

Original Research Article

Association between tuberculosis and bronchial asthma

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ABSTRACT

Background: Everything that wheezes is not asthma. In patients of tuberculosis (TB), wheezing can be because of bronchial asthma, or many other causes. Asthma and other causes of wheezing need to be differentiated, as the treatment should be planned accordingly.

Methods: Patients of active/quiescent tuberculosis who presented to Department of Tuberculosis and Chest Diseases, Government Medical College, Patiala, Punjab, India, with complaints of breathlessness and had rhonchi on examination were subjected to bronchodilator reversibility testing to prove if they were suffering from concomitant asthma. Patients thus found to have tuberculosis along with asthma were analyzed with respect to age, sex, rural urban differences and timing of diagnosis of either disease. Patients who developed asthma after tuberculosis were further analyzed for duration between completion of anti-tubercular treatment (ATT) and onset of asthma, family history of asthma and correlation of radiological manifestations and lung function measurements. Aim was to find association, if any, between tuberculosis and asthma.

Results: Over 6 months, 69 patients of tuberculosis along with asthma were found. Only 21/69 (30.4%) patients developed tuberculosis after asthma. 48/69 (69.6%) patients developed asthma after tuberculosis. Majority (25/48=52.1%) of them developed asthma within 5 years of completion of ATT ($p=0.020$). Only 2/48 (2.9%) patients had a positive family history for asthma. Lung function abnormalities correlated with the extent of radiological involvement in these patients who developed asthma after tuberculosis ($p \leq 0.0001$).

Conclusions: Patients of active/quiescent tuberculosis who present with breathlessness and have rhonchi on examination should be treated for asthma only after confirmation of the diagnosis, as there can be other reasons for the same.

Keywords: Asthma, Bronchodilator reversibility test, Rhonchi, Tuberculosis

INTRODUCTION

In patients of active/ quiescent tuberculosis (TB), rhonchi are not uncommonly present on auscultation. It is a known fact that the various causes of the rhonchi in active/quiescent tuberculosis include extraluminal obstruction by lymph glands, lesions in the wall of the bronchi like tubercular lesion or stricture in a healed

tubercular focus, intraluminal obstructions due to secretions or the proliferative tubercular lesions of the wall of the bronchus.

Besides this, the patient may have compensatory emphysema, traction of bronchi because of fibrosis and drug allergies due to anti tubercular drugs. If the cause of rhonchi is bronchial asthma, it may be present beforehand

in such patients, or they may develop it subsequently. It is practically important to prove the cause of rhonchi because its management will differ, depending upon the exact cause. If asthma is the reason, it should be recognized at an early stage and treated as per guidelines otherwise airway remodeling may occur leading to poor control of asthma.

Overuse of inhaled as well as oral steroids given for treating breathlessness and rhonchi in a patient of tuberculosis who is not an asthmatic may result in reactivation of quiescent tuberculosis.¹ Even otherwise, the use of inhaled steroids in higher doses and oral steroids for treatment of advanced stages of asthma may be a factor for the development of tuberculosis.

METHODS

The patients of active/quiescent tuberculosis presenting to the outpatient clinics of the Department of Tuberculosis and Chest Diseases, Government Medical College, Patiala, Punjab, India, over a period of 6 months, with complaints of breathlessness and had rhonchi on examination were screened.

The patients who had their sputum smear positive for acid fast bacilli (AFB) and were on anti-tubercular treatment (ATT) were labeled as ‘active tuberculosis’ cases while those who had taken ATT in the past and were declared cured, were labeled as ‘quiescent tuberculosis’ cases. Also, all the patients of suspected asthma were questioned for history of TB in the past to ascertain the relationship between the two diseases, if any. All such patients were subjected to bronchodilator reversibility testing which is one of the hallmark investigation for proving bronchial asthma. 69 patients were found to have asthma based on positive bronchodilator reversibility testing.

For bronchodilator reversibility testing, 400µg of levo-salbutamol was used by nebulization and after 15 minutes, reversibility was checked. A change in forced

expiratory volume in one second (FEV1) ≥200ml and 12% than the prebronchodilator value of FEV1 was considered to be positive. Only these patients were analyzed with respect to the age, sex, rural urban differences and timing of diagnosis of either disease.

The patients who developed asthma after tuberculosis were further analyzed for duration between completion of ATT and onset of asthma, family history of asthma and correlation between radiological manifestations and lung function measurements in the form of peak expiratory flow rate (PEFR).

The lung lesions were categorized as per national tuberculosis association (NTA) classification into minimal TB, moderate-advanced TB and far-advanced TB.² Data so gathered was tabulated and statistically analyzed.

Statistical analysis

Discrete categorical data was represented in the form of either a number or a percentage. The normality of quantitative data was checked by measures of Kolmogorov–Smirnov tests of Normality. Mean ages of diverse groups were compared using one-way ANOVA. Proportions were compared using Chi-square. Analysis was conducted using IBM SPSS STATISTICS (version 22.0). p value of ≤0.05 was considered to indicate statistical significance.

RESULTS

69 patients of active/quiescent tuberculosis, were diagnosed to be suffering from bronchial asthma along with. 27 were males and 42 were females, with a rural: urban ratio of 15:8. The age groups involved are shown in Table 1. 24 (34.8%) patients belonged to the age group of 31-40 years while 13 (18.9%) to the 51-60 years age group. 21/69 (30.4%) patients developed tuberculosis after their asthma.

Table 1: Age groups involved (n=69).

Age group	21-30 years	31-40 years	41-50 years	51-60 years	>60 years
Number of patients	12 (17.4%)	24 (34.8%)	12 (17.4%)	13 (18.9%)	8 (11.5%)

Majority (48/69=69.6%) had tuberculosis preceding the onset of bronchial asthma. Table 2 shows the further analysis of these 48 patients who developed asthma after tuberculosis, showing the time duration between the onset of asthma and the completion of ATT. Majority (25/48=52.1%) patients developed asthma within 5 years and 11/48 (22.9%) between 6-10 years of completion of ATT. The results were found to be statistically significant (p=0.020).

Amongst the 48 patients who developed asthma after tuberculosis, only 2 (2.9%) patients had a positive family history for asthma. Figure 1 shows the co-relation between radiological extent of the disease and PEFR (peak expiratory flow rate) with far advanced radiological shadowing being associated with poorer mean PEFR. As the lesions increased on radiology, mean PEFR values also decreased significantly (p ≤0.0001).

Table 2: Time durations between the completion of ATT and onset of asthma (n=48), in patients who had tuberculosis preceding the onset of bronchial asthma.

Time duration (years)	Number of patients	Percentage
≤5	25	52.1
6-10	11	22.9
11-15	5	10.4
16-25	4	8.3
>25	3	6.3

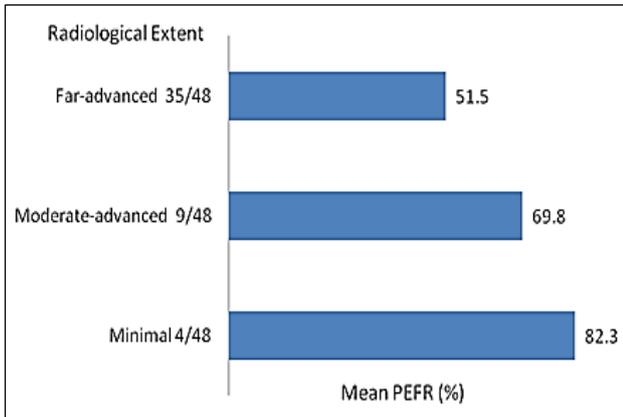


Figure 1: The co-relation between radiological extent of lung involvement and PEFR, (n=48), in patients who had tuberculosis preceding the onset of bronchial asthma.

DISCUSSION

Tuberculosis and bronchial asthma are two common public health problems. There is a possibility of their co-existence in some patients as well. Certain factors can lead to the predisposition of bronchial asthma in patients of tuberculosis and vice versa.

Various predisposing factors for tuberculosis include malnutrition, physical and mental strain, poor housing conditions with overcrowding, certain occupations like quarrying and knife grinding, alcoholism and smoking, immune compromised states like human immuno virus infection, diabetes mellitus, Hodgkin's disease, leukaemia etc and patients on steroids and immunosuppressive drugs.³ Similarly, the patients may develop bronchial asthma due to familial predisposition and genetic factors, obesity, environmental factors like exposure to indoor allergens, viral infections, smoking, indoor and outdoor air pollution and dietary factors.⁴

The use of steroids, physical and mental stress and poor socio economic status because of loss of wages due to asthma may predispose the patient to tuberculosis.⁴ A meta-analysis has concluded that the use of inhaled corticosteroids in patients with chronic respiratory diseases increases the risk of tuberculosis.⁵ Also, in patients of bronchial asthma who are on oral steroids,

there are high chances of developing tuberculosis.⁶ Multiple factors as stated above may be implicated in the patients who develop tuberculosis after their bronchial asthma.

Similar is the case in patients of tuberculosis who develop bronchial asthma afterwards. There are reports of Loeffler's syndrome being caused due to usage of para-amino salicylic acid (PAS) in tuberculosis patients was common.⁷ The patients of tuberculosis can develop bronchial asthma because of drug allergy or broncho pulmonary damage, whereby the allergens may gain access, causing inflammation and allergic manifestations.

Besides bronchial asthma, the rhonchi found on auscultation in patients of tuberculosis can be because of complications of tuberculosis itself, pressure by enlarged glands or endobronchial tuberculosis. Airway obstruction is one of the known complications/sequelae of tuberculosis which can be the cause of rhonchi in these patients.⁸ Bronchospasm, perhaps due to the development of bronchial hyper sensitivity to tuberculo-proteins, may appear for the first time after tuberculosis has become manifest. So, in patients of tuberculosis presenting with breathlessness and having rhonchi on auscultation, if misdiagnosis of asthma is done, then unnecessarily patient may be given higher doses of inhaled or oral steroids to control the symptoms which may be harmful to the patient. Therefore, in such patients, diagnosis of bronchial asthma should be confirmed.

In present study, 69 patients of active/quiescent tuberculosis were diagnosed to be suffering from bronchial asthma along with, based on bronchodilator reversibility testing.

Only 21/69 (30.4%) patients developed tuberculosis after their asthma. Majority (48/69=69.6%) had tuberculosis preceding the onset of bronchial asthma. This is in comparison to the study by Popescu et al, where in 90% of the patients, bronchial asthma developed after tuberculosis and 10% patients presented with bronchial asthma and subsequently developed pulmonary TB.⁹

Further analysing these 48 patients who developed tuberculosis after their asthma, it was seen that 52.1% of these patients developed bronchial asthma within 5 years of having tuberculosis. This is in comparison to the study by Rajasekaran et al where 76.3% patients had developed bronchial asthma within three years of stopping anti-tuberculosis treatment.¹⁰

Only 2/48 patients had a positive family history for asthma. This is in comparison to the study by Rajasekaran et al where only one third of the patients had familial history of bronchial asthma.¹⁰

In patients developing asthma after tuberculosis, familial predisposition is not a common factor. Other factors, which may be responsible for the increased chances of

development of asthma in patients of active/quiescent TB, need to be explored. If found, they can explain the reason for such an association.

When the radiological manifestations in these 48 patients were analysed, far advanced lung lesions predominated in our patients, compared to the moderate lesions predominance in study by Rajasekaran et al.¹⁰ This finding may suggest that the bronchopulmonary damage may be a crucial factor in patients developing post tuberculosis bronchial asthma, and this damage also correlates with the objective impairments in the form of poor PEFr readings in these patients.

Development of tuberculosis and bronchial asthma is regulated by Th 1 and Th 2 sub-groups of T lymphocytes respectively.^{11,12} The clinical manifestations of both the diseases do not occur simultaneously because the levels of these subgroups of lymphocytes are not increased at the same time in an individual.

In patients of tuberculosis, once they get treated, Th 1 response, which was accelerated during active Tuberculosis, gets reduced. The reduction in Th 1 response may result in mounting of Th 2 response which is a crucial factor for the unmasking of asthma in overt asthmatics.

As per hypothesis, when Th 1 response increases, then Th 2 response decreases and vice versa. So, the patients may not have Tuberculosis and asthma together. In current study, out of the 69 patients having tuberculosis and asthma together, one of the salient observations was that 59 (85.51%) patients were having quiescent tuberculosis and only 10 (14.49%) patients had active tuberculosis. Out of these 10 cases of active tuberculosis, only 2 were fresh newly diagnosed cases of tuberculosis, rest 8 patients had been treated and declared cured for tuberculosis in the past also. So, this proves the hypothesis that active tuberculosis and asthma occurring concurrently is a remote possibility. However, asthma may be existing in treated cases of tuberculosis.

CONCLUSION

Asthma in quiescent tuberculosis or active but treated patients of tuberculosis (who had taken ATT in the past and declared cured) is not an uncommon entity. A patient of tuberculosis having breathlessness and rhonchi because of the complications and sequelae but not because of asthma should not be started on higher doses of inhaled or oral steroids, as this may do more harm than good. Bronchodilator reversibility testing should be done in such patients, and only on confirmation of the

diagnosis of asthma should such patients be treated for the same according to the available guidelines.

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