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"Assessment of Airflow Obstruction in Post-Tubercular COPD Patients And non-Tubercular COPD Patients: A Comperative Study"

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Abstract
Objective(s): *To assess the airflow obstruction in post-tubercular COPD and non-tubercular COPD patients.*
Method(s): *86 patients of age 40-80 years, having exertional dyspnea with or without cough, expectoration and /or having past history of pulmonary tuberculosis and complete anti-tuberculosis therapy, smoking were recruited for study. Included patients had radiological evidence of scarring, fibrosis, cavitations, emphysema and other destructive lung changes. Presence of any active disease, history of occupational exposure, asthma, IHD, ILD, bronchiectasis, anemia and renal failure patients were excluded. 37 patients having COPD with history of TB were selected as cases and 49 patients of COPD without history of TB were selected as controls. Spirometry was done on Spirolab using vitalograph.*
Result(s): *vital capacity (FVC %) was significantly lower in cases relative to control group (48.24±21.81 vs. 57.27±14.10, P <0.05). Statistically significant difference was observed between both groups in FEV1 predicted (40.11±17.21vs. 49.02±14.00, P<0.05).On comparison of FEV1/FVC ratio in both groups, statistically significant difference was observed (52.32±9.84 vs. 57.48±9.93, P<0.05).*
Conclusion(s): *Study shows that pulmonary tuberculosis is definitely associated with pulmonary damage and airflow obstruction despite of microbiologic cure. So it endorses for early diagnosis of COPD in post tubercular patients.*
Keywords*: Anti tubercular treatment, chronic obstructive pulmonary disease, forced expiratory volume, Forced vital capacity, pulmonary function tests.*

I. Intoduction

Tuberculosis (TB) caused by Mycobacterium tuberculosis is one of the oldest diseases known to affect human beings. It commonly affects the lungs but can affect other parts of the body in around thirty-three percent (33%) of TB cases. Tuberculosis is a major cause of death worldwide. Tuberculosis is the most common communicable disease in the world which affects one third of the world's population. New infections occur at a rate of about one per second[1]. In 2007, there were an estimated 13.7 million chronic active cases globally[2]. In 2010, there were an estimated 8.8 million new cases. About 1.5 million deaths have occurred in 2010 in developing countries and1.9 million cases (i.e. 21%) out of 8.8 million new cases occur in India every year[2].It is estimated that two out of every five Indians are infected with TB and 3.22 lakh Indians die due to TB every year[3]. In other words it is estimated that two persons die of tuberculosis every minute. More people in the developing world contract tuberculosis because of compromised immunity due to high rates of HIV infection[4]. The classic symptoms of active tubercular infection are chronic cough with blood-tinged sputum, fever, night sweats and weight loss. Infection of other organs causes a wide range of symptoms. Diagnosis of active TB relies on radiological (commonly chest X-rays) as well as microscopic examination and microbiological culture of body fluids[5].Treated post tubercular patients are left with permanent changes in lung anatomy and are at higher risk of pulmonary sequel and premature mortality[6-9].

These result in pulmonary sequelae that are characterized by bronchial and parenchymal structural changes, including bronchovascular distortion, bronchiectasis, emphysematous changes, and fibrotic bands. Moreover, these changes remain permanently in the lungs after a microbiological cure[10].Studies of pulmonary function in individuals with pulmonary tuberculosis demonstrated variable patterns and severity of impairment[11-13]. Smoking is the major risk factor for airflow obstruction and is also associated with increased incidence of morbidity and mortality from TB[14]. Pulmonary function tests (PFTs) independently quantify lung function and impairment, and are used to evaluate persons with chronic lung disease[15].To determine the pattern and extent of pulmonary function abnormalities that are associated with tuberculosis, we conducted a case-

control study using a PFT of patients in COPD with previously infected and treated pulmonary tuberculosis and a comparison group with COPD without tuberculosis.

II. Material And Methods

We conducted a case control study in the Department of Medicine, SMS Medical College Hospital, Jaipur, Rajasthan. In this, 86 patients of age 40-80 years, having exertional dyspnea with or without cough, expectoration and /or having past history of pulmonary tuberculosis and complete anti-tuberculosis therapy, smoking were recruited for study. Only those patients were included who had radiological evidence of very typical post-TB lesions in the form of scarring, fibrosis, cavitations, emphysema and other destructive lung changes in their latest chest radiographs. Presence of any active disease, history of occupational exposure, asthma, IHD, ILD, bronchiectasis, anemia and renal failure patients were excluded. 37 patients having COPD with history of TB (post-tubercular COPD) were selected as cases and 49 patients of COPD without h/o TB(non-tubercular COPD) were selected as controls.

Patients with inclusion criteria were interviewed after their consent and data were recorded on pre-designed forms as case number, age, gender and timing of the anti-TB treatment. Patients were then called for spirometry on Spirolab using vitalograph, UK according to convenience without any pre-medication. Three attempts were recorded and only considered if the variation between two best readings was less than 5%. Spirometric values were recorded as FVC, FEV1 and FEV1/FVC. Those not meeting the American Thoracic Society Criteria for quality for spirometry and those showing significant post dilator reversibility (more than 12%) were excluded. The subjects showing an obstructive ventilatory defect were then classified as mild, moderate and severe according to the GOLD guidelines.

The statistical analysis was performed using 'Sigma Stat version 12.5' data analysis software developed by SyStat Software Inc, USA. Descriptive statistics were used to describe the data i.e. mean and standard deviation for numeric variables and frequency along with percentages for categorical variables.

III. Method Of Assessment

Selected patients were evaluated clinically by taking history of presence or absence of cough, expectoration and dyspnea as well as smoking habits. Dyspnea was evaluated by 6MWT (six minute walk test). The forced vital capacity and the forced expiratory volume in 1 second were measured using standard equipment; the best of 3 measurements were used. Airway obstruction was defined as FEV1/FVC <70. Severity of obstruction was graded according to GOLD COPD guidelines[16].

IV. Result

In this study Mean age for cases was 60.70 $\pm$ 9.23years while mean age for controls group was 63.22 $\pm$ 9.95years. Table 1 shows that the patients who were treated for MTB in past (cases) more often reported symptoms of cough (89% vs.83%), hemoptysis (44% vs. 22%), sputum production (83% vs. 44%) and wheezing (40% vs. 27%) in comparison to those who suffered from pure COPD(controls).

It shows cases develop more symptoms of airflow obstruction as a consequence of tubercular infection. Table 2 shows correlation of airflow obstruction with duration of past tubercular infection. Maximum number of cases 17 in 0-10years of duration since ATT among them 47% cases had FEV1% between 30-49and 29% cases had less than 30%. In 21-30years duration of ATT maximum percentage of cases had very severe airflow obstruction (FEV1 <30%). In maximum duration (31-40 years of ATT) 50 percent cases had FEV1 % between 30-49 %.Results show that recent infection has more severe airflow obstruction compared to that of long duration. As COPD Gold Guidelines[16] interpretation of FEV1 % 30-49 is severe airflow obstruction and <30 as very severe airflow obstruction. As table 3 shows 16 (43.24%) cases and 25 (51.02%) controls had severe airflow obstruction and 12 (32.43%) cases v/s 4 (8.16%) controls had very severe airflow obstruction. The observation signifying that previous tubercular infection has positive correlation with airflow obstruction.Baseline characteristics of all studied groups are shown in Table 4.

All the patients were divided into two groups in case and control, in that order, a significantly lower expected vital capacity (FVC%)in patients with a history of tuberculosis relative to control group were found (48.24±21.81 vs. 57.27±14.10, P <0.05). On comparison of patients with a history of tuberculosis to without a history of tuberculosis, statistically significant difference was observed between both groups in FEV1 predicted (40.11±17.21vs. 49.02±14.00, P<0.05).On comparison of FEV1/FVC ratio in both groups, statistically significant difference was observed (52.32±9.84 vs. 57.48±9.93, P<0.05).No statistically significant difference between case and control groups was found with respect to age (60.70 $\pm$ 9.23 VS 63.22 $\pm$ 9.950,p>0.05), smoking in pack /years (39.18±23.96VS 35.98±21.56,>0.05), and 6MWT (328.91±156.15 VS. 328.24±145.23,>0.05).

V. Discussion

In 1993, the world health organization (WHO) declared tuberculosis a "global emergency". Worldwide, 8 million new cases of active TB were reported[17,18].Despite many advances in modern medicine, both tuberculosis and COPD patients remain undertreated especially in the developing world. A significant proportion of patients with pulmonary tuberculosis may develop obstructive lung disease as a sequel to the disease. The development of additional airflow obstruction in tubercular patients may pose additional threat in terms of morbidity and mortality, as well as financially to the affected population. This study mainly focuses on the development of chronic airflow obstruction associated with tuberculosis. It reviews changes in pulmonary function in relation to clinical, functional and demographic variables.

This study shows that cases more often reported symptoms of cough (89% vs.83%), hemoptysis (44% vs. 22%), sputum production (83% vs. 44%), breathlessness (97% vs. 100%), and wheezing (40% vs. 27%; Table 4) in comparison to controls. The results are comparable to a study done by S.K.Verma *et al.*[19] at Lucknow. This may be due to the fact that MTB infection makes some permanent change in lung parenchyma and bronchi leading to frequent symptoms.

This study reveals 28/37 (75%) cases had FEV1 less than 50% i.e., severe to very severe airflow obstruction that is similar to the results of study by S.K.Verma *et al*[19]. It shows Maximum number of cases 17 in 0-10years of duration since ATT among them 47% cases had FEV1% between30-49. In maximum duration (31-40 years of ATT) 50% cases had FEV1 % between 30-49 % so it shows that the prevalence of airflow obstruction increases with duration since treatment completion this study correlates with the study done by Brashier B *et al*[20].Our study also showed that 17 cases stopped ATT 0-10years before; among them 76% cases had FEV1% less than 50%.In 11-20years duration of ATT subgroup 80% of cases had FEV1% less than 50%.With 21-30years of duration of ATT stoppage maximum 88% of cases had FEV1% less than 50%.In contrast, in maximum duration group (31-40 years of ATT) only 66 % cases had FEV1 % less than 50%.This is in contrast to the results of study by S.K. Verma *et al.* showing that recent infection was associated with more severe airflow obstruction compared to that of long duration[19].The reason given for this observation was that with the long duration tubercular lesions heal and patients are improved from obstructive pathology to some extent. But, our results show that there is rather a nonlinear relationship between duration since treatment and the degree of airflow obstruction. We advocate the need of further studies on this subject. A study conducted by Inam Muhammad Baig *et al*[21] in 2010 found that 65% of those patients showing an obstructive ventilatory defect had been treated more than 10 years earlier. An earlier study Willcox PA *et al*[22] revealed that the obstructive changes become pro-nounced after 10 years of follow-up in treated cases and co-related with the residual scarring on chest radiograph regardless of the findings on original chest radiographs. The prevalence of airflow obstruction in patients with pulmonary tuberculosis ranges from 28% to 68%[22,23]. **Gothi D et al**. studied the prevalence of obstructive airways disease ($FEV_1/FVC < 70\%$) in 100 patients fully treated for pulmonary tuberculosis in a tertiary care teaching hospital. The prevalence of obstructive defect was 46%**[24].** Obstruction was mild ($FEV_1 > 60\%$) in 75%, moderate (FEV_1 40–59%) in 10% and severe ($FEV_1 < 40\%$) in 15%.The results of above study are similar to our study. We found that the obstruction was mild ($FEV_1 > 60\%$) in 20%, moderate (FEV_1 40–59%) in 42% and severe ($FEV_1 < 40\%$) in 35%. Lee *et al.* did a study on Korean population which is similar our study, they involved 21 people with chronic airflow obstruction following pulmonary tuberculosis showed higher airflow resistance and lower positive bronchodilator response when compared with people with

The results of our study showed a significantly lower expected vital capacity (FVC % predicted) in cases v/s control group (48.24±21.81 vs. 57.27±14.10, $P < 0.05$) and a statistically significant difference was also observed between both groups in FEV1 % predicted (40.11±17.21vs. 49.02±14.00, $P<0.05$).The FEV1/FVC % ratio predicted in both groups also showed statistically significant difference (52.32±9.84 vs. 57.48±9.93, $P<0.05$). All these observations are similar to that reported in Jotam GP et al study.[25,26]

VI. Conclusion

Pulmonary tuberculosis is associated with frequent pulmonary damage despite of microbiologic cure. The impairment is variable, ranging from none to severe. Previously unmeasured burdens of tuberculosis in microbiologically cured patients may include chronic pulmonary impairment and excess mortality. PFTs and other measures may need consideration after a cure. When earlier data are considered with our findings, it is apparent that a microbiological cure is not protective against substantial pulmonary sequelae of pulmonary tuberculosis. These findings support the aggressive treatment of TB or other case preventing strategies like screening with PFTs for COPD worldwide, and indicate that, for many persons with tuberculosis, microbiological cure is the beginning, not the end, of their illness .In this study we evaluated the association between tuberculosis & severity of airflow obstruction. So it endorses for early diagnosis of COPD in post tubercular patients.

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Table 1: Respiratory symptoms in cases and controls

Symptom	Cough	Sputum	Dyspnea	Hemoptysis	Wheezing
Cases (COPD in post-TB pt)	**33(89)**	**31(83)**	**36(97)**	**22(44)**	**15(40)**
Controls (COPD in non-TB pt)	**41(83)**	**44(89)**	**49(100)**	**8(22)**	**27(55)**
Total	**74**	**75**	**85**	**30**	**42**

Values expressed as n (%).

This table shows that cases more often reported symptoms of cough (89% vs.83%), hemoptysis (44% vs. 22%), sputum production (83% vs. 44%), breathlessness (97% vs. 100%), and wheezing (40% vs. 27%; in comparison to controls.

Table 2: Comparison of FEV 1 % predicted with duration since ATT taken by the cases (patients with post TB)

Years	≥80	50-79	30-49	<30	Total Number of cases
0-10	Nil	4(23.52%)	8(47.05%)	5(29.41%)	17
11-20	Nil	2(40%)	2(40%)	1(20%)	5
21-30	Nil	1(11.11%)	3(33.33)	5(55.55%)	9
31-40	1(16.66)	1(16.66)	3(50%)	1(16.66)	6

This table displays correlation of airflow obstruction with duration of past tubercular infection. In 21-30years duration of ATT maximum percentage of cases had very severe airflow obstruction (FEV1 <30%). In maximum duration (31-40 years of ATT) 50 percent cases had FEV1 % between 30-49 %.Results show that recent infection has more severe airflow obstruction compared to that of long duration.

Table 3: FEV1% Predicted in cases and controls

FEV1 % Predicted	Case (COPD in post-TB pts)	Control (COPD in non-TB pts)
≥80	1(2.7%)	1(2.04%)
50-79	8(21.62%)	19(38.77%)
30-49	16(43.24%)	25(51.02%)
< 30	12(32.43%)	4 (8.16%)
Total	37	49

Table 3 shows 16 (43.24%) cases and 25 (51.02%) controls had severe airflow obstruction and 12 (32.43%) cases v/s 4 (8.16%) controls had very severe airflow obstruction.

Table 4: Correlation Between Different Characteristic Of Cases And Controls

	Case n=37 (COPD in post-TB pt)	Control n=49 (COPD in non-TB pt)	P value	Significance
AGE	60.70 ± 9.23	63.22 ± 9.95	0.228	NS
FVC % predicted	48.24±21.81	57.27±14.10	0.032	Sig
FEV1 % predicted	40.11±17.21	49.02±14.00	0.012	Sig
FEV1/FVC ratio	52.32±9.84	57.48±9.93	0.019	Sig
Smoking in pack years	39.18±23.96	35.98±21.56	0.518	NS
6MWT	328.91±156.15	328.24±145.23	0.984	NS

***All Values in Mean ± SD**

This table shows a significantly lower expected vital capacity (FVC%)in cases 48.24±21.81 v/s .controls 57.27±14.10, P <0.05). It shows statistically significant difference between both groups in FEV1 predicted (40.11±17.21vs. 49.02±14.00, P<0.05).On comparison of FEV1/FVC ratio in both groups, statistically significant difference was observed (52.32±9.84 vs. 57.48±9.93, P<0.05).