Original research article

Study of effect of smoking on Forced expiratory flow during 25-75% of expiration (FEF25-75%)

[1] Dr Arunkumar H K, [2] Dr Triveni A J, [3] Dr Avdhut Deshpande, [4] Dr Anupriya Avdhut Deshpande

[1] Assistant Professor, Department of TB & CHEST, Gadag institute of medical sciences, Gadag, Karnataka.

[2] Associate Professor, Department of Biochemistry, Gadag institute of medical sciences, Gadag, Karnataka.

[3] Associate professor, Department of Skin and VD, Prakash Institute of Medical Sciences and Research, Urun - Islampur, Maharashtra .

[4] Professor and Head, Department of Physiology, Prakash Institute of Medical Sciences and Research, Urun - Islampur, Maharashtra .

Corresponding Author: Dr Anupriya Avdhut Deshpande

Abstract
Cigarettes, the most popular method of smoking, consist of finely shredded tobacco rolled in light-weight paper. Smoke from the average cigarette contains around four thousand chemicals, some of which are highly toxic and at least 43 of which cause cancer. Nicotine, a major constituent of tobacco smoke is both poisonous and highly addictive1. FEF25- 75 %(L/sec) is the average flow rate over the middle of vital capacity. This test indicates the patency of smaller airways less than 2 mm in diameter. Aim of this study was to estimate effect of smoking on Forced expiratory flow during 25-75% of expiration ($FEF_{25-75\%}$) in asymptomatic smokers. The study was designed as cross section study which included 449 subjects of which 224 were in group 1 (0-10 Pack Year), 139 were in group2 (11-20 Pack Years), and 87 were in group 3 (21- 30 Pack Years). The mean value of FEF 25-75% POST in group 1 (0-10pack years) is 3.197+1.153, Group 2 (11-20 pack years) is 2.397+1.162, and Group 3 (21-30 pack years) is 1.368+0.663 respectively. Smoking causes significant deterioration of lung function which can easily detected by using a spirometer. FEF25-75 % (L/sec) is a simple test that could be useful in early diagnosis of peripheral airway obstruction and its treatment, thereby improving the quality of life.
Key words: Asymptomatic smokers, FEF25-75 %.

Introduction
Smoking is one of the major cause of preventable morbidity and mortality in both developed and in developing country. Smoking is one of the main risk factor for a number of chronic diseases including cancer, lung diseases and cardiovascular diseases. Moreover inhalation of smoke from even a single cigarette has been shown to cause brief broncho-constriction in smokers and non-smokers.[1] Cigarettes kill an estimated 5 million people annually worldwide. The World Health Organisation (WHO) reported that, tobacco smoking killed 100 million people worldwide in the twentieth century and warned that it could kill one billion people around the world in 21st century. By the early 2030, tobacco related death would increase to about 10 million a year.[2] The overall prevalence of current tobacco use from the National Household Survey of Drug and Alcohol Abuse in India (NHSDAA) is 55.8%.[3] Functional defect in smokers with chronic obstructive pulmonary diseases is that of air flow obstruction. Cigarette smoking is overwhelmingly the most important cause of cough and mucous

overproduction.[4] Chronic exposure to cigarette smoke reduces small airways function significantly. Smoking increases inflammatory cells in lung which produces free radicals. The oxidative stress is involved in the development of smoking related respiratory conditions and other pathologies. They significantly leads to progressive deterioration lung function and affects all the parameters of pulmonary function tests. The adverse effects of cigarette smoke on the lungs may be separated into two distinct conditions. These are chronic bronchitis which involves large air ways and usually clears up when the subject stop smoking. While COPD which involves medium and small air ways.[5] The various changes in the inflammatory phenotype observed in smokers with asthma and COPD have suggested several potential mechanisms.[6] The finding of increased circulating leucocyte elastase in some smokers may be relevant to the induction of lung damage caused by smoking. Activated neutrophils act both as effector cells of tissue damage and as amplifiers of the inflammatory process. Their azurophil granules contain a spectrum of proteinases capable of degrading the structural components of the interstitium-elastin, collagen, proteoglycans and basement membranes.[7]
Forced expiratory flow between 225-75 % of forced vital capacity is dynamic lung function test which are used to assess the patency of respiratory airways. The values of their flow rates are known to decrease not only in COPD but also in otherwise healthy smokers. Airway obstruction in cigarette smokers is diagnosed relatively late. Earlier detection of airflow obstruction and smoking cessation may result in significant health gain. If cigarette smokers stop smoking peak expiratory flow rates improve with passage of time. **Mean Forced Expiratory Flow during 25-75% of expiration (FEF25-75%):** This is the mean expiratory flow rate during middle 50% of FVC. It is a sensitive indicator of small airway disease where most of chronic obstructive pulmonary diseases start. Normal value – 300 litres per minute.

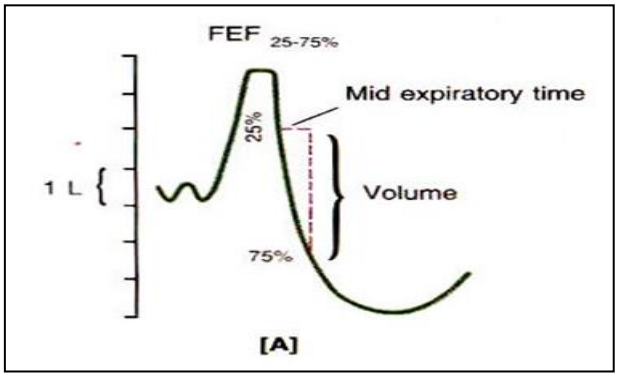

Figure 1: Forced expiratory flow during 25-75% of expiration (FEF25-75%)

Aim of this study was to estimate effect of smoking on Forced expiratory flow during 25-75% of expiration (FEF25-75%)**.** This study is aimed to detect the lung function changes in asymptomatic smokers with increasing pack years to assess whether early detection of lung function abnormalities can help to provide early intervention of tobacco cessation.

Material and Methods:
This study was carried out in the Department of Pulmonary Medicine, JSS Medical College Hospital, Mysuru over a period of 2 years. The subjects for study were selected from relatives and friends of patients in JSS Hospital, after fulfilling the inclusion and exclusion criteria.

Type of study:
Cross sectional study
Sample size:
449

Inclusion Criteria:
Clinically asymptomatic adult smokers >18 years of age
Grouped into following:
I) <10 pack years II) 10-20 pack years III) 21-30 pack years

Exclusion criteria:
1) Subjects have active pulmonary TB
2) Contraindications for spirometry like
a) History of abdominal/chest/eye surgery, MI in past 3 months.
b) Pneumothorax
c) Respiratory infections in past 3 weeks
Clinically asymptomatic adult smokers were screened for inclusion and exclusion criteria after explaining them about the study. Written and informed consent was taken for the study after explaining the procedure and its significance in their vernacular language. A pre tested structured proforma was used to collect the relevant information. A brief personal , smoking, medical, occupational history were taken and a clinical examination of all the systems was done to exclude medical problems and to prevent confounding of results. The physical characters such as height in centimeters and weight in kilograms of all the subjects were recorded and fed to the computer to get predicted values for pulmonary function tests. We used NDD for assessing the pulmonary functions. This spirometer has a mouth piece attached to a transducer assembly which is connected to an adaptor box and this is connected to the computer by a serial cable. Software from Recorders and Medicare system is loaded onto the computer. This software allows the calculation of the predicted values for age, sex, weight and height and it also gives the recorded values of all the parameters. Subject was motivated prior to the initiation of manoeuvre. He was made to sit on a stool, then place the mouth piece firmly in his mouth. He was asked to take a maximum inspiration following which we would attach a nose clip and ask him to execute a maximum forced expiration with full efforts which was followed by a maximum forced inspiration. . Mean Forced Expiratory Flow during 25-75% of expiration (FEF25-75%) was included in this study .

Statistical methods used: All the data collected were entered into MS Access database, statistical analysis was conducted using Epi info version 7 (CDC, Atlanta, USA) and IBM SPSS version 20 . Descriptive statistics: The continuous variables like age was presented as mean (standard deviation) and categorical/nominal variables were presented as frequencies. Pearson's correlation was used to analyse the correlation of variables like pack years with spirometry values. Comparison of means was done for assessing the difference of lung function parameter FEF25-75% between the pack year groups .Sub-group analysis to assess dose response relationship between pack-year groups and severity of lung function abnormalities was carried out.

Results:
During the study period, a total 472 subjects were screened for inclusion and exclusion criteria: 22 subjects were excluded from the study for the one of the following reasons: refused to perform PFT or unable to perform PFT or refused to sign consent form.
In present study total of 449 subjects were included are grouped in to:
224 in to 0-10 pack years.
139 in to 11-20 pack years.
87 in to 21-30 pack years.

Table 1: Comparison age among group 1,2& 3

Comparison age among group 1,2& 3			
Variable	Study group	Mean	SD
AGE (yrs)	0-10 pack years	49.25	16.11
	11- 20 pack years	56.93	10.05
	21-30 pack years	65.94	7.94

Table 2: Comparison of BMI among group 1,2,& 3

Comparison of BMI among group 1,2,& 3			
Variable	Study group	Mean	SD
BMI	0-10 pack years	23.26	4.68
	11- 20 pack years	22.73	4.64
	21-30 pack years	20.72	3.38

Table 3: FEF 25-75 % PRE among group 1,2,& 3

FEF 25-75 % Pre among group 1,2,& 3						
FEF25-75%-PRE	Pack years	N	Mean (L/S)	SD	Min	Max
	0 to 10 years	223	2.8735	1.056	.75	5.50
	11 to 20 years	139	3.4149	10.79	.42	92.00
	21 to 30 Years	87	1.1983	.569	.37	3.23

Table 4: FEF 25-75 Pre bronchodilator % PRED among group 1,2,& 3

FEF 25-75 Pre bronchodilator % Pred among group 1,2,& 3								
	Pack years	N	Mean (L/S)	SD	Min	Max	P value	Post HOC
FEF25-75%-PRE BRONCHODILATOR %PRED	0 to 10 years	223	86.43	25.823	23	160	<0.001	All three groups
	11 to 20 years	139	64.35	24.028	21	125		
	21 to 30 Years	87	41.77	16.627	4	85		

The mean value of FEF25-75%PRED in 0-10pack years is 86.43±25.82,in 11-20 pack years is 64.35±24.02 and in 21-30pack years is 41.77±16.62. There is a significant difference in FEF25-75% PRED values in all the three groups.

Table 5: FEF 25-75 % Post among group 1,2,& 3

FEF 25-75 % Post among group 1,2,& 3						
FEF25-75%-POST	Pack years	n	Mean (L/S)	SD	Min	Max
	0 to 10	223	3.1974	1.15394	.59	6.78
	11 to 20	139	2.3973	1.16277	.41	5.36
	21 to 30	87	1.3689	.66321	.07	3.59

The mean value of FEF25-75%-post in 0-10pack years is 3.19±1.15,in 11-20 pack years is 2.39±1.16 and in 21-30pack years is 1.36±.66.

Table 6: FEF 25-75 % Pred Post Bronchodilator among group 1,2,& 3

FEF 25-75 % Pred Post Bronchodilator among group 1,2,& 3								
	Pack years	N	Mean (L/S)	SD	Min	Max	p value	Post HOC
FEF25-75%-%Pred Post Bronchodilator	0 to 10	223	96.54	26.696	30	188	<0.001	All three groups
	11 to 20	139	73.31	27.471	22	153		
	21 to 30	87	48.44	18.177	13	92		

There is a significant difference in FEF25-75% PRED values in all the three groups.
The mean value of FEF25-75%-%PRED in 0-10pack years IS 96.54±26.69, in 11-20 pack years is 73.31±27.47, and in 21-30pack years is 48.44±18.177. There is a significant difference in FEF25-75% PRED values in all the three groups.

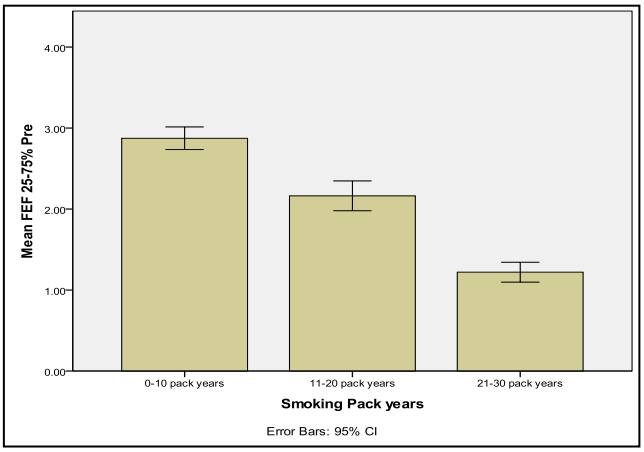

Figure 2: FEF 25-75 % PRED POST BRONCHODILATOR AMONG GROUP 1,2,& 3

Discussion:

The study was designed as cross section study which included 449 subjects of which 224 were in group 1 (0-10 Pack Year), 139 were in group2 (11-20 Pack Years), and 87 were in group 3 (21- 30 Pack Years). The mean value of FEF 25-75% POST in group 1 (0-10pack years) is 3.197+1.153, Group 2 (11-20 pack years) is 2.397+1.162, and Group 3 (21-30 pack years) is 1.368+0.663 respectively. Evidence accumulated in the past 30years,shown an Irrefutable association between the long term inhalation of cigarette smoke and the development of obstructive airway disease.[8]The available data indicate that the life expectancy of habitual smokers is reduced by 15-20 years and approximately half will die as a consequence of their habit. [9] Cigarette smoking has extensive effects on the respiratory function and it has been clearly implicated in the aetiology of a number of respiratory diseases, particularly chronic bronchitis, emphysema and bronchial carcinoma. Tobacco smoke contains number of substances which may exert some effects upon body. During burning of tobacco in cigarettes various processes such as pyrolysis, prosynthesis, distillation, sublimination, hydrogenation, oxidation, decarboxylation, dehydration result in generation of more than 4000 identifiable compounds present in tobacco itself or new compound generated thereof. The tobacco smoke inhalation causes an immediate rise in the airway resistant which persist for at least an hour. This is due to vagally mediated smooth muscle constriction presumably by way of stimulating submucosal irritant receptors. Experimental studies have shown that prolong cigarette smoking impairs cilliary movements, inhibition of function of alveolar macrophages leads to hypertrophy and hyperplasia of mucus secreting glands. It is

probable that smoke also inhibits antiproteases and causes polymorphonuclear leucocytes to release proteolytic enzymes acutely.[10] In smokers, changes occurs in respiratory system due to inflammation, and fibrosis. So all dynamic pulmonary parameters under consideration are significantly lower than normal values. Pulmonary function is a good test to describe the pattern of pulmonary disease.

FEF 25-75% : In our study, the mean value of FEF 25-75% post in group 1 (0-10pack years) is 3.197+1.153, Group 2 (11-20 pack years) is 2.397+1.162, and Group 3 (21-30 pack years) is 1.368+0.663 respectively.This suggests that as negative relationship with duration of smoking, as the pack years increases the FEF 25-75% value decreases. Thisresults were in consistent with Jetty Jerusha et al, Rubeena Bano and Nadeem Ahmad et al,[11] Mehmet Polath et al.[12] The early changes in smokers are probably due to narrowing of the small airways.
The present study illustrates the usefulness of the forced expiratory spirogram in evaluating the early changes in lung function in smokers.A progressive reduction in mean flow rates and an increase in the incidence of severe obstruction have been found with increasing pack-year exposure. However, only a small fraction of smokers will develop significant airway obstruction, a finding suggesting that other genetic and/or environmental factors are also operative in the production of airway obstruction. Smoke components likely to cause airway obstruction are not completely known but nicotine, irritants such as acrolein and free radicals might play a role. The manner of smoking is another factor influencing the lung's exposure to cigarette smoke; a considerable inter- and intra-subject variability has been documentedin the inhaled volume and puff volume, After the first few cigarette puffs, an inflammatory response develops involving several cell types, especially neutrophils, alveolar macrophages, CD8þ T-lymphocytes, and possibly eosinophils. In susceptible subjects, a bronchiolitis develops whichwill progress with continuing smoking. After variable time, airway inflammation is followed by airway remodelling, a term defining the structural changes that occur in the airway wall due to acute inflammatory events and/or chronic inflammation and repair. At the same time, the antiprotease activity of the lung may be compromised by the oxidation, by cigarette smoke, of antiprotease protective mechanisms (e.g. a1 AT). Without opposition, the proteolytic activity may damage the lung parenchyma leading to destructive emphysema. This proteolytic lung destruction combines with airway inflammation and remodelling to produce decrease lung recoil and increased peripheral airway resistance, the two main factors responsible for decreasing maximal expiratory flow from the lung in cigarette smoke-induced chronic airway obstruction.[13] FEF25-75% is a reliable marker of early airflow limitation. Abnormal FEF25-75% had a high probability of being bronchial hyper responsiveness, is probably due to eosinophilic airway inflammation.

Conclusion:
From the statistical analysis of the results obtained in the present study, it may be concluded that smoking causes significant deterioration of lung function which can easily detected by using a spirometer. FEF25-75 % (L/sec) is a simple test that could be useful in early diagnosis of peripheral airway obstruction and its treatment, thereby improving the quality of life.

References:
1. Bano R, Mahagaonkar AM, Kulkarni NB et al. A study of the pulmonary function test among smokers and non-smokers in a rural area. Pravara Med Rev 2009; 4(1):11-16.
2. Rexhepi A, Brestovci B. Influence of smoking and physical activity on pulmonaryfunction. The Int J of P Med 2008;11(2):1 – 9.
3. Dwarakanath N, Gandhavalla V M, Munisekhar K. The correlation of FCV%,

FEV1%, PEFR corresponding to pulmonary function in smokers and non-smokers. Int J Physiother Res 2014; 2(4):663-66.
4. Jerusha J,Ssanthi V. Comparative study of pulmonary function tests in smokers and non smokers. B of Pharm and Med Sciences 2014;2(I2):2201-2208.
5. Louise A. H, Karen H, Stephen S H, Bruce R L, Xianghua L, Steven G et al. Exposure to a tobacco-specific lung carcinogen in adolescent versus adult smokers. Cancer Epidemiol Biomarkers Prev. 2008;17(12):3337-3343.
6. Tamimi A, Serdarevic D, Nicola A H. The effects of cigarette smoke on airway inflammation in asthma and COPD: Therapeutic implications.Respiratory Medicine. 2012; 106: 319-328.
7. Ogushi F, Hubbard R C, Vogelmeier C, Fells G A, and Crystal R G. Cigarette smoking is associated with a reduction in the association Rate constant of lung alpha -1-antitrypsin for neutrophil elastase. J Clin Invn. March 1991;87:1060-1065.
8. Gordon L A. Functions of lung. In: Anthony S, Douglas S and Gordon L A, editors. Crofton and Douglas's Respiratory diseases. 5th edn. Malden USA; Blackwell Sciences:2000.p-26
9. Tests of Pulmonary Function: How Respiratory Physiology Is Applied to Measure Lung Function.In: West and John B editors. Respiratory Physiology: The Essentials, 8th edn. California; Lippincott Williams & Wilkins:2008.p-159.
10. Harpreet R, Wilde M, Madden B.Pulmonary function tests. *Ulster Med J* 2011;80(2):84-90.
11. Rubeena B, Ahmad N, Mahagaonkar A M. Study of pulmonary functions in smokers and non-smokers in sugarcane harvesters in rural Maharashtra. WIMJOURNAL. 2014; 1, (1):33-37.
12. Polatly M, MD, Erdinç M, MD. The Early Effect of Smoking on Spirometry and Transfer Factor. Turkish Resp J. December 2000; 1(2):31-34.
13. Bohadana A, Teculescu D, Martine Y. Mechanisms of chronic airway obstruction in smokers. Respiratory Medicine .2004; 98: 139–151.