

# A Prospective, Randomised, Observational Study for an Evaluation of Chronic Obstructive Pulmonary Disease (COPD) in Post-Tubercular (Post-TB) Versus Non-Tubercular (Non-TB) Patients at Tertiary Care Teaching Hospital in Rajasthan

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## Abstract

## Original Research Article

**Background:** Post tuberculosis airway impairment has emerged as a distinct clinical entity, which is almost indistinguishable from other forms. India is in second place for harbouring the greatest number of morbidity and mortality cases from obstructive airway disease however there is paucity of studies on TB-associated COPD compared with its other varieties. **Materials and Method:** This prospective, randomised, observational study was carried out in 130 patients of Post-Tuberculosis (Cases) against 52 patients of Non-Tubercular COPD (Controls) admitted at tertiary care TB and Chest Hospital in Rajasthan during same period for comparisons in terms of Degree of Airflow Obstruction (FEV1%), Exercise capacity (6min. walk distance) and BODE index. **Results:** Mean FEV1% in Post-Tubercular COPD group was significantly lower 43.88 (SD=15.45) against in Non-Tubercular COPD 51.07(SD=14.28) (P<0.05). The mean 6MWD in Post-Tubercular COPD group was significantly lower 276.34 (SD=106.48) against in Non-Tubercular COPD group 308.26 (SD=67.31) (P<0.05). Distribution of patients according to BODE Index in Quartile-1 more patients were from Non-tubercular COPD (30.8%) as compared to Post-Tubercular COPD (11.5%), while in Quartile-4 more patients were from Post-tubercular COPD (25%) against Non-Tubercular COPD (7.7%). (p <0.05). **Conclusion:** Prior history of TB has an important role in the development of COPD and negatively impacts the long-term course of COPD, so early diagnosis of COPD in post tubercular patients is necessary to prevent further complications.

**Key words:** Post Tubercular COPD, FEV1%, 6MWD, BODE Index.

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## INTRODUCTION

Chronic obstructive airways disease as a complication of pulmonary tuberculosis has been re-studied recently in many regions of the globe [1, 2]. Post tuberculosis airway impairment has emerged as a distinct clinical entity, which is almost indistinguishable from other forms. Pulmonary functional impairment as a complication of tuberculosis manifests in various patterns but mainly as airflow limitation [3, 4]. In the executive summary of the 2006 update of the Global initiative for chronic obstructive lung disease (GOLD)

guidelines [5], the role of tuberculosis in the development of chronic airways obstruction has been recognized. According to the GOLD Workshop summary, chronic bronchitis and emphysema can occur as complications of pulmonary tuberculosis [6]. A study performed to assess the impact of pulmonary tuberculosis on the prevalence of COPD, found that the prevalence of COPD increased from 3.7-5% by including participants with history of TB treatment [7].

Most of the evidence on the causative association between TB and COPD has been derived

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from studies on lung function evaluation in treated TB patients and from population-based surveys on COPD [8-12]. However, a serious limitation is the confounding caused by concurrent exposure to risk factors such as tobacco smoking, dust and biomass fuel, childhood respiratory illnesses, and a lack of diagnostic precision when distinguishing COPD from other forms of structural lung disease (e.g. bronchiectasis) found in patients who had Pulmonary tuberculosis [13]. India is the highest TB burden country in the world and hence is likely to harbour significant burden of TB-associated COPD. Furthermore, India has a growing population of COPD and is in second place for harbouring the greatest number of morbidity and mortality cases from obstructive airway disease, after China [14]. Ironically, there is paucity of studies on TB-associated COPD from this geographical region [15, 16].

The potential effect of TB on the development of COPD was believed to be mediated by mechanisms of chronic inflammation [17-19] Radovic et al. [20] demonstrated that after 6 months of anti-TB treatment, serum markers of systemic inflammation such as erythrocyte sedimentation rate and fibrinogen decreased significantly but were still abnormally high. Recently, Tang et al. found that serum concentrations of cytokines such as soluble interleukin-2 receptor (sIL-2R), IL-6 and tumour necrosis factor (TNF- $\alpha$ ) in COPD patients with TB were higher than those without TB or those with TB but without COPD, suggesting that COPD combined with TB may result in excessive inflammation [21].

There are few documented evidences regarding prevalence of Post-Tubercular obstructive airway disease and its comparison with Non-Tubercular COPD available in India. Therefore, the present study was planned to evaluate the association between history of pulmonary tuberculosis and chronic obstructive airway disease.

## MATERIALS AND METHODS

This was prospective, randomised, observational study carried out in 130 patients of Post-Tuberculosis and 52 patients of Non-Tubercular COPD admitted at TB & Chest Hospital (Bari) under the Department of Respiratory Medicine, R.N.T. Medical College, Udaipur (Rajasthan) in the period between April 2019 to September 2019. In this study, 130 adult patients of age 40-80 years who were having history of Pulmonary Tuberculosis (TB) and were completely cured with Anti-tuberculosis treatment (ATT) and were having radiological evidence of typical post TB lesions in the form of scarring, fibrosis, cavitation, emphysema and other destructive lung changes in their latest chest radiographs and were bacteriologically negative on recent sputum AFB (Acid-Fast Bacilli) and sputum CBNAAT (Cartridge Base Nucleic Acid Amplification Test) results were included as Post-Tuberculosis

patients and patients without history of Tuberculosis between the age of 40-80 years were included as Non-Tubercular COPD patients. Patients with presence of any other Respiratory or systemic illness, any clinical features leading to a probability of active pulmonary TB, patients who were not able to perform Spirometry and 6 Minute Walk Test (6MWT) or having contra-indication to spirometry and six-minute walk test and those showing more than 12% - and 200-ml reversibility in the post-bronchodilator FEV1 were also excluded from the study.

With prior approval from Institutional Ethics Committee of R.N.T. Medical College and after taking a detailed written informed consent in patient's native language (Hindi) all the patients were evaluated as per Predesigned Case Record Form (CRF). For selected Post Tuberculosis patients, spirometry was being performed and the frequency of obstructive airway disease (i.e., Post bronchodilator FEV1/FVC <0.7) among Post Tuberculosis patients was obtained. Hence, the number of patients having Post Tubercular Obstructive airway disease (considered as Cases group) were compared against the equal number of Non-Tubercular COPD patients (COPD patients without history of tuberculosis) of age 40-80 years (considered as Control group) admitted at TB & Chest Hospital (Bari) during same period in terms of Degree of Airflow Obstruction (FEV1%), Exercise capacity (6min. walk distance) and BODE index. (Body-mass index (B), the degree of airflow Obstruction (O) as assessed by FEV1 and Dyspnoea (D) assessed by mMRC scale, and Exercise capacity (E) measured by the six-minute-walk test, to be calculated for grading of severity of COPD).

The quantitative data was represented as their mean  $\pm$  SD. Categorical and nominal data was expressed in percentage. The t-test was used for analysing quantitative data and categorical data was analysed by using chi-square test. Pearson's correlation coefficient was used to determine the correlation between parameters. The significance threshold of p-value was set at <0.05. All analysis was carried out by using SPSS software version 16.

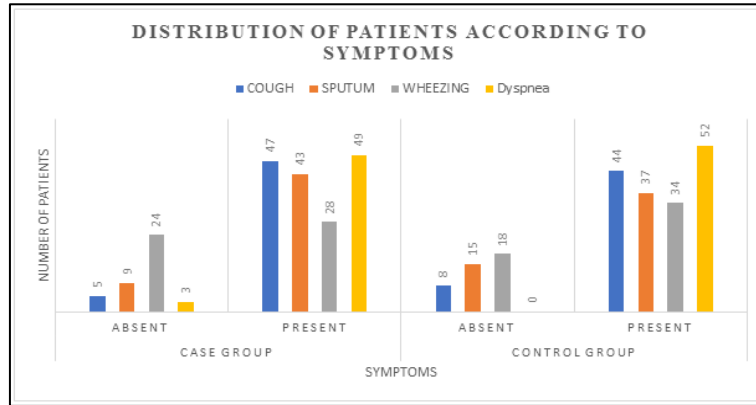
## RESULTS

Majority of Post-Tubercular COPD patients belonged to age 51-60 (44.2%) as compared to Non-Tubercular COPD patients in which majority were aged between 61-70 (46.15%). The mean age in Post-Tubercular COPD patients was 56.73 (SD=8.16) and in Non-Tubercular COPD patients was 61.3 (SD=8.90). The difference is statistically significant as the p value is <0.05. Most patients in both the groups were males. Male to female ratio in Post-tubercular COPD group was 2:1 and in Non-Tubercular COPD group was 3.7:1. Mean BMI in Post-Tubercular COPD patients was 20.75 $\pm$ 2.95 and in Non-Tubercular COPD patients was 21.65 $\pm$ 3.37. Majority of patients in both Post-

Tubercular COPD (67.3%) and Non-Tubercular COPD (63.4%) were having normal BMI. The difference is not significant.

The maximum no. of patients (52) was having obstructive ventilatory defect on spirometry i.e., 40%. Normal spirometry pattern was present only in 19 (14.6%) patients. 33 (25.4%) patients were having

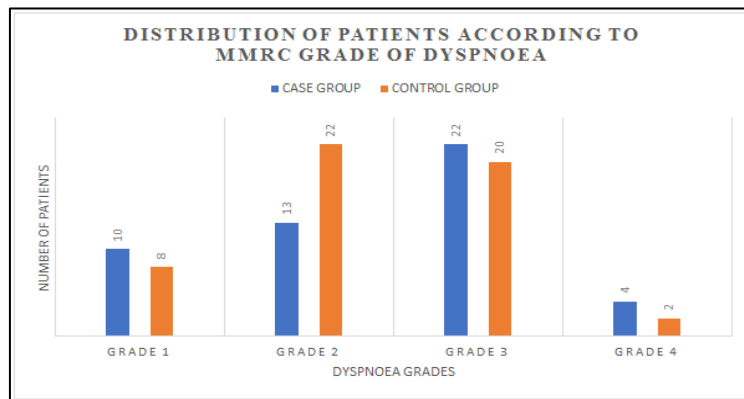
restrictive pattern and 26 (20%) patients were having mixed spirometry pattern. The most common symptoms among both the Post-Tubercular COPD (94.23%) and Non-Tubercular COPD (100%) patients. While wheezing was more common in Non-Tubercular COPD patients (65.38%) as compared to Post-Tubercular COPD patients (Figure-1).



**Fig-1: Distribution of patients according to Symptoms**

Almost 50% of Post-Tubercular COPD patients were having mMRC Grade-3 & Grade-4 Dyspnoea as compared to Non-Tubercular COPD

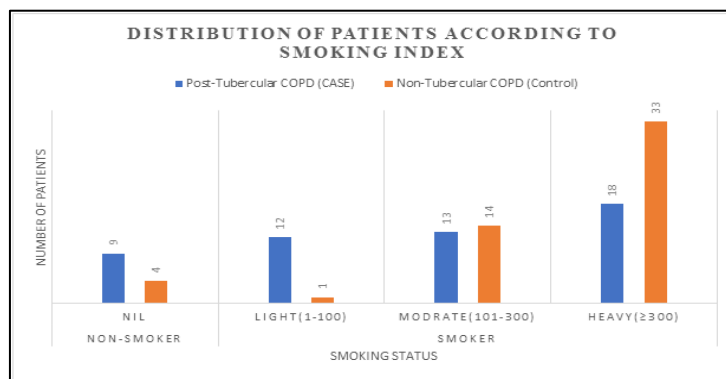
patients in which 42.3% patients were having mMRC Grade-3 & Grade-4 Dyspnoea. (Figure-2). The difference is not significant.



**Fig-2: Distribution of patients according to mMRC Grade of Dyspnoea**

Heavy smokers were significantly more in Non-Tubercular COPD (63.46%) as compared to Post-Tubercular COPD (34.61%) while Non-Smokers were

more in Post-Tubercular COPD (17.3%) as compared to Non-Tubercular COPD (7.69%). The difference is statistically significant (Figure-3).



**Fig-3: Distribution of patients according to Smoking index**

Mean FEV1 in Post-Tubercular COPD group was 43.88(SD=15.45) and in Non-Tubercular COPD group it was 51.07(SD=14.28). The difference is statistically significant as the p value is <0.05. (Table-1)

Mean FVC in Post-Tubercular COPD group was 70.90 (SD=4.28) and in Non-Tubercular COPD group was 73.05(SD=9.05). The difference is not significant (p-value>0.05).

**Table-1: Distribution of patients according to Severity of COPD (Gold Guidelines)**

Severity of COPD	FEV1 (% Pred.)	Post-Tubercular COPD	Non-Tubercular COPD	P-value
GOLD-1 (Mild)	≥80	3(5.76%)	2(3.84%)	0.07
GOLD-2 (Moderate)	50-79	16(30.76%)	25(48.07%)	0.001
GOLD-3 (Severe)	30-49	25(48.07%)	23(44.23%)	0.099
GOLD-4 (Very Severe)	< 30	8(15.38)	2(3.84%)	0.001
	Total	52(100%)	52(100%)	
	MEAN±SD	43.88±15.45	51.07±14.28	0.001

About 86.6% of Non-Tubercular COPD patients were able to walk between range of 250-349m and ≥350m in 6 minutes as compared to Post-Tubercular COPD patients in which only 55.8% patients could walk between the range of 250-349m and

≥350m in 6 minutes. The mean 6MWD in Post-Tubercular COPD group was 276.34 (SD=106.48) and in Non-Tubercular COPD group was 308.26 (SD=67.31). The difference is significant as the p value is <0.05 (Table-2).

**Table-2: Distribution of patients according to 6MWD**

6MWD (in meters)	Post-Tubercular COPD		Non-Tubercular COPD		P-value
	No of patients	%	No of patients	%	
≥350	18	34.6	20	38.5	0.63
250-349	11	21.2	25	48.1	0.001
150-249	18	34.6	7	13.5	0.003
≤149	5	9.6	0	0.0	0
TOTAL	52	100.0	52	100.0	
MEAN±SD	276.34±106.48		308.26±67.31		0.001

Distribution of patients according to BODE Index shows in Quartile-1 maximum no. of patients are from Non-tubercular COPD (30.8%) as compared to Post-Tubercular COPD (11.5%). While in Quartile-4

maximum no. of patients are from Post-tubercular COPD (25%) as compared to Non-Tubercular COPD (7.7%). The difference is statistically significant as the p value is <0.05 (Table-3).

**Table-3: Distribution of patients according to BODE Index**

BODE INDEX	Post-Tubercular COPD (n=52)	Non-Tubercular COPD (n=52)	P-value
QUARTILE-1 (0-2)	6 (11.5%)	16 (30.8%)	0.001
QUARTILE-2 (3-4)	16 (30.8%)	17 (32.7%)	0.52
QUARTILE-3 (5-6)	17 (32.7%)	15 (28.8%)	0.09
QUARTILE4(7-10)	12 (25%)	4 (7.7%)	0.001
Total	52(100%)	52(100%)	

Majority of Post-Tubercular COPD patients (73%) had no. of hospitalization ≥2 times in last one year while majority of patients in Non-Tubercular COPD (57.5%) were hospitalized only once in last one year. Mean number of hospitalizations in last one year for Post-Tubercular COPD group was 2.78(SD=1.85) and for Non-Tubercular COPD group was 1.53(SD=1.37). The difference is statistically significant as the p value is <0.05.

COPD group was 9995.19 (SD=2720.98). The difference is statistically significant as the p value is <0.05. Majority of patients in both Post-Tubercular COPD (88.5%) and Non-Tubercular COPD (78.8%) were having high ESR level. The mean ESR in Post-Tubercular COPD was 49.38±20.9 and in Non-Tubercular COPD group 42.36±21.9. The difference is not significant.

Leukocytosis was more common in Post – Tubercular COPD patients (48%) as compared to Non-Tubercular COPD patients (25%). Majority of patients of Non-Tubercular COPD (71.2%) were having normal TLC. Mean TLC count in Post-Tubercular COPD group was 11230.76 (SD=5231.37) and in Non-Tubercular

Hyperinflation was present in 53.8% patients of Post-Tubercular COPD and 78.84% patients of Non-Tubercular COPD. The difference was statistically significant p-value <0.05. Among patients having hyperinflation, patients with flattened diaphragm were significantly more in Non-Tubercular COPD patients (73.1%) as compared to Post-Tubercular COPD patients

(60%). The difference is statistically significant. Cardiomegaly was present in 17.3% patients of Post-Tubercular COPD and 11.5% patients of Non-Tubercular COPD. The difference is not significant.

## DISCUSSIONS

In present study, 50% of Post-Tubercular COPD patients were having mMRC Grade-3 & Grade-4 Dyspnea as compared to Non-Tubercular COPD patients in which 42.3% patients were having mMRC Grade-3 & Grade-4 Dyspnea. This shows that patients with Post-Tubercular COPD have more worsened dyspnea as compared to Non-Tubercular COPD. The results were comparable with the study by Bairwa R et al. [2, 3] and Zakaria et al. [9]. This may be due airway involvement in Post-Tuberculosis patient there is more parenchymal involvement. Cavitation, extensive fibrosis, emphysematous changes, bulla formation, lung scarring & destroyed lung in Post-Tuberculosis patient also contribute to the worsening of dyspnea. In present study Heavy smokers were significantly more in Non-Tubercular COPD (63.46%) as compared to Post-Tubercular COPD (34.61%) while Non-Smokers were more in Post-Tubercular COPD (17.3%) as compared to Non-Tubercular COPD (7.69%). Jain NK et al. [24] suggested that Smoking, however, is not the sole factor in the pathogenesis of COPD. Caballero et al. [12] from Columbia has reported that the association between TB and airway obstruction was stronger than that observed between smoking and airway obstruction.

In present study the mean 6MWD in Post-Tubercular COPD group was 276.34 (SD=106.48) and in Non-Tubercular COPD group was 308.26 (SD=67.31). The difference is significant (p value <0.05). Decrease in exercise capacity is more in Post-tubercular COPD patients because these patients have poor muscle strength and are more cachexic as compared to Non-Tubercular COPD patients. We also observed the negative correlation between mMRC grades of dyspnea and 6MWD in both Post-Tubercular COPD ( $r = -0.564$ ,  $p < 0.001$ ) and Non-Tubercular COPD patients ( $r = -0.402$ ,  $p = 0.003$ ) i.e., with increasing mMRC grades of dyspnea there was decrease in 6MWD. Since severity of dyspnea was more in Post-tubercular COPD patient, hence 6MWD was lesser in Post-Tubercular COPD patient as compared to Non-Tubercular COPD patient. Similar results were recorded in the study of Manoj Kumar Khandelwal [25] in which they found that higher the grade of dyspnea (MMRC grade), lower the 6-minute walk distance ( $P < 0.05$ ). Tamakuwala Grinish et al. [26] also showed that there was strong negative correlation between 6MWD and MMRC grade ( $p < 0.05$ ).

In present study, in Quartile-1 BODE Index (0-2 Points) maximum no. of patients are from Non-Tubercular COPD group (30.8%) as compared to Post-Tubercular COPD group (11.5%). While in Quartile-4

BODE Index (7-10 Points) maximum no. of patients are from Post-tubercular COPD (25%) as compared to Non-Tubercular COPD (7.7%). In present study, the mean number of hospitalizations in last one year for Post-Tubercular COPD group was 2.78(SD=1.85) and for Non-Tubercular COPD group was 1.53(SD=1.37). The difference is significant as the p value is <0.05. This was comparable to the reports from the study of Yakar et al<sup>35</sup> (2017), in which the mean number of hospitalizations in last one year for Post-Tubercular COPD group was 2.46 (SD=2.54) and for Non-Tubercular COPD group was 1.56(SD=1.97). They reported that higher number of hospitalizations was associated with worsening of dyspnea, faster decline in FEV1 and increase severity of BODE Index.

In present study, mean TLC count in Post-Tubercular COPD group was 11230.76 (SD=5231.37) and in Non-Tubercular COPD group was 9995.19 (SD=2720.98). The difference is significant (p value= 0.0001). Similar results were recorded in the study by Yakar et al. [27] in which mean TLC count in Post-Tubercular COPD group was 12247(SD=6648) and in Non-Tubercular COPD group was 10731 (SD=4927) with p value= 0.01. For leukocyte value significantly higher in those with TB history, possible explanation for this could be that severe inflammation and bacterial infections facilitated by TB sequel might also be leading to higher leukocyte level. In present study, the mean ESR in Post-Tubercular COPD was  $49.38 \pm 20.9$  and in Non-Tubercular COPD group  $42.36 \pm 21.9$ . The difference is not significant. This was comparable to the reports from the study by Radovic et al. [28] and Yakar et al. [27].

## CONCLUSION

Present study has revealed that patients with a history of TB were diagnosed with COPD 5 years earlier, had poor pulmonary function, were hospitalized more often due to COPD exacerbations and had poor exercise capacity. Taking all these findings into account, we may conclude that a prior history of TB has an important role in the development of COPD and negatively impacts the long-term course of COPD. So, it endorses for early diagnosis of COPD in post tubercular patients to prevent further complications occurring from COPD.

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