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PREVALENCE OF ALLERGIC: BRONCHO-PULMONARY ASPERGILLOSIS IN PATIENTS WITH PULMONARY TUBERCULOSIS

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ABSTRACT

Background: Allergic Bronchopulmonary Aspergillosis (ABPA) is a hypersensitivity airway disease caused by Aspergillus species, and is common in chronic lung disease patients such as Pulmonary Tuberculosis (TB). In TB patients, the immunocompromised state and lung parenchymal loss may predispose to ABPA, which guarantees the exacerbation of the pulmonary condition and complicate the disease.
Objective: To determine the prevalence of ABPA in patients with Pulmonary Tuberculosis and assess the impact of co-morbid ABPA on pulmonary-function, disease progression and treatment outcome in patients.
Study design: A cross-sectional study.
Place and duration of study: From 01 December 2024 to 31 May 2025 Pulmonology Department, Fatima Jinnah Institute of Chest Diseases, Quetta.
Methods: A Cross-sectional study was carried out among tuberculosis patients of tertiary care hospital. ABPA was diagnosed on the basis of clinical examination, radiograph and laboratory studies (serum Ige, Aspergillus skin prick test and sputum culture). The prevalence of ABPA was determined and correlated with clinical features, pulmonary findings and clinical response to treatment. Chi-square and p-value calculation

were applied in the statistical analysis.
Results: A total of 150 patients with pulmonary tuberculosis were included in the study and the median age was 42.3 years (SD ± 12.4). Of these 38 (25.3) patients had ABPA. ABPA was more frequent in patients with cavitary TB (40%) compared with non-cavitary TB (15 percent, p = 0.001). There is a significant reduction in forced expiratory volume (FEV1) in patients with ABPA compared with those without the disease (mean FEV1: 63% -7.4 and 77% -9.2 respectively, p = 0.02). Also, the serum Ige was higher in ABPA-positive patients (mean Ige: 523 IU/mL +- 129.5) than in the non-ABPA group (mean Ige: 175 IU/mL +- 85.6; p < 0.01). Bronchiectasis (p = 0.004) was more common in ABPA patients than in non-ABPA TB patients (60 vs 35, respectively).
Conclusion: ABPA is an important co-morbidity of pulmonary tuberculosis with a prevalence of 25.3. Abstract Background: Active Bovine tuberculosis (ABPA) is known to have a negative impact on lung function, especially in those with cavitary TB and high serum IgE and bronchiectasis. It is possible that ABPA can be treated and minimized in its effects on lung health by early diagnosis and treatment of the disease, and may improve overall TB patients' prognosis.

INTRODUCTION

Allergic Bronchopulmonary Aspergillosis (ABPA) is a hypersensitivity condition caused by the Aspergillus species (primarily Aspergillus fumigatus) and is characterized by chronic lung inflammation. It is most commonly seen in patients with chronic pulmonary diseases such as asthma, cystic fibrosis and most importantly Pulmonary Tuberculosis (TB) [1]. ABPA is considered to be a consequence of an inappropriately robust immune response to fungal colonization of the airways that involves a complex set of inflammatory reactions; immunoglobulin E (Ige) and other immune cells are mobilized [2]. Pulmonary TB is a disease that has led to increased morbidity and mortality in the world and especially in high-burden countries like South Asia and Sub-Saharan Africa [3]. Pulmonary TB is a disease that has become a major source of morbidity and mortality worldwide and especially in heavily burdened countries like South Asia and Sub-Saharan Africa [4]. TB most commonly affects the lungs, which can cause the symptoms below; Cough, hemoptysis (blood in sputum), chest pain Confirmed inflammatory responses and lung destruction, bronchiectasia and fibrosis are frequent secondary effects of TB that offer a milieu that predisposes patients to the development of opportunistic infections like ABPA [5]. In addition, it is known that TB treatment and particularly corticosteroids have immunosuppressive properties that can also contribute to fungus susceptibility and hypersensitivity in TB patients [6]. Although the association of TB and ABPA is discussed in relation to some of these studies, there remains a lack of understanding on the true prevalence of ABPA in patients with TB, particularly in a setting in which TB has a high prevalence. This is critical in improving diagnosis and treatment and management strategies overall. Pathophysiology of ABPA in the context of TB is multifactorial and includes the following: immune dysregulation, structural lung damage, fungal colonization. Cavitary TB or patients with post TB sequelae are especially vulnerable to develop ABPA due to the concomitant presence of poor

immune response and the presence of optimal environment to support Aspergillus growth [7]. It is extremely important to identify ABPA in TB patients early enough to ensure they receive treatment quickly, which can include corticosteroids and antifungal treatment to calm the inflammation and inhibit overgrowth of the fungus. However, corticosteroid administration in TB patients must be closely monitored to avoid relapsing TB and, therefore, diagnosis and treatment of ABPA is even more difficult [8]. Despite the reports of studies documenting the prevalence of ABPA in TB patients, its prevalence remains poorly defined, especially in regions where TB endemicity is high. Objective: This study aims to establish the prevalence of ABPA in patients with pulmonary TB in a tertiary care unit and its impact on pulmonary function, disease progression and outcome of treatment. We would like to highlight the occurrence of two conditions co-occurring to stress the importance of close screening and management measures in this high-risk group [9].

Methods:

Design: it was a cross-sectional study design conducted in a tertiary care hospital in a high endemic area for TB. Methods: We included patients who had pulmonary TB as established disease, and who were on treatment or follow-up in the study. ABPA was diagnosed on the basis of clinical presentation, positive Aspergillus skin prick test, elevated serum Ige and/or positive Aspergillus culture of sputum. A radiological investigation (chest X-ray and CT scan) was performed to search for lung damage including bronchiectasis. To quantify lung function, spirometry to determine forced vital capacity (FVC) and forced expiratory volume (FEV1) was performed. SPSS 24.0 software was used for analysis. The study was done in compliance with the ethics and approved by the institutional review board.

Inclusion Criteria:

Included study participants were patients with confirmed pulmonary tuberculosis (culture or clinically diagnosed), aged 18-65 who are on treatment or follow-up in hospital.

Exclusion Criteria:

Patients who had a history of fungal infections, other than ABPA, or known immunodeficiency (e.g., HIV, diabetes) or declined to participate in the study were excluded.

Ethical Approval Statement:

This study was carried out in accordance with the Declaration of Helsinki (Approval No. XYZ1234). All the subjects provided written informed consent before they were admitted to the study and informed consent was ensured, confidentiality observed and voluntary participation ensured.

Data Collection:

Data was collected via patient interview, clinical and laboratory studies. Demographic, clinical, radiological and sputum culture data as well as serum Ige and pulmonary function testing data were recorded. Data were anonymized in order to maintain patient confidentiality and stored securely for analysis.

Statistical Analysis:

Statistical analyses were performed by using SPSS 24.0. Demographic and clinical data were summarized as descriptive statistics (mean, standard deviation). Associations between ABPA and TB-related variables were assessed using chi-square test and t-tests. A value of less than $p=0.05$ was considered as statistically significant.

Results:

One hundred and fifty patients with pulmonary TB were selected and the average age of the population was 42.3 years (SD + 12.4). Out of the 38 patients (25.3), 25 patients were diagnosed with ABPA. Among them, 65% were cavitary TB and 35% non-cavitary TB. Also ABPA was significantly more frequent among cavitary TB patients (40

vs. 15%, p = 0.001) Mean serum Ige was significantly higher in ABPA compared to non-ABPA (523 IU/mL +- 129.5 vs. 175 IU/mL +- 85.6, p = 0.01). Forced expiratory volume in 1 second (FEV1) on spirometry was significantly lower in the ABPA than in the non-ABPA group (63% +- 7.4 vs 77% +- 9.2, p = 0.004) and bronchiectasis was reported in Chest CT demonstrated characteristic mucus plugging and bronchial dilation in ABPA positive patients resulting in prolonged treatment duration and usage of antifungal therapy which adds to treatment cost and prolonged hospitalization.

Table 1: Demographic Characteristics of Study Participants (n = 150)

Characteristic	Value (n = 150)
Mean Age (years)	42.3 (SD ± 12.4)
Gender	
Male (%)	90 (60%)
Female (%)	60 (40%)
Smoking History	
Current smokers (%)	40 (26.7%)
Former smokers (%)	50 (33.3%)
Non-smokers (%)	60 (40%)

Table 2: Prevalence of ABPA Among TB Patients

TB Classification	ABPA Positive (%)	ABPA Negative (%)	Total (%)
Total	38 (25.3%)	112 (74.7%)	150 (100%)
Cavitary TB	26 (40%)	39 (60%)	65 (43.3%)
Non-Cavitary TB	12 (15%)	73 (85%)	85 (56.7%)

Table 3: Serum Ige Levels in ABPA and Non-ABPA Groups

Group	Serum Ige (IU/mL) - Mean (SD)	p-value
ABPA Positive (n = 38)	523 (± 129.5)	<0.01
ABPA Negative (n = 112)	175 (± 85.6)	

Table 4: Lung Function (FEV1 and FVC) in ABPA vs Non-ABPA Groups

Group	FEV1 (%) - Mean (SD)	FVC (%) - Mean (SD)	p-value
ABPA Positive (n = 38)	63 (± 7.4)	75 (± 10.2)	0.02
ABPA Negative (n = 112)	77 (± 9.2)	80 (± 9.5)	

Table 5: Radiological Findings in ABPA vs Non-ABPA Groups

Radiological Finding	ABPA Positive (%)	ABPA Negative (%)	p-value
Bronchiectasis	60% (n = 23)	35% (n = 39)	0.004
Mucus Plugging	48% (n = 18)	20% (n = 22)	0.01
Other Abnormalities	30% (n = 12)	18% (n = 20)	0.1

Discussion

Co-morbidity between ABPA and Pulmonary Tuberculosis (TB) is a major clinical practice problem especially in areas where TB remains endemic. In our case, the prevalence of ABPA was found to be 25.3% of patients with pulmonary TB, which is similar to the previous studies suggesting overlap of these two diseases. The aim of the present discussion is to compare our findings with previous study, clarify the mechanisms underlying the ABPA in TB patients, and identify the implication of the findings in diagnosis and treatment. Several studies have shown that the incidence of ABPA among TB patients is many times higher than in the general population, particularly those with tuberculous damage to the lung. Wang et al. (2019) carried out a study which found the prevalence of ABPA in TB patients to be between 20% and 30% which aligns with our study of 25.3. Similarly, Agarwal et al. (2017) reported that 28% of TB patients in the Indians had ABPA and prevalence was more in patients with cavitary TB or bronchiectasis (10). These data demonstrate the relevance of ABPA to TB patients and suggest that TB-mediated lung damage makes patients vulnerable to fungal colonization and the resulting hypersensitivity reaction. The pathophysiology of TB and ABPA is complex. TB causes chronic inflammation and tissue necrosis and can suppress the immune system of a host. The cavitary structure of the lungs of TB patients, especially those with cavitary disease, provides an ideal niche for fungus colonization, Aspergillus spp. [11]. In our study we confirmed that 40 percent of patients treated for cavitary TB developed ABPA, which is consistent with other studies. For example, a study by Bansal et al. (2018) showed that cavitary lesions in TB-infected subjects lead to an increase in the risk of developing ABPA due to the formation of fungal growth in the cavities [12]. The presence of bronchiectasis as one of the most common sequelae of TB aggravates the risk of fungal infection and allergic reactions. TB patients are known to also use corticosteroid therapy, which also contributes to the development of ABPA. Corticosteroids have also been found to be effective in controlling TB-related complications such as inflammation and flare-ups; however, it may suppress the immune system, exposing the lungs to fungal infections. The study done by Ghosh et al. (2020) demonstrated a strong impact of corticosteroid administration in TB patients on ABPA formation especially during the time of intensive treatment [13]. This is in agreement with our finding where most of the ABPA positive patients had corticosteroids as part of TB treatment. Although corticosteroids are needed to treat TB complications, their propensity to increase fungal colonization makes their use critical in treating TB patients with ABPA, a condition associated with Abate high serum Ige levels (523 IU/mL +- 129.5 in ABPA-positive patients) indicative of an underlying immune response to Aspergillus antigens characteristic of ABPA. This was reflected by Chaudhary et al. (2019) who found Ige level in patients with TB who had ABPA was significantly higher than in patients without. The elevated Ige levels are part of the inflammatory cascade, airway remodeling, bronchiectasis, and progressive lung tissue injury on untreated. Furthermore, elevated levels of Ige were significantly associated with decreased lung function as reflected by decreased FEV1 values in our ABPA-positive group. Our findings are consistent with other studies including Desai et al. (2017) showing the abnormalities of lung function of TB patients with ABPA including bronchiectasis, a well-established complication of TB and ABPA [15]. With regard to radiologic results, our study showed that 60% of all patients with ABPA had bronchiectasis, which is a well-recognized complication of both TB and ABPA. Bronchiectasis is a chronic inflammatory and

infectious disease that leads to permanent dilation of airways. In the studies by Singhal et al. (2016) and Gupta et al. (2018) in TB and ABPA patients, bronchiectasis is a prominent finding because it is usually seen in the presence of the chronic inflammatory reaction to the Aspergillus colonization [16,17]. In addition, the presence of mucus plugging - another well-known radiological finding of ABPA - was also found in our cohort. These findings are consistent with reports by Patel et al. (2017) and Chen et al. (2019) who report mucus plugging as a common feature of ABPA in asthma and TB patients [18,19]. The overlapping clinical features of the two diseases is one of the biggest problems in management of ABPA in TB patients. Cough, wheezing and chest tightness are some of the symptoms common to both TB and ABPA, making the latter diagnosis not easy unless other examination is done. It is particularly concerning in areas that are affected by a high TB burden where healthcare professionals may be drawn only to the TB treatment and not be able to diagnose ABPA. Thus, the early diagnosis and treatment of ABPA is critical to prevent further lung damages and improve the patient's outcome [20].

Conclusion:

ABPA is frequent in 25.3% of pulmonary TB patients with a high prevalence in cavitary TB patients. The condition creates a negative impact on the functioning of the lungs and complicates treatment. Therefore, early diagnosis and appropriate management such as antifungal therapy would be crucial to and potentially improve the prognosis and prevent chronic pulmonary injury in this high-risk group.

Limitations:

We used cross-sectional, which doesn't allow for causation. The sample size was in one tertiary care center and may not be representative of the whole population. Moreover, using the clinical and radiological criteria as the basis of diagnosis of ABPA may lead to under-diagnosis and mis-diagnosis of the disease.

Future Findings:

Further longitudinal study should be advanced to examine the long-term outcome of TB patients and ABPA. Furthermore, multi-center trials are needed to standardize diagnostic method (e.g. biomarkers) and to assess the benefit of early antifungal treatment in order to prevent TB-related morbidity and to improve overall survival.

Abbreviations

1. **ABPA** – Allergic Bronchopulmonary Aspergillosis
2. **TB** – Tuberculosis
3. **Ige** – Immunoglobulin E
4. **FEV1** – Forced Expiratory Volume in 1 second
5. **FVC** – Forced Vital Capacity
6. **SPSS** – Statistical Package for the Social Sciences
7. **CT** – Computed Tomography

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Authors Contribution

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