

Research Article

To study the burden of post tubercular obstructive airway diseases in patients visiting chest OPD at a tertiary level chest OPD in North India: a descriptive cross-sectional study

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Summary

Abstract COPD and tuberculosis are on the rise in developing countries. There is evidence of post-tuberculosis lung function deterioration and the occurrence of obstructive airway diseases in such patient groups.

Objectives: To study the burden and severity of obstructive airway disease in subjects with a history of pulmonary tuberculosis and find the demographic trends, features, and clinical presentations in tuberculosis-associated obstructive pulmonary disease (TOPD) and non-tubercular obstructive airway disease (non-tubercular OAD).

Methodology: We investigated 125 patients divided into two groups, i.e., post-tubercular airway disease (n = 50) and airway disease due to other aetiology (n = 75). Age, gender, and BMI were analysed. Dyspnea grade was analysed using the Modified Medical Research Council (m MRC) scale. Spirometry was performed to find the pattern of airway disease in both groups. The severity of obstruction and lung functions were analysed using GOLD guidelines and spirometry.

Results: The males accounted for 71.2%, and females –28.8% of the patients. There were more females in the tubercular airway disease group. The mean age of the tubercular group (46.94 ± 14.67) was significantly lower than that of the non-tubercular airway disease (58.47 ± 6.14). No significant difference was found for BMI. Obstructive airway disease was more common in both groups (46% and 49.30%, respectively), and the severity of obstruction was higher in the TOPD group. The severity of cough and dyspnea was higher in that group. FVC and FEV1 were significantly reduced in TOPD compared to non-tubercular obstructive airway disease (non-tubercular OAD). The mean latency of COPD symptoms after completion of ATT was found to be 5.38 ± 6.77 years.

Conclusion: Post-tuberculosis subjects presented with lung function decline without confounding factors like smoking; thus, early screening of COPD is required once diagnosed; appropriate treatment should be initiated as early detection and treatment of these patients can help in better disease management and optimum treatment outcomes.

Key words: Biomedical research, demography, developing countries, lung, post-tubercular, respiratory disorders, smoking, tuberculosis, spirometry, treatment outcome



Academic editor: Ivelina Yordanova

Received: 5 February 2025

Accepted: 17 April 2025

Published: 19 June 2025

Citation: Masood I, Neyazi N, Abbas Waseem SM, Hussain H (2025) To study the burden of post tubercular obstructive airway diseases in patients visiting chest OPD at a tertiary level chest OPD in North India: a descriptive cross-sectional study. Journal of Biomedical and Clinical Research 18: 159–169. <https://doi.org/10.3897/jbcr.e148797>

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Introduction

According to the study of Menon et al. (2022) the burden of non-communicable diseases (NCDs) is on the rise. People from low- to middle-income countries suffer from both NCDs and infectious diseases, which often have a reciprocal relationship (Tadyanemhandu et al. 2018; Coates et al. 2020). Among infectious diseases, tuberculosis continues to be a global health concern. Reports suggest that 26% of the global burden of incident cases of tuberculosis was from India alone in 2020 (Global Tuberculosis Report 2021). Also, the literature suggests that obstructive airway disease is the third leading cause of mortality worldwide, and importantly, obstructive airway diseases have also been linked with a history of tuberculosis. Reportedly, there is a threefold high probability of airway obstruction in patients who have been treated for TB (Byrne et al. 2015; GBD 2017). According to Gupte et al. (2019) pulmonary function deterioration is reported even after treatment for tuberculosis. There appear to be multiple contributory factors, with smoking reported to be a confounding factor both for TB and obstructive airway disease (Chakrabarti et al. 2007). Links between COPD and tuberculosis require attention and exploration, as both diseases are on the rise in developing nations. Another critical issue is whether COPD and tuberculosis-associated obstructive pulmonary disease (TOPD) should be treated as separate entities (Sarkar et al. 2017). Given the importance and link between post-treatment tuberculosis and obstructive airway disease, the present study was undertaken as it is still an unexplored domain and requires much research. An understanding of the etiologies of COPD in post-tubercular and non-tubercular subjects could help draw demographic trends and clinical features and suggest better diagnostic algorithms and optimum treatment strategies. Also, early screening and interventions can help to improve the quality of life. Importantly, owing to geographical and environmental variations, there appears to be a disparity in the reported prevalence in India, and considering the standard links between the two, studies are needed to expand the knowledge about the spectrum of TOPD.

Materials and methods

This descriptive cross-sectional study was conducted over three months in the outpatient department of a tertiary care hospital. One hundred and twenty-five patients with stable COPD without acute exacerbation attending the outpatient department of the Respiratory Medicine Clinic were enrolled in the present study after obtaining informed and voluntary consent. Confounding factors like smoking and exposure to biomass fuel were excluded. The study subjects were further divided into two groups.

The first group consisted of 50 patients following inclusion and exclusion criteria. Patients with COPD per GOLD guidelines with a history of pulmonary tuberculosis in the past and those with a record of complete ATT intake per revised RNTCP guidelines were included in the study. Those with active pulmonary tuberculosis and currently taking ATT, active smokers, and subjects with a history of asthma, bronchiectasis, or any other respiratory disorders before tuberculosis were excluded. Also, COPD patients with comorbidities like sleep apnoea, lung cancer, and interstitial lung diseases were excluded. Patients with

moderate to severe anaemia, a history of recent myocardial infarction, congestive heart failure, and unstable angina were also excluded from the study.

The second group consisted of seventy-five stable COPD patients without acute exacerbation and without a history of pulmonary tuberculosis or any prior TB contact.

A detailed clinical examination and history taking were performed. Various investigations like chest X-ray for foci of tuberculosis, electrocardiogram to rule out cardiac pathologies, sputum AFB for active tuberculosis, and pre and post-bronchodilator spirometry to compute FEV1/FVC for COPD severity as per GOLD guidelines (Agustí et al. 2023) and modified MRC dyspnea scale (Agarwal et al. 2023) to assess the severity of symptoms were carried out. Patients were classified into mild, moderate, or severe obstructive airway diseases based on FEV1/FVC values, dyspnea scoring, exacerbation frequency, and presence of complications (like respiratory failure, i.e., pO_2 less than 60% and SPO_2 less than 88% and pCO_2 more significant than 50 mm Hg; cor pulmonale and secondary polycythemia, i.e., hematocrit above 55%) (Gupta et al. 2013).

The data collected was analysed for the following objectives:

1. To study the burden and severity of obstructive airway diseases in patients with a pulmonary tuberculosis history.
2. To find out the demographic trends and features associated with COPD in post-treatment tuberculosis.
3. To compare the clinical presentation of COPD in post-treatment tuberculosis and non-tubercular airway disease.

Statistical analysis

The software package for statistical analysis, SPSS-22.0, and Microsoft Excel were used to analyse the data collected. Parametric and non-parametric tests were used for the analysis of data. Student's t-test and chi-square test were utilised. The results obtained are presented in the form of tables and graphs. The data are presented as mean \pm SD and frequency. A p-value of <0.05 was considered significant.

Results

A total of 125 subjects were included in the present study. They were further divided into two groups. The first group comprised 50 subjects with tubercular-associated airway disease. The second group comprised 75 subjects with non-tubercular airway disease. In the former group, 56% were males and 44% were females, whereas in the latter group, 81.33% were males and 18.67% were females. There was a significant difference in mean ages between the two groups ($p < 0.001$). The mean BMI of subjects with airway disease associated with other aetiology was higher than that of subjects with post-tubercular airway disease, but the difference was insignificant ($p = 0.41$) (Table 1).

In the post-tubercular airway disease group, the intake of ATT ranged between six to twenty-four months. The results showed that 68% had taken ATT for six months, whereas 2% had taken it for 24 months (Table 2).

Table 1. Comparison of BMI and demographic profile between tubercular associated airway disease and airway disease due to other aetiology.

| Variable | Tubercular associated airway disease (n = 50) | Non-tubercular airway disease (n = 75) | P value |
|-------------------------|---|--|---------|
| Gender | | | 0.001* |
| Male | 28(56%) | 61(81.33%) | |
| Female | 22(44%) | 14(18.67%) | |
| Age (years) | 46.94 ± 14.67 | 58.47 ± 6.14 | <0.001* |
| BMI(Kg/m ²) | 20.79 ± 3.88 | 21.27 ± 2.42 | 0.41 |

The results are represented as numbers and percentages for qualitative data (gender) and analysed using the chi-square test. For quantitative data represented in mean ± SD, the student's t-test was used for analysis and a p-value of <0.05* was taken as significant.

Table 2. Duration of intake of ATT in tubercular associated airway disease group (n = 50).

| ATT intake in months | Number (%) |
|----------------------|------------|
| 6 | 34 (68%) |
| 9 | 3 (6%) |
| 12 | 5 (10%) |
| 18 | 7 (14%) |
| 24 | 1 (2%) |

Numbers and percentages represent the data on the duration of ATT intake in months.

The latency between discontinuation of ATT and the appearance of cough and dyspnea in the tubercular group was 5.38 ± 6.77 years (range 6 months to 27 years) (Table 3).

Table 3. Latency period of stoppage of ATT and appearance of cough in post tubercular group.

| Symptoms | Latency in years post-ATT | minimum | maximum |
|-------------------|---------------------------|----------|----------|
| Cough and dyspnea | 5.38 ± 6.77 | 6 months | 27 years |

Seventy per cent of the subjects with post-tubercular airway disease reported cough (Table 4).

Table 4. Cough in post tubercular airway disease group(n = 50).

| Cough | Number (%) |
|-------|------------|
| Yes | 35(70%) |
| No | 5(30%) |

The modified medical research council (m MRC) dyspnea scale results showed that grade two and three dyspnea was present in 32% and 38% of subjects with post-tubercular airway disease, and 18% had grade four dyspnea. In non-tubercular airway disease, grade 1 and 2 dyspnea cases prevailed, i.e., 36% and 46.67%, respectively, whereas the frequency of grade 4 dyspnea was lower (5.33%). The difference was significant (p < 0.001) (Table 5).

Table 5. mMRC dyspnea scale in post tubercular airway disease and airway disease associated with other etiologies.

| mMRC severity Grade | Post tubercular airway disease Number (%) | Non-tubercular airway disease Number (%) | P value |
|---------------------|---|--|---------|
| 1 | 6 (12%) | 27 (36%) | <0.001* |
| 2 | 16 (32%) | 35 (46.67%) | |
| 3 | 19 (38%) | 9 (12%) | |
| 4 | 9 (18%) | 4 (5.33%) | |

The data was represented as numbers and percentages, and the difference was analysed using the non-parametric chi-square test, and p-value <0.05* was taken as significant.

The results of spirometry summarised in Table 5 show that 46% of subjects with post-tubercular airway disease had obstructive pattern, and 34% had restrictive airway disease. In non-tubercular airway disease due to other aetiology, a restrictive pattern was present in 42.67%, and an obstructive pattern was reported in 49.33%. Thus, results showed that an obstructive pattern was more common in both post-tubercular and non-tubercular airway disease, i.e., the difference was insignificant (p = 0.079) (Table 6).

Table 6. Pattern in post-tubercular and non-tubercular airway disease.

| Spirometry pattern | Post tubercular airway disease Number (%) | non-tubercular airway disease Number (%) | P value |
|--------------------|---|--|---------|
| Obstructive | 23(46%) | 37(49.33%) | 0.079* |
| Restrictive | 17(34%) | 32(42.67%) | |
| Mixed | 10(20%) | 6(8%) | |

The data was represented as numbers and percentages and was analysed using the non-parametric chi-square test. A p-value of <0.05 was taken as significant. The difference was insignificant, with a p-value >0.05*. The results show that most patients had obstructive airway disease in both post-tubercular and non-tubercular disease, i.e., 46 and 49.33 per cent, respectively. The patients were classified as having obstructive and restrictive patterns as per the FEV1/FVC % ratio, with the obstructive pattern defined as a ratio of less than 70%.

As per the results of GOLD summarised in Table 6, in the post-tuberculosis obstructive pulmonary disease (TOPD) group, the majority of subjects (36%) had moderate obstruction followed by severe obstruction (28%). In COPD, due to other aetiology, the majority (54.67%) had mild obstruction followed by severe (18.67%) obstruction. The difference was significant (p = 0.018) (Table 7).

Table 7. Severity of obstructive airway disease in post-tubercular (TOPD) and non-tubercular obstructive airway disease.

| GOLD Stage | TOPD Number (%) | Non-tubercular OAD Number (%) | P value |
|-------------|-----------------|-------------------------------|---------|
| Mild | 12 (24%) | 41(54.67%) | 0.018* |
| Moderate | 18 (36%) | 13(17.33%) | |
| Severe | 14(28%) | 7(9.33%) | |
| Very Severe | 6(12%) | 14(18.67%) | |

The data was represented as numbers and percentages and was analysed using the non-parametric chi-square test. A p-value of <0.05* was taken as significant. In non-tubercular obstructive airway disease (OAD) patients majority (54.67%) had mild obstructive pattern, whereas in the post-tubercular obstructive pulmonary disease (TOPD) group, the majority had moderate (36%) followed by severe (28%) obstruction as per the spirometry reports.

The spirometry values showed a significant reduction in the FVC ($p = 0.012$) and FEV1 ($p = 0.001$) values in the TOPD group compared to COPD due to other aetiology. The FEV1/FVC % was lower in the former group than in the latter group. However, the difference was insignificant ($p = 0.851$). Similarly, PEFr was insignificantly ($p = 0.212$) reduced in TOPD compared to COPD due to other aetiology (Table 8).

Table 8. Pulmonary Function Test Values in TOPD and Non-Tubercular OAD.

| Pulmonary Function | TOPD | Non-tubercular OAD | P value |
|--------------------|---------------|--------------------|---------|
| FVC(liters) | 1.90 ± 0.75 | 2.19 ± 0.84 | 0.012* |
| FEV1(liters) | 1.32 ± 0.58 | 1.63 ± 0.87 | 0.001* |
| FEV1/FVC % | 70.46 ± 18.78 | 74.07 ± 17.55 | 0.851 |
| PEFR(liters) | 3.46 ± 1.62 | 3.51 ± 1.47 | 0.212 |

The spirometry test results are shown as mean ± SD. The difference between the lung functions between TOPD and non-tubercular OAD was analysed using the parametric unpaired student's t-test. A p-value of <0.05* was taken as significant.

Discussion

Our study showed a significant association between post-treatment tuberculosis and obstructive airway diseases. Compared to other OADs, the clinical presentation was more severe, if not identical.

Out of 125, $n = 50$ (40%) were non-smoker post-treatment tuberculosis patients, and $n = 75$ (60%) were OAD patients with other etiologies like smoking, biomass fuel exposure, and a history of prior pulmonary tuberculosis. Of 125 subjects, 71.20% were males and 28.80% were females. However, the number of females in the post-tubercular OAD was higher (44%) than in the non-tubercular OAD group (18.67%). Sixty, i.e., 81.33% of subjects with non-tubercular OAD, were found to be males, whereas 56% of subjects with post-tubercular OAD were males. It may be because smoking is the most common aetiology of COPD, and men are associated with evermore increasing rates of cigarette and bidi consumption (Mishra et al. 2016).

The mean age in post-tubercular and non-tubercular airway disease groups was 46.94 ± 14.67 and 58.47 ± 6.14 years, respectively. Thus, the mean age of the former group was significantly lower ($p < 0.001$) than the latter group. The results obtained align with the previous study by Gunen and Yakar (2016). Further analysis of the results showed that the obstructive pattern was more common in patients post-tuberculosis and, thus, providing valuable insight into the early onset of COPD in patients post-tuberculosis and, therefore, needs to be explored and evaluated further by designing follow-up longitudinal studies.

Also, in the present study, the difference in the mean BMI between post-tubercular (20.78 ± 3.88) and non-tubercular airway disease (21.27 ± 2.42) groups was found to be insignificant ($p = 0.41$). The results corroborate with earlier findings that even though obesity is known to increase morbidity in COPD patients, BMI, per se, is not a significant factor in differentiating post-tubercular and non-tubercular airway disease (Cecere et al. 2011).

Cough was a widespread complaint in the patients of post-tubercular OAD. 35/50, i.e., 70% had a history of recurrent coughing episodes. This was significantly higher than in a study by Zakaria and Moussa (2015) where only

44% of patients presented with cough. However, there was no significant correlation (Chi-Square test p value = 0.064) between cough and type of ventilatory defect (obstructive, restrictive, or mixed). Also, there was no correlation (Mann Whitney U test p value = 0.0921) between the presence or absence of cough and severity of airflow limitation. These results contradicted a less-known cross-sectional study where patients with mild to moderate airflow obstruction reported cough and sputum production more frequently than those with severe disease (Von Hertzen et al. 2000). This study was not done in a non-smoking cohort; thus, the results differ from ours. Cough occurs due to minor airway inflammation, as many inflammatory mediators like prostaglandins are tussive agents (Smith and Woodcock 2006). Thus, cough can always be used as a case-finding tool for patients at risk of progressive airway obstruction.

The anti-tubercular treatment history was elicited from post-tubercular patients: 34/50 (68%) of these patients followed the regimen of 6 months, and the rest followed nine months, 12 months, 18 months, and 24 months. (6%, 10%, 14%, and 2%, respectively). This shows that most of them suffered from drug-sensitive tuberculosis. Thus, it proves that drug-sensitive or multidrug-resistant tuberculosis strains of *Mycobacterium tuberculosis* make no significant difference in the pathophysiology of obstructive airway disease. There is also no correlation (p value = 0.83) between the duration of treatment and the severity of the limitation of pulmonary function. Nor is there any association between the duration of the ATT regimen and the type of ventilatory defect (obstructive, restrictive, or mixed). Similar findings were seen by Basha et al. (2022).

The latency can be defined as the time between completion of the anti-tubercular treatment regimen and the occurrence of symptoms like dyspnea, cough, etc., suggestive of compromised pulmonary functions and the latency periods ranging from a minimum of 6 months to a maximum of 27 years. In our study, 28% (14/50) of the patients presented with OAD within six months of completion of treatment. Hnizdo et al. (2000) noted a maximum loss of FEV1 values six months after post-tubercular treatment. Seventy-six per cent of our patients (38/50) had a latency of <5 years. Only 12% (6/50) had a latency of 5–15 years, and the rest had a Latency of >15 years. These findings predict that post-tubercular OAD will most likely present in the first five years of the following decade, specifically during the first six months of the post-tubercular treatment period. Like cough and anti-tubercular treatment duration, latency also had no association with the type or severity of the ventilatory defect.

Dyspnea or difficulty breathing was recorded by asking the patients about their limitations of activities according to the mMRC. The results of the descriptive statistics showed that the post-tubercular OAD group had higher values for dyspnea (median score = 3) than the non-tubercular OAD group (median score = 2). This difference was statistically significant ($p < 0.001$), proving that patients with prior history of tuberculosis had a more severe form of dyspnea and more activity limitation, with most of the patients being in mMRC grade 3 (36%) and grade 4 (18%) as compared to plain COPD patients where the majority were in mMRC grade 1 (36%) and grade 2 (46.67%).

The obstructive type of ventilatory defect is most prevalent in both post-tubercular and non-tubercular airway disease groups, followed by restrictive and mixed ventilatory defects. No significant correlation was found between these two variables ($p = 0.079$).

The COPD was graded according to the severity of airflow limitation as assessed by spirometry. In the post tubercular group (TOPD), the majority of patients belonged to grade 2/Moderate (36%) and Grade 3/Severe (28%), whereas, in the non-tubercular obstructive airway disease group, the majority of patients fell into Grade 1/Mild (54.67%). These findings showed that post-tubercular patients had significantly higher GOLD Grades of COPD than the non-tubercular OAD group ($p = 0.018$).

The mean forced vital capacity in the TOPD patients was 1.9 ± 0.75 compared to the non-tubercular patients, which was 2.19 ± 0.84 . The FVC was significantly lower in the TOPD patients ($p = 0.012$). Also, the mean FEV1 value in the TOPD patients was 1.32 ± 0.58 as opposed to 1.62 ± 0.87 in other patients, showing that even FEV1 was significantly reduced in post-tubercular OAD ($p = 0.001$).

On the other hand, differences between the mean peak expiratory flow rates and FEV1/FVC values were not significant in the two groups.

The above findings indicate that the pulmonary function parameters were further reduced, and the severity was much higher for the post-tubercular OADs than the non-tubercular OADs. Aggarwal et al. (2017) have seen similar findings, probably because tuberculosis affects the lungs by multiple mechanisms like minor airway impairment, bronchiectasis, destruction of extracellular matrix proteins, interstitial granulomas, and nodule formation, as well as reducing the diffusion capacity by fibrosis and emphysematous changes (Dheda et al. 2005).

Limitations of the study

This was a short-duration study confined to one hospital. Therefore, the findings may not apply to a general population. Since it was strictly an OPD-based study, patients with acute or indifferent presentations of this disease may have yet to be noticed. The sample collection was biased in terms that people having smoked along with a history of ATT intake could not be included, and no findings could be known about them. We do not know if the presentation of post-tubercular OAD may vary with drug-sensitive or multi-drug resistant strains or what happens to spirometry values in patients with a history of multiple treatments for pulmonary tuberculosis. We could not elicit differences in outcomes concerning ATT intake history, for example, if there is a difference in the presentation of defaulters and relapsed patients. Radio-logical evidence could have given more clues to fibrosis status in the lung parenchyma. Active case finding and passive case reporting are needed for tuberculosis and COPD. All these limitations are indicators for further improvement; the demographic data, especially the gender distribution, cannot be blindly relied upon since there is always bias in health-seeking behaviour between men and women and between elderly and young patient groups.

Therefore, more evidence-based conclusions need to be derived, expanding over more geographical locations to cover more of the population and different age and gender groups so that results can be more generalised.

Conclusion

The study aimed to find the burden, severity, trends, and features of post-tubercular OADs and their difference from OADs of other etiologies. A significant number of patients with a history of treated pulmonary tuberculosis,

without confounding factors like previous smoking, presented to OPD with clinical and spirometry features of decreased lung function. Compared with other COPDs, post-tubercular airway disease had younger and more varied ages of presentation. The ratio of female to male patients with post-tubercular obstructive pulmonary disease (TOPD) was significantly higher compared to non-tubercular obstructive airway disease. TOPD had a high frequency of cough symptoms. Symptoms like dyspnea were more pronounced in TOPD, with a median score of 3 rather than a score of 2, as seen in COPD of other etiologies. The severity of airflow limitation, as seen by GOLD grades, was higher in post-tubercular COPD. Diminution of functional vital capacity and forced expiratory volume in one second was more prevalent in post-tubular COPD. This severity is attributable to the fact that tuberculosis causes aggressive inflammation of the lungs, leading to accelerated fibrosis and air trapping, causing more severe COPD.

Suggestions

The study's outcome points out a strong association between tuberculosis and COPD.

Features of decreasing lung function appear as early as six months. Thus, early and timely screening of COPD must be done after anti-tubercular treatment is completed.

The treatment outcome of post-tubercular COPD is worse than other COPDs, even though the clinical presentation is very similar.

Since post-tubercular OADs present in younger age groups, more aggressive treatment and frequent follow-ups are required to prevent long-term complications.

Acknowledgements

The authors acknowledge the support of the technical staff and thank the study participants.

Additional information

Conflict of interest

The authors have declared that no competing interests exist.

Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

Funding

It was an ICMR approved and granted STS project (2023) (reference ID: Reference Id: 2023-11433).

Author contributions

All authors have contributed equally.

Data availability

All of the data that support the findings of this study are available in the main text.

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