A cross-sectional study to investigate short duration toxic consequences of smoking to lungs of asymptomatic smokers through spirometry and 6 min walk test

Bhupendra Kumar Jain[1], Ashwin Songra[2]

[1]Associate Professor and Head, Department of Pulmonary Medicine, Chhindwara Institute of Medical Sciences, Chhindwara, Madhya Pradesh, India, [2]Assistant Professor, Department of Pulmonary Medicine, Amaltas Institute of Medical Sciences, Dewas, Madhya Pradesh, India

A B S T R A C T

Background: Cigarette smokers have a lower level of pulmonary function and physical fitness than non-smokers. Very little information is available for the short-term effects of smoking to lungs of asymptomatic smokers. **Aims and Objectives:** The main focus of this study is to evaluate short duration toxic consequences of smoking to the lungs of asymptomatic smokers through spirometry and 6 min walk test (6MWT). **Materials and Methods:** The present study is an observational cross-sectional study conducted in a tertiary care hospital which includes 160 individuals, 80 smokers and 80 non-smokers. The spirometric variables and 6MWT were performed to quantify smoking exposure. The whole statistics was analyzed using SPSS 21 and the mean between two groups was compared after applying standard Chi-square test. The means across more than 2 groups were compared after applying the standard analysis of variance (ANOVA) test. **Results:** Most of lung function parameter such as forced expiratory volume in 1 s (FEV1), FEV1%, FEV1/forced vital capacity % (FVC%), maximum mid-expiratory flow 25–75%, peak expiratory flow rate (PEFR), PEFR%, and maximum voluntary ventilation % is decreased significantly in asymptomatic smokers than non-smokers except FVC and FVC%. The 6MWT distance is also reduced gradually and significantly in asymptomatic smokers from 1–5 pack-years to 15–20 pack-years. **Conclusion:** Lung function parameters and 6MWT decreased significantly in asymptomatic smoker with increased quantum of pack-years. Therefore, early screening of high-risk smokers would lead to reduction of the clinical disease.

Key words: Lungs; Smoking; Spirometry; 6 min walk test

INTRODUCTION

Cigarette smokers have a higher prevalence of respiratory symptoms, lung function aberration, and a higher decline in forced expiratory volume in 1 s (FEV1) than non-smokers.[1] Cigarette smokers have a lower level of pulmonary function than those persons who are non-smokers. Smoking damages the young people's achievement in terms of physical fitness and exercise capacity. Person who smokes a pack or more of cigarettes each day generally lives 7 years less than individual who never smoked.[2] The early

symptoms of cough and sputum production which are manifestation of chronic obstructive pulmonary disease (COPD) are usually missed by the smoker and are regarded as normal or seasonal cough. A person attends medical physician when they got breathing problems of mild-to-moderate degree, but half of the respiratory reserves are lost at that time.[3] Meta-analysis of Indian study reveals prevalence of COPD to be 5% in males while it is 2.7% in females above 30 years of age.[4] Most of literature reveals long-term toxic effect of smoking (>20 pack-years) to lung function. Therefore, the main purpose of this study is to

Address for Correspondence:
Bhupendra Kumar Jain, Associate Professor, Department of Pulmonary Medicine, Chhindwara Institute of Medical Sciences Chhindwara, Dewas - 480 001, Madhya Pradesh, India. **Mobile:** +91-9406533632. **E-mail:** drbhupendrakjain@gmail.com

investigate short duration toxic consequences of smoking (<20 pack-years) to lungs of asymptomatic smokers by spirometry and 6 min walk test (6MWT).

Aims and objectives

The main focus of this study is to evaluate short duration toxic consequences of smoking to the lungs of asymptomatic smokers through spirometry and 6 min walk test (6MWT).

MATERIALS AND METHODS

A minimum of 160 patients who visited Sri Aurobindo Medical College and Mohak Superspeciality Hospital, Indore, who have been diagnosed as free from any cardiovascular, neurological, and gastroenterological disease by thorough clinical examination were taken into account. Complete ethical approval taken from college ethical committee before starting study. Sample size has been taken on the basis of average number of asymptomatic smokers between 20–50 years age group in around 24 months. The random selection of individuals includes 80 asymptomatic smokers and 80 healthy non-smokers.

Inclusion criteria
For cases
1. Informed and willing young smokers with no prior history of any chronic disease
2. Age 20–50 years of age
3. Body mass index (BMI) between 18 and 25 kg/m²
4. Smoker 1–20 pack-years (PYs).

For control
1. Informed and willing healthy subject from executive health check-up with no prior history of any chronic disease
2. Age 20–50 years of age
3. Non-smoker
4. BMI 18–25 kg/m².

Exclusion criteria
The following criteria were excluded from the study:
1. Acute metabolic complications
2. Smoker >20 PYs
3. Alcohol dependence
4. Comorbid disease.

For the comparison between smokers and non-smokers, the whole sample of population was divided into two groups. Group 1 has individuals of age 21–35 years and Group 2 has individuals of age 36–50 years.

The volume of smoking exposure was calculated based on PYs. PYs are calculated by formula Number of

PYs=Number of cigarettes smoked per day/20×Number of years smoked. Subjects were asked to stop smoking for 4–6 h before tests. Smokers are divided into four groups, Group A comprises 1–5 PYs, Group B consists of 6–10 PYs, Group C consists of 11–15 PYs, and Group D consists of 16–20 PYs.

Study tools
1. History
2. Examination
3. BMI
4. Pulmonary function test
5. 6 min walk distance (SMWD).

The spirometric studies was conducted to find out the range of values for various pulmonary function parameters including forced vital capacity (FVC), forced expiratory volume in 1 s (FEV1) in 1 s of FVC, FEV1%, peak expiratory flow rate (PEFR), maximum mid-expiratory flow rate (MMEF), and maximum voluntary ventilation (MVV). Equipment used was a Master Screen PFT SYSTEM (JAEGER M S PFT) Machine. Spirometry is performed by an experienced respiratory technician as per the recommendations of the American Thoracic Society guidelines.[5] FVC, FEV1, and FEV1% were measured after the administration of 400 μg of salbutamol as per the guidelines given by chronic obstructive lung disease (GOLD).[1] Based on spirometry, subjects were categorized as COPD if FEV1/FVC <0.70 and mild grade if FEV >80% of predicted normal value, moderate grade COPD if FEV1 50–70% of predicted normal value, severe grade COPD if FEV1 30–50% of predicted normal, and very severe grade COPD if FEV1 <30% of predicted normal value.

The 6MWT is a practical simple test that requires a 100-feet hallway and flat hard surface for walking. 6MWT was carried out as per the American Thoracic society guideline by trained respiratory technicians. This test measures the distance that a patient can quickly walk on a flat, hard surface in a period of 6 min.[6] This test is performed by both case and control to quantify effects of smoking.

Statistical methods
The whole data were entered into Microsoft Excel sheet and analyzed using Statistical Package for the Social Sciences (SPSS) software, version 21. We calculated the means and standard deviations for the linear variables and proportions for the categorical variables. The means between two groups were compared using standard Chi-square test. The means across more than two groups were compared using the standard test analysis of variance (ANOVA). If $P<0.05$, result is trumpted as statistically significant.

RESULTS

A total of 160 persons including both males and females who met inclusion criteria were included in the study. It includes 80 asymptomatic smokers as case and 80 non-smokers as controls.

The whole population of smokers is divided into four groups on the basis of number of pack-years they used to smoke.

Figure 1 shows that Group A includes 1-5PYs, Group B have 5-10PYs, Group C have 10-15PYs and Group D have 15-20PYs. Maximum smokers belonged to Group A (32) followed by Group C (22 smokers), Group B (16 smokers) and Group D (10 smokers).

Table 1 shows that difference between anthropometric measures of smokers and non-smokers group, that is, age, height, weight, and BMI, is not statistically significant (P>0.05) which signifies a proper group selection.

Table 2 shows that there is difference in mean values of spirometric parameters of smokers and non-smokers. Mean values of all the variables are more in non-smokers than smokers.

There is statistically significant difference between smokers and non-smokers group in spirometric parameters of

FEV1, FEV1%, FEV1/FVC%, MMEF 25–75, MMEF 25–75%, PEFR, PEFR%, and MVV% (P<0.001), while there is no significant difference in parameter of FVC and FVC% of two groups (P=0.164 and P=0.774, respectively).

Table 3 shows that the mean distance walked in 6 min, that is, 6MWT=424.7 in smoker which is significantly less than non-smokers, that is, 478.8 (P<0.05).

Table 4 shows the spirometric variables correlation among different groups of smokers. Group A has maximum mean FEV1% (i.e., 88%) while Group D has least value of FEV1% (i.e., 71.5%), so as the trend of maximum number of variables except FVC. This suggests gradual progressing toxic effect of smoking to the lungs with increased quantum of smoking PYs. P value is significant (P<0.05) for all the variables except FVC and FVC%. The spirometric variable which is most effected in Group A is MMEF 25–75% (i.e., 73.7%) to MMEF 25–75% in Group D (i.e., 53.09%). The earliest spirometric variable affected in smokers is MMEF 25–75% which suggests involvement of small airway obstruction. Thus, we conclude by this table that as the number of pack-years of smoking increases, there is statistically significant decrease in most of the spirometric variables except FVC and FVC%.

Figure 2 suggests that as the duration and intensity of smoking increase, the mean SMWD decreases.

SMWT is inversely proportional to smoking PYs. The correlation between smoking PYs and 6MWT is statistically significant (P<0.05). This table suggests that physical fitness of smokers in terms of 6MWT performance gradually decreases from 464 meters in Group A (1–5 PYs) to 343 m in Group D (16–20 PYs).

Table 5 shows the comparison of spirometric values between the smokers and non-smokers of different age groups (A and B). The variables FVC, FEV1, FEV1%, FEV1/FVC%, MMEF 25–75, MMEF 25–75%, PEFR, PEFR%, and MVV% have value lesser in smokers than non-smokers of age-matched controls and the difference in spirometric variables is found to be statistically significant (P<0.001). Furthermore, when the smokers of both the groups are compared, the mean value of all the variables

Table 1: Anthropometric values and physical performance of two groups

Variables	Smokers* N=80	Non-smokers* N=80	P value
Age (yrs)	35.46±9.08	35.75±8.07	0.890
Height (cm)	172.11±6.89	171.31±6.10	0.441
Weight (kg)	67.38±8.36	65.32±6.46	0.087
BMI	22.71±2.14	22.27±1.85	0.164

*All data are expressed as mean (standard deviation). BMI: Body mass index, Yrs: Years, cm: Centimeter, Kg: Kilogram

Table 2: Pulmonary function test of smokers and non-smokers

Variables	Smokers*	Non-smokers*	P value
FVC	4.06±0.69	4.20±0.58	0.164
FVC%	87.22±9.08	87.64±9.10	0.774
FEV1	3.04±0.50	3.46±0.54	0.000
FEV1%	79.97±11.79	88.60±11.91	0.000
FEV1/FVC%	77.21±13.05	82.80±5.95	0.001
MMEF 25–75	2.84±0.90	3.67±0.76	0.000
MMEF 25–75%	65.95±18.21	88.86±20.95	0.000
PEFR	6.94±1.48	8.46±1.09	0.000
PEFR%	75.09±17.21	90.76±13.62	0.000
MVV%	81.31±20.34	95.621±13.24	0.000

*All data are expressed as mean (standard deviation). FVC: Force vital capacity, FEV1: Forced expiratory volume in 1 s, MMEF: Mid-maximum expiratory flow rate, PEFR: Peak expiratory flow rate, MVV: Maximum voluntary ventilation

Table 3: Physical performance of smokers and non-smokers

Variables	Smokers N=80 (mean±SD)	Non-smokers N=80 (mean±SD)	P value
SMWD	424.72±46.12 8.58±5.62	478.88±30.22	0.000

SMWD: 6 min walk distance

Table 4: Correlation of PFT with smoking pack-years

Variables	Group A n=32 (1–5 Py)	Group B n=16 (5–10 Py)	Group C n=2 (10–15 Py)	Group D n=10 (15–20 Py)	Df	P value
FVC	3.91±0.72	4.19±0.80	4.22±0.61	4.01±0.43	1.082	0.36
FVC%	89.45±8.4	87.55±9.26	86.44±9.80	81.3±5.80	2.187	0.09
FEV1	3.22±0.47	3.06±0.57	2.98±0.54	2.82±0.31	2.586	0.05
FEV1%	88.22±7.41	78.91±8.63	74.73±13.32	71.55±5.22	12.88	0.00
FEV1/FVC%	86.56±12.03	73.20±5.15	71.74±11.67	70.24±2.71	13.23	0.00
MMEF 25–75	3.48±0.84	2.43±0.68	2.45±0.60	2.09±0.53	15.21	0.00
MMEF 25–75%	73.79±20.58	61.13±14.42	61.57±13.60	53.09±10.92	5.011	0.003
PEFR	7.35±1.60	6.99±1.66	6.58±0.93	5.79±0.98	3.452	0.02
PEFR%	81.80±19.24	75.20±17.06	69.34±9.18	60.16±9.98	5.694	0.001
MVV%	94.51±22.13	75.23±18.27	73.63±9.46	66.33±6.50	10.50	0.00

FVC: Force vital capacity, FEV1: Forced expiratory volume in 1 s, MMEF: Mid-maximum expiratory flow rate, PEFR: Peak expiratory flow rate, MVV: Maximum voluntary ventilation
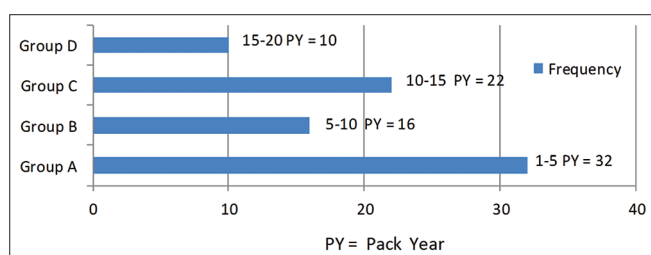

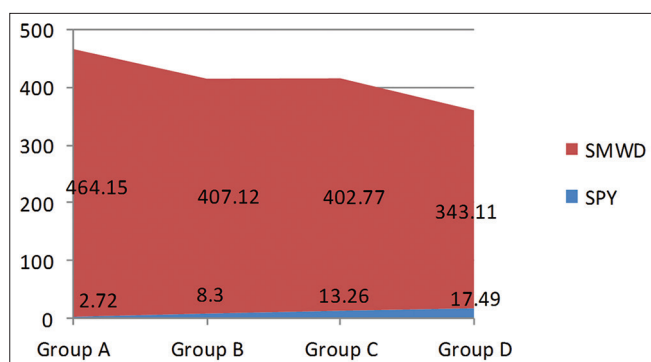**Figure 1:** Distribution among smokers population

Figure 2: Comparison of 6 min walk distance with smoking pack-years

is lesser in all the smokers of Group 2 which may be due to the age-related decrease in spirometric variables and increased smoking PYs. This table suggest early large airway obstruction (FEV1%) in 36–50 years smokers group (i.e., 75%) to normal large airways (84%) in 21–35 years smokers group while small airway obstruction MMEF (25–75%) decrement is mainly observed in 36–50 years smokers group, that is, 61.9%, and 21–35 years smoker group, that is, 68.35%.

MMEF 25–75% parameter is normal in both non-smoker groups. This table suggests that small airway variable is effected maximum in early smokers.

Table 6 shows that mean SMWT distance is decreased in smokers of both 21–35 years and 36–50 years age

group as compared to the non-smokers of same age group. As the age increases, the mean SMWT distance decreases. Furthermore, the decrease in SMWT distance is significantly more in cases of smokers of older age group. Smokers of 36–50 years age group are heavy smokers with maximum smoking PYs. It suggests that age and quantum of smoking PYs are negatively correlated to SMWT distance.

Figure 3 suggests that the prevalence of COPD in smoker is 23.7%, that is, total 19 smokers fulfill the criteria of COPD as per GOLD spirometric variables criteria. Among them, maximum smokers have moderate COPD (15), three have mild COPD while one has severe COPD. Smokers of Group "C" have maximum number of COPD patients, that is, 8.

DISCUSSION

COPD is frequently under-recognized or diagnosed at an older stage of life, when there are very few treatment modalities to hamper the progressive nature of COPD. Spirometry screening of asymptomatic smokers will be helpful to diagnose a trivial number of smokers with airway obstruction who are at high risk of development to COPD disease. In this study, we have evaluated the results of spirometry screening and 6MWT distance on asymptomatic smokers between 1–20 PYs and compared with asymptomatic healthy controls of same age group.

In our study, proper matching of the smokers and non-smokers group was there as both groups had no significant difference in the mean anthropometric parameters such as age, height, weight, and BMI when mean and standard deviation in both groups were compared. All the smokers smoked only cigarettes and no smoker is taking tobacco in any form other than smoking.

Table 5: Comparison of pulmonary function test of two groups

Spirometric variables	Age groups			
	Group 1 (20–35 years)		Group 2 (35–50 years)	
	Smokers (n=42)	Non-smokers (n=43)	Smokers (n=38)	Non-smokers (n=37)
FVC	4.070±0.72	4.29±0.49	4.06±0.66	4.10±0.65
FVC%	89.45±8.32	86.60±8.29	84.76±9.25	88.84±9.82
FEV1	3.21±0.53	3.57±0.51	2.86±0.40	3.34±0.55
FEV1%	84±11.54	87.45±11.92	75.51±10.37	89.93±11.75
FEV1/FVC%	82.59±13.73	83.96±6.57	71.27±9.12	81.46±4.80
MMEF 25–75	3.19±0.90	3.95±0.55	2.39±0.69	3.34±0.84
MMEF 25–75%	68.35±19.57	90.01±18.15	61.95±15.92	87.53±23.73
PEFR	6.98±1.65	8.35±1.076	6.76±1.27	8.60±1.09
PEFR%	75.95±18.50	87.71±10.41	72.58±15.48	94.31±15.87
MVV%	89.62±22.21	95.35±12.01	72.29±12.99	95.93±14.54

FVC: Force vital capacity, FEV1: Forced expiratory volume in 1 s, MMEF: Mid-maximum expiratory flow rate, PEFR: Peak expiratory flow rate, MVV: Maximum voluntary ventilation

Table 6: SMWD of both age groups

Variables	Age groups			
	Group 1 (20–35 years)		Group 2 (35–50 years)	
	Smoker* (n=42)	Non-smoker* (n=43)	Smoker* (n=38)	Non-smoker* (n=37)
SMWD	447.14±45.50	482.18±27.06	399.94±31.95	475±33.12
SPY	6.52±5.41		10.86±4.93	

*All data are expressed as mean (standard deviation). SMWD: 6 min walk distance, SPY: Smoking pack-years
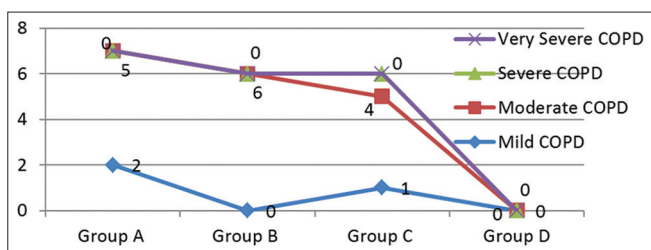

Figure 3: Prevalence of chronic obstructive pulmonary disease among smokers

In our study, spirometric variables such as FEV1% and FEV1/FVC ratio are decreased in smokers suggesting obstructive type of lung disease. Similar results were observed in recent Mexico study conducted by Sansores et al., in which 2961 smokers were observed with a smoking history of at least 10 pack-years.[7]

George et al[8] found that age, body weight, body surface area and FVC did not show statistically significant difference between non smokers and smokers whereas FEV1, FEV1/FVC, PEFR, and MVV was found to be significantly higher in non smoker as compared to smokers (P value=0.00).

In our study as the intensity and duration of smoking increased FEV1, FEV1%, FEV1/FVC%, PEFR, PEFR%, and MVV% gradually decreased and there is statistically significant relation between the smoking PYs and the above mentioned spirometric variables. More is the PYs of cigarette smoked, more is the reduction in lungs spirometric variables. There is a significant difference in these variables when compared between all the four groups on the basis of number of pack years. This suggests that severity of COPD is directly proportional to number of PYs and even early smoking between 1 and 20 pack year can lead to considerable damage to lung function.

This is similar in accordance with the studies done by Hegde et al.,[9] and Targowski et al.,[10] Hegde et al., studied the correlation between smoking index in pack-years and FEV1% using the correlation coefficient test and observed a highly significant inverse correlation between smoking pack-years and FEV1%, that is, as the smoking pack-years increased the FEV1 gradually decreased (r=−0.97, P<0.01).

Examination of the mid-portion of expiratory flow rate may provide information on small airway involvement. The FEF rate between 25 and 75% of the FVC (FEF$_{25-75}$) is usually signifies measurement of small airways pathology.[11] A recent Indian study observes that small airway obstruction develops more commonly in smokers with higher quantum of cigarette consumption and involves 51% smokers at 10 PYs or more.[12] We found the difference in MMEF rate (MMEF 25–75%) variable of smokers and non-smokers as statistically significant (P<0.05). MMEF rate (MMEF 25–75%) is decreased more in Group 2 (36–50 years) smokers than Group 1 (20–35 year) smokers.

Ritesh[13] in his study concluded that value of PEFR and maximum voluntary ventilation (MVV) is lower in active tobacco smokers than non-smokers. The actual value of PEFR and MVV decreases as the number of years tobacco smoking increases. Therefore, pulmonary function variables value is lower in moderate smokers than in mild smokers and highly decreased in heavy smokers than in mild and moderate smokers which are also seen in our study.

The mean values of all the spirometric variables are more decreased in smokers of Group 2 (35–50 years age group) than Group 1 (20–35 years age group) except FVC%. The reason is increased duration and intensity of smoking in Group 2 in our study. Non-smokers of Group 1 have values of all parameters more than Group 2 non-smokers. This is suggestive of age-related decline in pulmonary functions.

In our study, out of the total 80 smokers, 23% of smokers fit in some category of COPD in GOLD staging, though they were asymptomatic which means that they were completely free from cough, sputum production, and dyspnea. Similarly in a study done by Barthwal and Singh,[14] smokers above 40 years and with smoking index above 200 showed obstruction in 26% on spirometry. In a large scale study done at Poland, 11,027 smokers older than 40 years were screened for airflow obstruction with the help of spirometry and it was found that the prevalence of airway obstruction was 24.3%.[15]

The 6MWT provides information regarding functional capacity, response to treatment, and prognosis across a range of chronic cardiopulmonary diseases. A SMWD <350 m is usually correlated with higher mortality in COPD, chronic heart failure, and pulmonary arterial hypertension. A change in 6MWT distance of more than 50 m is clinically important in most disease states.[5] In our study, the mean distance walked in SMWD by non-smokers is 478.88±30.22 while that by smokers is 424.72±46.12. This variable difference in between the two study groups is statistically significant (P<0.001). Among the smokers, we found that as the number of pack-years increases, SMWD decreases with least distance walked by Group D smokers (343 m). Thus, the degree to which lung function and exercise capacity of smokers decreases is inversely proportional to the duration and the quantity of cigarettes being smoked.

Cahan et al.,[16] in their study found that non-smokers walked significantly farther (413±14 m; mean ± standard error) and took more steps (665±14 steps) than either current (352±7) or former smokers (370±7).

Among the two groups of smokers on the basis of age, there is statistically significant difference between the distance walked in SMWT by smokers of Group 1 and Group 2. Smokers of more aged group walk lesser than young smokers indicating that smoking significantly affects the functional exercise capacity of smokers.

Limitations of the study
Limitation: The spirometric variables and 6MWD abnormality could not be compared with male and female gender as most of smoker patient are male. In addition, the small size of our sample might impose some restriction on the interpretation of our data.

CONCLUSION

Spirometry testing should target on those at risk of developing COPD particularly from smoking and thus spirometry was able to detect under-recognized airflow obstruction (FEV1). Thus, early screening of high-risk group would lead to reduction of the clinical burden of disease. If the intensity and duration of smoking increased, lung function such as FEV1, FEV1%, FEV1/FVC%, MMFR 25–75%, PEFR, PEFR%, and MVV% is reduced gradually. Most of spirometric variable except FVC and FVC% are significantly decreased in asymptomatic smokers than non-smokers. Among asymptomatic smokers with impaired pulmonary function tests, obstructive pattern is more common. The SMWD was significantly decreased in asymptomatic smokers as compared to non-smokers and it reduces gradually from Group A (1–5 PYs) to Group D (15–20 PYs). Early diagnosis of lung function impairment with spirometric variable and 6MWD in smokers may help in detection of young individual smoker who are prone for rapid deterioration of lung function with increased quantum of pack-years. Smoking cessation programs are highly productive in such individual.

ACKNOWLEDGMENT

REFERENCES

1. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016. Available from: https://www.goldcopd.org [Last accessed on 2016 Mar 17].

2. Health Effects of Smoking among Young People. Available from: https://www.who.int/tobacco/research/youth/health_effects/en [Last accessed on 2017 Apr 26].

3. Mannino DM, Gagnon RC, Petty TL and Lydick E. Obstructive lung disease and low lung function in adults in the United States: Data from national health and nutrition examination survey 1988-1994. Arch Intern Med. 2000;160(11):1683-1689.
    https://doi.org/10.1001/archinte.160.11.1683

4. Jindal SK, Aggarwal AN and Gupta D. A review of population studies from India to estimate national burden of chronic obstructive lung disease and its association with smoking. Indian J Chest Dis Allied Sci. 2001;43(3):139-147.

5. American Thoracic Society. Standardization of spirometry: 1994 update. Am J Respir Crit Care Med. 1995;152(3):1107-1136.
    https://doi.org/10.1164/ajrccm.152.3.7663792

6. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166(1):111-117.
    https://doi.org/10.1164/ajrccm.166.1.at1102

7. Sansores RH, Velazquez-Uncal M, Perez-Bautista O, Villalba-Caloca J, Falfán-Valencia R and Ramírez-Venegas A. Prevalence of chronic obstructive pulmonary disease in asymptomatic smokers. Int J Chron Obstruct Pulmon Dis. 2015;10:2357-2363.
    https://doi.org/10.2147/copd.s91742

8. George JM, Sen K and Raveendran C. Evaluation of the effect of smoking on pulmonary function in young healthy adults. Int J Biomed Res. 2014;5(5):569.
    https://doi.org/10.7439/ijbr.v5i5.569

9. Hegde RR, Phadtare JM and Ramraj NN. Study of smoking Index, spirometry and severity of chronic lung disease. Indian J Basic Appl Med Res. 2013;2(8):1043-1046.

10. Targowski T, Jahnz-Rózyk K, From S and Płusa T. Relationship between disease severity, smoking index age and direct costs of hospital treatment of COPD exacerbations. Pneumonol Alergol Pol. 2005;73(1):32-35.
    https://doi.org/10.5603/arm.27861

11. McNulty W and Usmani OS. Techniques of assessing small airways dysfunction. Eur Clin Res J 2014;1:1-17.
    https://doi.org/10.3402/ecrj.v1.25898

12. Singh GY, Singh NL, Banik U and Devi GK. Detection of early small airway obstruction in male adult smokers of an ethnic community in North East India. J Med Soc. 2014;28(1):14-17.
    https://doi.org/10.4103/0972-4958.135218

13. Ritesh MK. Comparative study of peak expiratory flow rate and maximum voluntary ventilation between smokers and non-smokers. Natl J Med Res. 2012;2(2):191-193.

14. Barthwal MS and Singh S. Early detection of chronic obstructive pulmonary disease in asymptomatic smokers using spirometry. J Assoc Physicians India. 2014;62(3):238-242.

15. Zielinski J and Bednarek M. Early detection of COPD in a high-risk population using spirometric screening. Chest. 2001;119(3):731-736.
    https://doi.org/10.1378/chest.119.3.731

16. Cahan MA, Montgomery P, Otis RB, Clancy R, Flinn W and Gardner A. The effect of cigarette smoking status on six-minute walk distance in patients with intermittent claudication. Angiology. 1999;50(7):7537-7546.
    https://doi.org/10.1177/000331979905000703