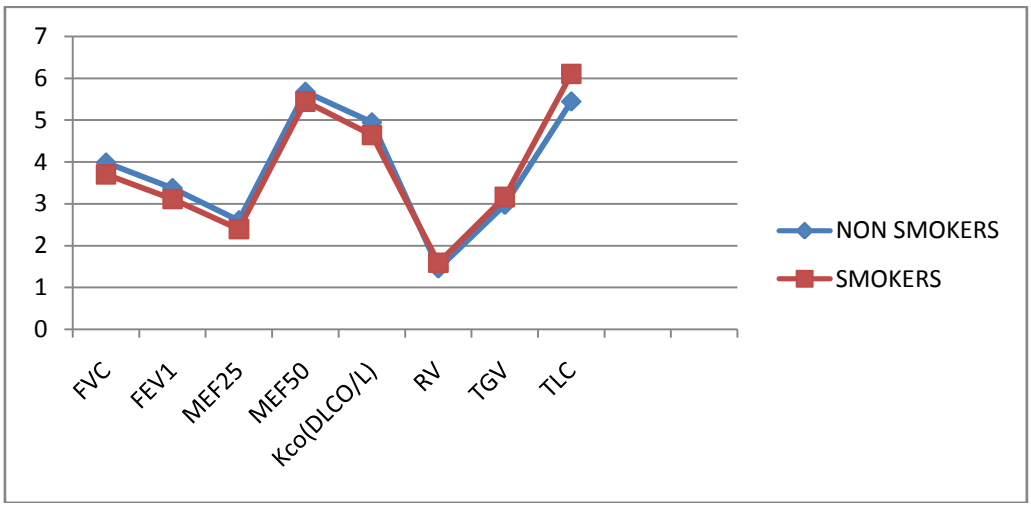
Similar observations were made by **Padmavathy KM (2008) and Bano R et al (2009),** who found that the obstructive lung changes were most common in smokers and were observed predominantly in bidi smokers (72.22%), followed by both cigarette and bidi smokers (22.22%) and those who smoked cigarettes only (5.55%). The lung function parameters among asymptomatic smokers with different types of smoking (cigarette smokers, bidi smokers and those who smoked both cigarettes and bidis) were not analyzed as the numbers were small in individual groups.

After obtaining PFT results and after counseling of the subjects, 14 out of 42 current smokers (33.33%) decided to quit smoking. Out of these, 13 were males and one was female.

Age Group	Six Minute Walk Distance(Meters)	
	Control Group (Non Smokers)	Study Group (Asymptomatic Smokers)
18-25 Years	568.33±18.05	553.89±19.32
26-30 Years	560.26±20.23	533.35±18.74
31-35 Years	540.86±28.22	524.00±19.55
36-40 Years	521.51±46.12	503.18±17.32
All Subjects	550.04±32.14	528.30±24.90

Lung Function Parameter	Non Smokers(N=55)			Smokers(N=47)		
	Predicted Value (MEAN)	Observed Value (MEAN ±SD)	% Ref. (MEAN ± SD)	Predicted Value (MEAN ±SD)	Observed Value (MEAN ±SD)	% Ref. (MEAN ± SD)
Fvc(L)	4.15± 0.96	3.98± 0.86	95.80± 5.6%	4.62± 0.82	3.70± 0.84	80.08± 10.12%
Fev1(L)	3.69± 0.82	3.37± 0.77	91.39± 6.2%	3.98± 0.78	3.11± 0.81	77.88± 11.37%
Fev1/ Fvc	86.87± 5.38	82.40±5.56	94.85± 4.02%	85.65± 7.24	72.33± 7.97	84.44± 8.08%
Pefr(L/S)	8.56± 1.52	8.06± 1.49	94.12± 5.89%	8.98± 1.58	7.63± 1.70	84.94± 9.34%

Mef25(L/S)	2.87± 0.27	2.60± 0.31	90.65± 5.19%	2.91± 0.29	2.39± 0.31	82.03± 8.25
Mef50(L/S)	6.01± 0.48	5.67± 0.52	94.41± 4.31	6.15± 0.54	5.44± 0.58	88.37± 7.10
Mef75(L/S)	8.30± 1.54	7.92± 1.32	95.38± 5.88	8.76± 1.56	7.44± 1.31	84.91± 8.92
Tgv(L)	3.05± 0.31	2.97± 0.29	97.17± 2.54%	2.94± 0.21	3.16± 0.19	107.48± 4.12%
Rv(L)	1.53± 0.13	1.45± 0.12	94.63± 3.93%	1.49± 0.11	1.59± 0.08	107.55± 5.49%
Tlc(L)	5.80± 0.89	5.44± 0.87	93.74± 3.46%	5.86± 0.68	6.10± 0.64	104.02± 5.59%
Kco (DLCO/L)	5.08± 0.38	4.94± 0.36	97.24± 3.54%	5.06± 0.42	4.64± 0.35	91.69± 5.31%



V. Conclusions

1. The six minute walk distance was significantly reduced in asymptomatic smokers as compared to non smokers.
2. 53.19% asymptomatic smokers had all lung function parameters within normal range versus 94.55% in non smokers.
3. The mean values of lung function parameters like FVC, FEV1, FEV1/FVC, MEF 25, MEF 50 and DLco/L in asymptomatic smokers despite of being well within normal range were significantly lower than non-smokers.
4. Static lung volumes like RV, TGV and TLC were increased in asymptomatic smokers as compared to non smokers with TLC being the most sensitive parameter.
5. The mean Lung diffusing capacity for carbon monoxide (DLco/L) was significantly reduced in asymptomatic smokers.
6. Among asymptomatic smokers with impaired pulmonary function tests, obstructive pattern was more common.
7. Post PFT counseling of asymptomatic smokers yielded good results in the motivation of the subjects to quit smoking.

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