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A study on association of obstructive airway disease in previously treated pulmonary tuberculosis patients

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ABSTRACT

Background: Pulmonary tuberculosis (TB) and obstructive airway disease are of growing concern in a developing country akin to India. A considerable number of TB patients develop post-tubercular respiratory disease. There are few Indian studies assessing the relationship between antecedents of PTB and COPD. PTB has a considerable impact on quality of life.

Objective: To evaluate the prevalence of obstructive airway disease in previously treated pulmonary tuberculosis patients and to evaluate the impact of post TB obstructive airway disease on QOL using SGRQ-C.

Materials and Methods: A prospective, observational cross-sectional study was conducted in a tertiary care health centre over six months, enrolling 116 study subjects who met the inclusion criteria included after acquiring Informed consent. Study subjects had been categorized primarily based on prior history of PTB. Therefore, this study involved two groups of study subjects, PTB associated COPD and COPD. Subjects were assessed for PFT through the aid of MIR Spirobank smart App and QOL using SGRQ-C scale.

Results: Of 116 patients, 19(22.6%) women and 65(77.4%) men and 5(15.6%) women and 27(84.4%) men were diagnosed as PTB associated COPD and COPD respectively. Dyspnea and cough with sputum were the most common symptoms presented by 76(94.04%) and 62(71.42%) patients respectively. The effect of airflow limitation (FEV1) was slightly increased in PTB associated COPD patients (25.65%) compared to COPD patients (26.4%) and study endpoint showed noteworthy decrease in QOL of PTB associated COPD(72%) patients compared to COPD(66.4%).

Conclusion: PTB-associated COPD constitutes a significant proportion of COPD within clinical setting. It is an independent risk factor for OAD in extensive TB burden countries. The results indicated that early diagnosis, appropriate management and control of TB are as critical as smoking cessation for reducing OAD. Early identification of Post tubercular COPD and early initiation of treatment in these patients improve the QOL and reduces morbidity and mortality.

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1. Introduction

Pulmonary tuberculosis (TB) and obstructive airway diseases are of growing concern in a developing country like India as we enter modernization. It has emerged as a global

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health challenge affecting all age groups, and the inflow of such sufferers has multiplied in the recent past, rendering it a burden on the healthcare system. An extensive number of TB patients develop post-tubercular respiratory disease. This COPD phenotype has been variably termed as post-tubercular obstructive respiratory disease.¹

Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*, and pulmonary tuberculosis is the most common form.² It is associated with frequent pulmonary damage despite microbiological cure, which causes progressive destruction of lung tissue, and this damage might not absolutely resolve after treatment.^{3–5} Patients with treated TB may remain lifelong sufferers of disabling structural and functional sequelae of the disease, which eventually impair quality of life.^{6,7}

Chronic Obstructive Pulmonary Disease (COPD), a common, preventable, and treatable disease, is characterized by persistent airflow limitation that is usually progressive and associated with increased chronic inflammatory response in the airways and the lung to noxious particles or gases.⁸ Patients with treated pulmonary TB present signs of permanent impairment of their lung function. Impairment is variable in pattern and severity, ranging from none to severe, and indicates restrictive, obstructive or mixed patterns.^{9–11} Patients are segregated based on the clinical and radiological criteria and the GOLD classification as referred to in the study. Thus, establishing the pattern of obstructive airway involvement in post-PTB and determining the most effective relief regimen is crucial in the management of the same.

COPD and TB constitute significant public health challenges, especially in low and middle-income countries. Individuals with chronic respiratory disease additionally face higher all-cause mortality, even with only mild lung impairment.^{12,13} In addition to pulmonary damage, extrapulmonary tuberculosis disease and drug toxicity can cause permanent impairment to other organ systems, as well as social and psychological sequelae.⁵

The World Health Organisation has envisioned that the prevalence will increase in the next 30 years, with a total of annual death higher than 4.5 million (TOPD).¹⁴ According to World Health Organization (WHO) reports that 9.6 million people developed active tuberculosis and 1.5 million died due to tuberculosis each year, making it the leading infectious cause of death globally.^{15,16} In a nationwide survey of 13, 86 adults in South Africa results suggested that the strongest predictor of COPD was a history of PTB. Furthermore, the risk of COPD was more strongly associated with PTB than the tobacco smoking or exposure to smoke from biomass fuel.¹⁷ The history PTB increased the risk of COPD by 4.1 times for men and 1.7 times for women. The burden of Obstructive Lung Disease (BOLD) study had also proved the history of tuberculosis as a risk factor for developing airflow obstruction in later life.⁴

There are few Indian studies evaluating the relationship between the history of pulmonary tuberculosis and COPD that reported a 13–46% of prevalence of airflow obstruction, and the prevalence increased with duration after treatment completion.^{18–20} It was also reported that the association of COPD with PTB constitutes a significant proportion of COPD patients in India, it affects younger people than the patient with conventional COPD, and they have more hospitalizations, reaffirming the idea that TOPD is a distinct clinical entity.¹ Very recently it has been that young patients, previously healthy and non-smokers, can develop residual chronic changes post-PTB, one year after completing the treatment.²¹

Pulmonary tuberculosis has a substantial adverse impact on a patient's quality of life. Patients perceived Health-Related Quality of Life (HRQoL) is decreased in all patients diagnosed with PTB.²² Perceptions of both mental and physical quality of life remain below the normal population.²³ However, in a population of multi-drug resistant (MDR) tuberculosis (TB) patients, the decreased perception of HRQoL was still prevalent 18 months after the patients were deemed cured of TB.²⁴ Adult PTB survivors have two-to-four fold higher odds of persistently abnormal spirometry compared with those without previous TB, which is associated with respiratory symptoms and reduced quality of life.²⁵

India stands as the highest affected rate of TB burden and hence, there are more chances of getting a significant burden in TB-associated COPD. India is found to be placed in the second position after China in the mortality and morbidity cases due to obstructive airway diseases. There are very few studies done on TB-associated COPD in the present geographical location.¹

It is still not known whether there is any difference in clinical presentation between smoking-related COPD and TB-associated chronic pulmonary disease.²⁶ The majority of published studies available in the literature have been centered on investigating the effects of TB history on COPD prevalence though there are very limited data available regarding the effects of TB-associated COPD on Health-Related Quality of Life (HRQoL).²⁷ Hence the objective of the present study was to evaluate the prevalence of obstructive airway disease in previously treated tuberculosis patients and evaluate the impact of post-TB obstructive airway disease on Quality of Life using St. George's Respiratory Questionnaire for COPD patients (SGRQ-C).

2. Materials and Methods

Prospective, Observational cross-sectional study was carried out over a period of 6 months in the Government Wellesley TB and Chest disease hospital attached to Vijayanagara Institute of Medical Sciences, Ballari District, Karnataka. The study was approved by the Institutional Ethics Committee and provided IEC number

as TVMCP/IEC/V PD/2021-22/02. A total of 116 patients were involved in the study. Out of them 84 patients were diagnosed as PTB associated COPD and 32 patients were diagnosed as COPD. An informed consent was obtained from the study subjects after explaining about the methodology.

Patients with relapsed PTB or active PTB, with history of other pulmonary disorders such as interstitial lung cancer, unstable angina, congestive heart failure, Obstructive sleep apnea and pregnant women were excluded from the study.

The demographic questionnaire was constructed to obtain data on key variables like age, sex and weight. The medical data includes the duration of the disease, pharmacological treatment of the disease, duration of the therapy, smoking history and previous history of PTB. We performed the spirometry using MIR Spirobank Smart App-Based Spirometer (Ispirometer App) and the test was performed on Sputum smear negative patients. And then the patients were classified into four stages of airflow limitation (FEV1) as per the COPD GOLD Guidelines 2022. The Quality of Life of both groups of patients was assessed and compared by using a standard questionnaire St. George's Respiratory Questionnaire (SGRQ-C) and the airflow limitation (FEV1) obtained by performing spirometry. We evaluated the prevalence of PTB associated COPD and compared the impact of TB associated COPD and COPD on the quality of life of the patients.

2.1. Statistical analysis

Data were compared as mean±SD. A probability value <0.05 was considered for statistical significance. Data from and survey-derived information was entered into an electronic spreadsheet (MS Excel). Results were summarized using MS Excel. Demographic characteristics, previous history, pulmonary function tests, and SGRQ-C data were used to assess response rates by comparing PTB associated COPD and COPD. All the tests were performed using IBM SPSS Statistics for Windows, version 23.0. (Armonk, NY: IBM Corp).

3. Results

3.1. Baseline characteristics of study subjects

In our study males were predominant compared to females and most of the patients fall under the age group of 51-70 yrs. Major population of the study subjects comprised of smokers than non- smokers shown in Figure 1. Prevalence of TB associated COPD among the COPD population was 72% shown in Figure 2. Symptoms of dyspnea and cough with sputum were significantly seen in both the study groups and the symptom of Hemoptysis was only seen in PTB associated COPD patients. Using the COPD GOLD guidelines 2022 study subjects based on airflow limitation (FEV1) were classified as mild, moderate, severe

and very severe as detailed in Table 1. Clinically significant pulmonary impairment defined as an FEV1 <80% of the predicted value, was identified in all the study subjects being attributed to obstructive pattern and the obstruction was slightly more in TB associated COPD patients compared to COPD patients explaining more obstruction as shown in Figure 3.

Table 1: Characteristics of the patients in the study sample (n=116)

Characteristic	TB associated COPD	COPD
Gender		
Male	65(77.4%)	27(84.4%)
Female	19(22.6%)	05(15.6%)
Age		
18-30yrs	06(7.1%)	00(0.00%)
31-40yrs	07(8.3%)	00(0.00%)
41-50yrs	14(16.7%)	04(12.5%)
51-60yrs	25(29.8%)	10(31.3%)
61-70yrs	24(28.6%)	10(31.3%)
71-80yrs	07(8.3%)	07(21.8%)
Above 80yrs	01(1.2%)	01(3.1%)
Smoking		
Smoker	52(61.9%)	24(75%)
Non-smoker	32(38.1%)	08(25%)
Previous history		
With PTB	84(100%)	00(0.00%)
Without PTB	00(0.00%)	32(100%)
Symptoms		
Dyspnea	77(94.04%)	31(93.75%)
Cough with sputum	60(71.42%)	19(50%)
Fever	26(33.33%)	08(29.42%)
Edema	08(8.3%)	06(17.64%)
Hemoptysis	04(5.9%)	00(0.00%)
Chest pain	02(1.1%)	01(5.8%)
COPD Stage		
Mild	00(0.00%)	00(0.00%)
Moderate	04(4.8%)	02(6.3%)
Severe	21(25%)	08(25%)
Very severe	59(70.2%)	22(68.7%)
FEV1(mean±SD)	25.65±10.22	26.4±14.97
P-value	0.863	0.063
P-value (b/w groups)	0.039	

3.2. Impact of demographic and clinical features on SGRQ-C components in terms of quality of life

Mean SGRQ scale scores in the study subjects were weighed according to demographic and clinical features. Symptoms scale score was greater among men and activity scale was significantly higher in women. SGRQ scores were significantly greater in older groups for all scales. Smokers presented significantly higher scores for only activity scales. SGRQ scores also worsened in a statistically significant

manner as FEV1% over decreased. The impact of SGRQ components on the quality of life between two groups assessed, which presented that patients with TB associated COPD showed poor quality of life compared to patients with COPD shown in Figure 4.

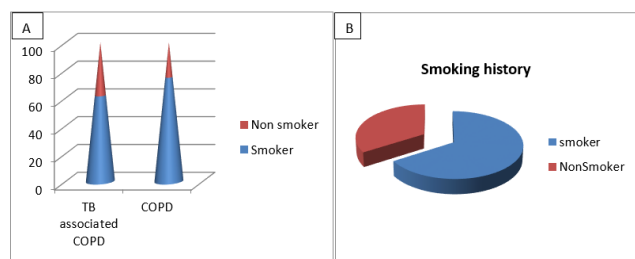


Fig. 1: a: Distribution of patients according to smoking status in two different groups; **b:** Distribution of the total study subjects according to smoking status

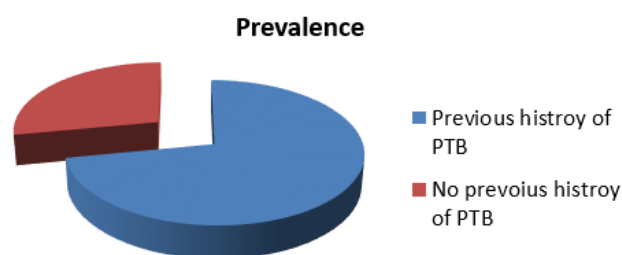


Fig. 2: Distribution of the total study subjects according to previous history of PTB

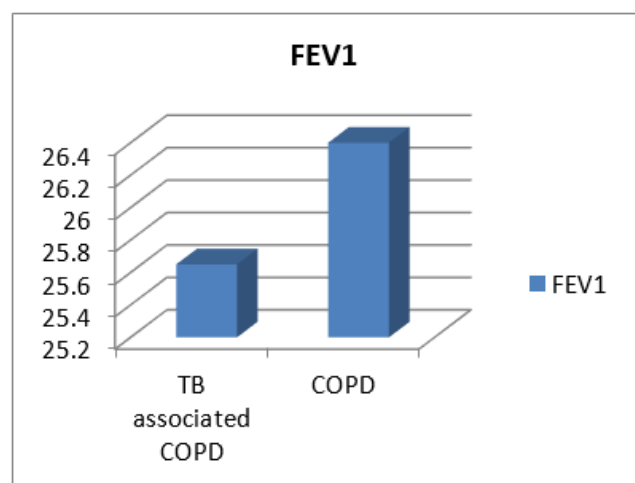


Fig. 3: Impact of lung function with TB associated COPD and COPD

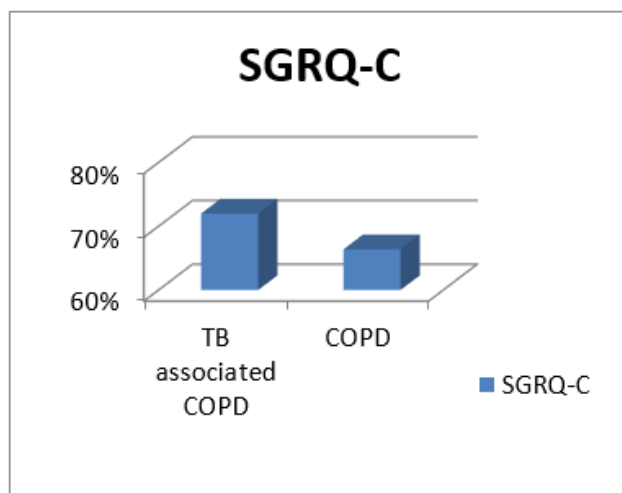


Fig. 4: Impact of SGRQ-C components with TB associated COPD and COPD

4. Discussion

The present study was conducted to find the hospital-based prevalence of TB associated COPD and to evaluate its characteristic features. The result showed that almost two third of COPD (72%) patients had associated TB in the past. It was seen that patients with TB associated COPD had almost similar grades of airway obstruction as compared to smoking related COPD. This gives strong evidence in favor of the casual association between TB and the development of COPD.

In the present study, out of 116 patients male 92 (79.3%) predominates over female 24 (20.7%) which is similar to the study conducted by Aggarwal et al.,¹ Upadhyay et al.,²⁶ of FEV1 in patients.²⁷

In the present study, the predicted value of FEV1 in patients with airflow limitation was 25.65±10.22 in TB associated COPD patients and 26.40±14.97 in COPD patients which is comparable to COPD of GOLD stage IV which is in contrast to the study that had airflow limitation comparable to COPD of GOLD stage III conducted by Kim et al.²⁸ This different rate of FEV1 decline may reflect differences like airflow limitation between destroyed lung by TB and COPD.

In the present study, we found a high symptom burden and poor HRQoL across all components of the SGRQ, particularly in activity and impact components. Increasing dyspnea showed a significant association with poor HRQoL across all component scores and fev1 was also strongly associated with poor HRQoL which is in comparable to the study conducted by Ozoh et al.²⁹

In our study among 84 TB associated COPD patients, 52(61.9%) were smokers and 32(38.1%) were nonsmokers. This result indicates that there is a significant contribution of smoking to parenchymal destruction as well as decreased

Table 2: St. George's Respiratory Questionnaire scale scores by demographical and clinical characteristics

	Symptoms	Activity	Impacts	Overall
Gender				
Male	68.74	83.78	62.15	69.95
Female	68.51	91.86	66.65	74.72
Age				
18-30yrs	73.5±19.5	89.2±18.7	65.6±28.9	74.3±23.4
31-40yrs	60.8±11.4	86.2±19.4	65.5±19.6	71±13.6
41-50yrs	69.5±12.5	85.6±16.7	61.3±23.2	70.2±15.8
51-60yrs	69.5±16.9	83.5±15.5	60.6±21.8	69.2±14.8
61-70yrs	69.8±14.2	86±8.5	64.8±23.8	71.7±18.2
71-80yrs	67±15.8	83.3±17.3	57.3±22.7	67±17.4
>80yrs	60.6±7.66	100±0	83.5±7.0	84.5±5.0
Symptoms(PTB associated COPD)				
Dyspnea	69.4±15.2	86±17	66±20.2	72.5±15
Cough with sputum	72±15.1	85.2±17.2	66.6±20.9	73±15.5
Fever	72.9±14.5	84.1±15.8	67.7±19.8	73.7±14
Edema	60.2±9	94.2±12.2	66.3±18.3	73.7±8.6
Hemoptysis	69.8±9.2	77.2±17.5	47.6±27.8	60.6±20
Chest pain	82.9	59.34	59.34	63.51
(COPD)				
Dyspnea	66.8±15	83.5±17.4	55.9±25.4	66.3±19.1
Cough with sputum	69.9±11	87.1±16.6	63±18.1	71.6±13.7
Fever	70.5±13	79.2±18.3	59.4±20.9	67.5±16.1
Edema	75.5±8.3	94.6±9.78	68±19	77.5±12.4
Hemoptysis	00	00	00	00
Chest pain	70.1±5.8	95.8±5.95	89.2±1.07	87.6±0.6
Smoking(PTB associated COPD)				
Smoker	69.6±15.2	83.8±16.6	65.5±21.9	71.6±15.4
Non smoker	69.1±15.1	89.4±16.6	63.07±20	72.2±15.5
(COPD)				
Smoker	66.7±16.8	81.3±18.4	53±26.2	64.1±20.4
Non smoker	68.9±5.5	90.7±11.9	68.3±17.2	75.3±10.2
P value				
PTB associated COPD	69.57	85.83	65.02	72.04
COPD	66.92	83.96	55.78	66.38
P-value	0.198	0.298	0.023	0.049

FEV1 values. Hence, smoking is one of the confounding factors in our study compared to the study conducted by Kim et al.²⁸

In the current study, the prevalence of TB associated COPD among the sample population was 72%. A similar study showed a prevalence of 16% among 500 patients conducted by Mohamed A et al and another similar study showed a prevalence of 32.4% conducted by Upadhyay et al.²⁶

Various mechanisms have been proposed for the development of COPD in TB patients. It includes endobronchial involvement leading to airway obstruction, bronchiolar narrowing, and bronchiolitis obliterans caused from peribronchial fibrosis and extensive emphysematous changes caused by residual chronic or recurrent inflammation affecting lung compliance. A common link to the pathogenesis of both conditions may lie in the destruction of the pulmonary extracellular matrix

due to the increased activity of matrix metalloproteinase enzymes precipitated by TB.

The risk of COPD has been found to increase with the increase in the radiological extent of TB, an increase in the number of previous TB episodes as well as with delay in initiating anti-TB therapy. In our study, we found that there is extensive parenchymal damage on Chest X-rays in TB associated COPD patients. Radiological findings are correlating with FEV1 values.

5. Conclusion

TB associated COPD constitutes a significant proportion of COPD in a hospital setting. It is an independent risk factor for obstructive airway disease in high TB burden countries. Post tubercular COPD as a cause of COPD in non-smokers should now be more recognized in countries where TB burden is high. The results of our study indicated

that early diagnosis of TB and appropriate management and control of TB is as important as smoking cessation for reducing obstructive airway disease. Early identification of Post tubercular COPD and early initiation of treatment in these patients improves quality of life and reduces morbidity as well as mortality.

6. Conflicts of Interests

None declared.

7. Source of Funding

None.


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