Study The Risk Of Chronic Obstructive Pulmonary Diseases Among Successfully Treated Old Pulmonary Tubercular Cases By Measuring Lung Function Indices - A Hospital Based Case Control Multi Group Study

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Abstract: Background: Pulmonary tuberculosis consider as an independent risk factor for COPD by few recent researcher apart from tobacco smoke and biomass fuel though not much explored hitherto, therefore study conducted to find out possible association in between two epidemics of era. Methods: A hospital based multi group case control study was conducted in tertiary care centre of teaching institute by including 200 subjects comprises in four groups ,Group 1: 50 successfully treated non-smoker, non-biomass fuel smoke exposed, successfully treated patients of Pulmonary Koch's, currently sputum negative. ; Group 2: 50 individuals with history of exposure to biomass fuel smoke. ; Group 3: 50 smokers, currently asymptomatic; Group 4: 50 normal (healthy) individuals, non smokers, non-biomass fuel smoke exposed and not having any history of tuberculosis.PFT was done in all included subjects. Data compiled and analyzed by using Standard statistical software spss23.p value <0.05 consider as significant. Results: Only 8(16%) subjects among old treated pulmonary tuberculosis having COPD (odd ratio= 2.19) contrary to this 14(28%) and12 (24%) subjects among smokers and biomass smoke exposed having COPD (odd ratio= 4.472; 3.63). However mean reduction in FEV1 % and FVC% in old tubercular group (55.33±25.46; 60.51±31.07) compare to healthy control (109.63±18.92; 94.89±12.94) was statistically significant (p=<0.05). Conclusion: Old pulmonary tuberculosis significantly associated with diminution of airflow in the lungs, as well as significant risk factor for COPD , though less in compare to tobacco & biomass smoke. [A Agrawal, Natl J Integr Res Med, 2018; 9(4):1-6]

Key Words: Tuberculosis, Lungs, COPD, Tobacco Smoke, Biomass Fuel smoke, Pulmonary function test.

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Introduction: In addition to tobacco fumes and biomass smoke, old tubercular infection has been implicated as a new emerging factor affecting the patho-physiology of lung and in-turn leading to air way obstruction. Pulmonary tuberculosis can cause parenchymal destruction by up regulation of several proteases and dysregulation of protease control[1.] It is characterized by bronchial stenosis, fibrosis and bronchiectasis [2, 3.] Research has also shown that tuberculosis increases the activity of matrix metallo-proteases, thus contributing to pulmonary damage [4.] However the effect of pathological changes in tuberculosis on Pulmonary Function Test (PFT) parameters is not very clear [5]. In fact, tobacco smoking as well as biomass smoke exposure in any form has significantly deleterious effects on pulmonary function and leads to pathological and histological changes in lungs which are similar to those seen in patients of COPD[6,7,8,9.] Besides this, both tobacco and biomass fuel smoke have been implicated as causative factors for COPD [10.] As per Global Initiative for Chronic Obstructive Lung Diseases (GOLD) guidelines update (http://goldcopd.org) provided by the WHO, the airway constriction in COPD and decline in PFT is a progressive phenomenon[11, 12]. This airway constriction is associated with a chronic inflammatory process in the membranous and respiratory bronchioles [13, 14, 15.] Few recent studies have endorsed the fact that similar obstructive changes are observed in PFT of patients with a history of tuberculosis which further potentiates the theory behind the association of tubercular infection with COPD [16,17,18,19]. All such patients may lead to an increase in the humongous burden of this disease in the world. Hence it is necessary to determine the type and extent of impairment of lung function as well as study the possible association between these two diseases in which one could be the risk factor for other chronic ailment, a fact which hasn't been thoroughly explored.

Method: The study was conducted in the department of Respiratory Medicine, of tertiary care teaching institute, BPS GMCW, Khanpur Kalan, Sonepat, Haryana during April 2014 to October 2017. A hospital based study designed as Multi group case control type which will include the patients visiting the Respiratory medicine OPD as well as admitted patients in the ward. The study subjects will be divided into four groups: Group 1: 50 successfully treated non-smoker, non-biomass fuel smoke exposed, successfully treated

patients of Pulmonary Koch's, currently sputum negative. ; Group 2: 50 individuals with history of exposure to biomass fuel smoke. ; Group 3: 50 smokers, currently asymptomatic; Group 4: 50 normal (healthy) individuals, non smokers, non-biomass fuel smoke exposed and not having any history of tuberculosis.

Patients with Pregnancy, Known case of respiratory illness including bronchiectasis, pneumonia, ILD, malignancy of or metastasis to the lung, extra-pulmonary tuberculosis and patients currently suffering from pulmonary tuberculosis. Patients with renal, hepatic or cardiac diseases. , HIV positive patients, Patients not fit for PFT, having any contraindication to PFT and having any anatomical anomaly , was excluded from the study:

Informed written consent of all subjects and prior approval of the institutional ethics committee was taken. All subjects was evaluated using a predesigned and pretested Performa which includes information regarding the personal profile with duration of exposure to biomass fuel, type of fuel used, position of kitchen, number of members in one room, common symptoms and detailed smoking history. If the subject has any respiratory problem, detailed Clinical examination and PFT will be performed only once by trained Resident doctor in the Department of Respiratory Medicine by using Pulmonary Function Equipment (BTL -08 Spiro PC, manufactured by Health and Medical Industry, United Kingdom, calibration 03-jun-13/003-0031080), with pre and post bronchodilator reports to confirm the diagnosis and staging based on the criteria of Global Initiative for Chronic Obstructive Lung Diseases guidelines update (http://www.goldcopd.org/) in required subjects.

Stage 1: FEV1 ≥ 80% of predicted- Mild
Stage 2: FEV1 50≤ FEV1 < 80% of predicted-Moderate
Stage 3: FEV1 30≤FEV1 <50% of predicted-Severe
Stage 4: FEV1 <30% of predicted-Very Severe

The chest radiograph was reviewed without sight of the lung function data and scoring was done on basis of previously reported scoring system by snider et al[18.] Radiographic scoring system of lung infiltration for pulmonary tuberculosis
Score   Features
0   no infiltrate
1   one third or less of the zone

2   infiltrate involving more than one third ,but less than two thirds of the zone
3   infiltrate involving more than two thirds of the zone

Each lung was divided into thirds and each third was scored according to the degree of infiltration using the index above. Minimum two visits of the patients will be needed to collect the complete information.

The data collected was analyzed by using standard statistical software SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp. Student T-test will be used to compare means of different continuous variables, Chi square/Fischer exact test to analyze categorical variables among different groups. Pearson Correlation & Regression analysis was done to find out the possible association and dependency among different variables of study subjects. $P < .05$ will be considered as significant.

Results: On view of demographic profile the mean age of study subjects in various groups have no significant variation however among smokers group male were predominantly present. Majority of study population comes from rural areas and belongs to middle as well as low socioeconomic strata besides this literacy rate was also very poor shown in table 1.

By analyzing Lung function indices as per GOLD guideline in various groups it was observed that only 8 (16%) subjects with old pulmonary tuberculosis having obstructive changes, however 37(74%) cases were found with restrictive changes, rest 5(10%) subjects have shown   insignificant changes in PFT (p=0.356), though among smokers this figure was quite high , 14(28%) subjects were with obstructive changes (p=0.017), although among biomass users this figure near to smokers group 12(24%) (p=0.053), while in healthy control group only 4(8%) subjects had shown mild obstructive changes. Odd ratio of old pulmonary tubercular cases for COPD was 2.19; CI =0.6146,7.807, however for , Smokers and Biomass users it is 4.472;CI = 1.356,14.75 ; 3.631; CI= 1.083,12.18.

Diminution in FEV1 % and FVC% among old tubercular group (55.33±25.46; 60.51±31.07) was observed far less than healthy control (109.63±18.92; 94.89±12.94 ; p=<0.05) shown in table 2 . On comparing the means by unpaired student t test reveal   statistically significant difference between   Old tubercular vs.

Healthy control , though it was insignificant among Tubercular vs. Biomass users and smoker group shown in table 3.

Correlation as well as regression analysis between PFT indices FEV1%, and radiographic score in the old tubercular group shows very weak positive correlation (r=0.008, p=0.953) . , though FVC% and FEF25-75% shows statistically insignificant inverse correlation (r= -0.145, p= 0.314:r= -0.019, p= 0.896) shown in fig 1. Multiple linear regressions between lung function indices (FEV1%, FVC%FEF25-75) with radiographic scoring were also statistically insignificant shown in table 4.

Table 1: Demographic detail of various study groups

Variables	Old Tubercular (G1) N=50	Smokers (G2) N=50	Biomass Fuel Users (G3) N=50	Healthy Control (G4) N=50	P Value
Age Mean± SD	48.02±15.57	56.4±11.8	49.14±12.53	44.40±16.42	P=0.26
Marital status					
M	46(92%)	50(100%)	50(100%)	46(92%)	p>0.05
UM	4(8%)	-	-	4(8%)	
Education					P>0.05
literate	10(20%)	8(16%)	11(22%)	15(30%)	
Illeterate	40(80%)	42(84%)	39(78%)	35(70%)	
rural	38(76%)	45(90%)	48(96%)	40(80%)	p>0.05
urban	12(24%)	5(10%)	2(4%)	10(20%)	
Housing condition					
kuccha	33(66%)	48(96%)	49(98%)	37(74%)	p>0.05
pukka	17(34%)	1(2%)	-	7(14%)	
semi pukka	-	1(2%)	1(2%)	6(12%)	
ventilation					
adequate	44(88%)	30(60%)	40(80%)	35(70%)	p>0.05
inadequate	6(12%)	20(40%)	10(20%)	15(30%)	p>0.05
socioeconomic status					
middle	32(64%)	32(64%)	48(96%)	49(98%)	P>0.05
lower middle	9(18%)	8(16%)	-	-	
lower	9(18%)	10(20%)	2(4%)	1(2%)	P>0.05

Table 2: Comperative value of predictive indices of lung function in various study groups.

SN	Parameter	Group1 (Old TB) Mean± SD N=50	Group 2 (Smoker) Mean± SD N=50	Group 3 (Biomass users) Mean± SD N=50	Group 4 (Healthy control Mean± SD N=50	p value
1.	FEV1/FVC	87.05±13.84	84.59±48.56	86.78 ±14.89	94.71±9.91	
2.	FVC%	60.51±31.07*	56.16±27.57	63.43±20.86	94.89±12.94*	<0.0001*
3.	FVC (L)	1.61±0.70	1.80±0.95	1.67±0.52	3.40±0.92	
4.	FEV1%	55.33±25.46*	64.45±31.32	71.28±23.39	109.63±18.92*	<0.0001*
5.	FEV1(L)	1.37±0.63	1.58±0.85	1.53±0.58	3.10±1.07	

FEV1: Forced expiratory Volume; FVC: Forced vital capacity; SD: Standard deviation

Table 3: Compare means of unpaired indices of lung function by student t test in various study groups.

| SN		GROUPS					
		Old Tubercular vs Healthy control		Old Tubercular vs Smoker		Old Tubercular vs Biomass users	
	Coefficient	FEV1%	FVC %	FEV1%	FVC%	FEV1%	FVC%
1	t	-12.106	-7.224	-1.60	0.739	-3.263	-0.553
2	p	0.0001	0.0001	0.113	0.461	0.002	0.582

FEV1: Forced expiratory Volume; FVC: Forced vital capacity

Table 4: Regression and correlation relationship for predicting indices of lung function from radiological scoring of old tubercular cases

SN		Regression Coefficient			Correlation Coefficient			
	Indices	f	β	p	r	r2	SE	p
1	FEV1%	0.003	0.008	0.953	0.008	0.000	25.72	0.953
2	FVC%	1.037	-0.145	0.314	-0.145	0.021	31.06	0.314
3	FEF25-75%	0.017	-0.019	0.896	-0.019	0.000	22.38	0.896

FEV1: Forced expiratory Volume; FVC: Forced vital capacity;FEF25-75: Mid expiratory Flow

Fig 1: Scattered plot showing Correlation in between lung function indices (FVC) and radiographic score in old tubercular cases

r= - 0.145
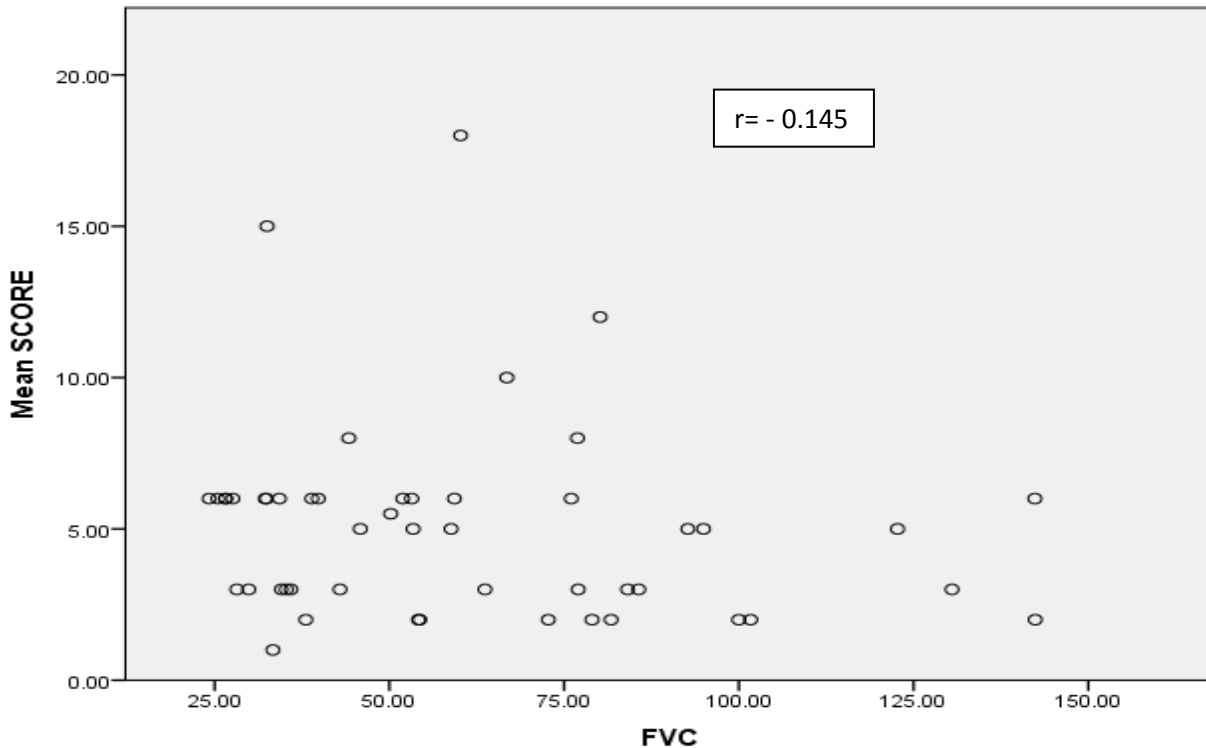
Discussion: Various eminent researchers have observed that old treated cases of tuberculosis results in airway obstruction while Impairment of airflow was related to the extent of tuberculosis which determined radiological [20, 21, 22.] In present study the mean FEV1% and FVC% shows significant diminution between old tubercular and healthy control group, as well as test of significance by comparing means for unpaired indices also shows statistically significant diminution, however 8 (16%) subjects have shown obstructive changes among old tubercular group in comparing to healthy control 4 (8%), in a similar prospective study conducted on 92 patients by Verma et al[22] reveal that only 15 (16.3%) subjects had

obstructive airway disease in which only 12 (13.04%) subjects having COPD 3 (3.26%) were asthmatic, 17 (18.48%) subjects having mixed obstruction without reversibility, hence total subjects having COPD were 29 (31.52%) which is very high figure contrary to this only 37 (40.21%) were having restrictive pathology which is very less in comparison to current observation, however odd ratio was not calculated by them besides this confounding factors may also interfering in the result of their study ,perhaps responsible for high prevalence of COPD cases .

Although various eminent researcher's had postulated that patients with radiological evidence of more advanced diseases at the time of initial diagnosis of TB appear to have worst lung function after treatment [20,23],however In present study no significant correlation was found between extent of radiological lesion in old tubercular cases and their corresponding lung function indices . However In few recent studies, negative correlation was reported in between radiological changes and lung function indices among untreated patients. It was also endorsed that residual damage to the lung tissue after completion of tuberculosis treatment includes varying degree of fibrosis, bronchiectatic changes, emphysema and bronchovascular distortion lead to change in lung function [1, 2,3].

Lee et al[24] observed in his cohort study that delays in anti TB treatment had a dose response relationship with the risk of developing COPD. Moreover in present study the risk of COPD was quite high in old tubercular cases as shown by odd ratio which is 2.19 near to the observation of Chung et al[17] shows odd ratio 2.544 ,though it is far less from odd ratio of tobacco smoke as well as biomass smoke . The incidence of endo bronchial tuberculosis in our patients is unknown which may lead to airway obstruction , however tobacco Smoking as well as biomass fuel smoke were proven risk factor responsible for chronic airway obstruction,[6,10,25,26] ,while tuberculosis of lung was also associated with obstructive pathology for some extent as reveal in present study .

Contrary to other postulate, which relate the radiological picture with possible association of lung function indices [17, 27], present study shows no such significant relationship .Besides this similar to other recent studies, restrictive lung pathology predominantly highlighted among old treated pulmonary tubercular cases. Rajasekharan et al[16] postulate that tuberculosis increase the activity of the matrix metalloproteinase enzyme which contribute to pulmonary damage similar to tobacco smoke, although obstructive changes in old tubercular group was less intense than smokers as well as biomass users , according to present study.

Conclusion: Present study shows fairly moderate risk of COPD in old treated pulmonary tubercular cases though it is less intense and statistically insignificant than previously known risk factor like tobacco smoke and indoor air pollution, however increasing prevalence of tuberculosis in developing world along with pollution and irrational uncontrolled tobacco use may potentiate disease burden drastically in this part of world where poor living condition and literacy rate always a major limiting factor for preventive strategies, hence It need more comprehensive research to endorse the phenomenon for better understanding of the patho physiology of airflow limitation as well as point the way of therapeutic strategies to limit the future load of COPD in high burden tubercular countries like us.

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