RJNMSR
Review Journal of Neurological & Medical Sciences Review

Volume 4, Issue 3, 2026

A RETROSPECTIVE STUDY OF CHRONIC PULMONARY ASPERGILLOSIS CASES IN TERTIARY CARE HOSPITAL (NISHTAR MEDICAL UNIVERSITY), SOUTH PUNJAB, PAKISTAN

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DOI: http://doi.org/10.5281/zenodo.21331809

Received	Accepted	Published
02 February 2025	15 March 2026	31 March 2026

ABSTRACT

Background: *Chronic pulmonary aspergillosis (CPA) is a progressive fungal disease induced by Aspergillus species which frequently occurs in patients with underlying structural lung diseases specifically pulmonic tuberculosis. Although CPA is increasingly becoming a global issue of concern, it is poorly diagnosed in areas with high prevalence of tuberculosis thus resulting in late treatment and unfavorable clinical responses.*

Objective: *The aim of the study was to analyze the clinical features, the risk factors, radiological appearances, and microbiological and serological results of patients with the diagnosis of CPA in a tertiary care unit in South Punjab, Pakistan.*

Methods: *A retrospective cross-sectional study was done at the Department of Pulmonology, Nishtar Medical University Hospital, Multan, between April 2024 and May 2025. The medical records of the suspected and confirmed CPA patients were examined. Diagnostic tests were high-resolution computer tomography (HRCT), serum Aspergillus-specific IgG serology, and sputum fungal culture in cases where done. They were analyzed with SPSS version 24 and summarized with descriptive statistics.*

Results: *A total of 51 participants were used at an average age of 47.1 with a standard error of 15.9 years old. The underlying condition was previously treated pulmonary tuberculosis (56.9%). It tested positive on serological testing of Aspergillus fumigatus IgG in 53 percent of patients. Aspergillus niger was the most commonly isolated culture that was available. The most prevalent type of radiological pattern was found as per aspergilloma by HRCT. Conclusion: CPA was largely related to post-tuberculosis lung disease. In the area of tuberculosis endemicity, the HRCT imaging and Aspergillus-specific IgG-testing are crucial to the early tuberculosis diagnosis.*

Keywords: *Chronic pulmonary aspergillosis, Aspergillus fumigatus, pulmonary tuberculosis, aspergilloma, HRCT*

INTRODUCTION

Chronic pulmonary aspergillosis (CPA) constitutes a progressive and potentially fatal lung fungus of the species of the genus *Aspergillus*, in particular of *Aspergillus fumigatus* [1]. The disease tends to develop in people who already have structural lung abnormalities of pulmonary tuberculosis (TB), chronic obstructive pulmonary

disease (COPD), bronchiectasis, sarcoidosis and other chronic pulmonary conditions [2]. CPA is more common in people with chronic lung pathology but with comparatively normal immune capacity as opposed to an invasive pulmonary aspergillosis, which is more common in severely immunocompromised individuals. Fungal diseases are a significant but unrecognized societal health challenge in the world [3]. CPA is estimated to have a population of over three million individuals around the globe with a significant number of them developing the disease as a chronic complication of the pulmonary tuberculosis they had gotten treatment before. The weight of CPA is especially significant in those countries that are still facing tuberculosis. Surprisingly, recent epidemiological data show that the rates of CPA are very high in South Asia, and Pakistan is no exception, where the prevalence of pulmonary tuberculosis is found to be high, making post-tuberculosis pulmonary complications very likely [4]. Pulmonary tuberculosis is the identified risk factor with the biggest influence on the development of CPA, with almost half of the CPA cases in the world being caused by tuberculosis [5]. Chronic lung damage in tuberculosis provides good environments where *Aspergillus* species can colonize and grow in residual cavities or fibrotic lung tissue. Additional predisposing factors comprise chronic lung diseases including, asthma, COPD, bronchiectasis, allergic bronchopulmonary aspergillosis (ABPA) and systemic disorders like diabetes mellitus [6]. These comorbidities also have effects of poor pulmonary defense mechanisms and promotion of fungal colonization and disease development. Clinical presentation of CPA can be most of the time nonspecific and can include chronic cough, haemoptysis, weight loss, fatigue, and dyspnea [7]. The radiological appearance of CPA includes cavitary lesion, fungal balls (aspergilloma), fibrosis, and pleural thickening which may be seen on the high-resolution computed tomography (HRCT) of the chest [8]. Besides the imaging, microbiological and serological tests are also imperative in diagnosis. *Aspergillus*-specific IgG antibodies and isolation of *Aspergillus* species of respiratory specimens are valuable diagnostic techniques which can be added to clinical and radiographic data [9]. Although CPA is clinically relevant, it is still often poorly diagnosed or misdiagnosed especially in low- and middle-income countries where diagnostic facilities might be insufficient [10]. The illness is frequently confused with either recurrent or persistent tuberculosis and thus there are delays in treating the condition. Moreover, little epidemiological evidence on the clinical features, diagnosis, and risk factors underlying CPA exists in Pakistan especially in South Punjab where tuberculosis is also most likely to occur [11]. The demographic factors, underlying pathology, radiography, as well as the microbiological results of CPA would be vital in enhancing the early diagnosis and treatment of the disease. These aspects have, however, not been studied in tertiary care hospitals in Pakistan. This is why the current research was carried out to determine the clinical features, predisposing factors, radiographic appearances, and microbiological and serological evidence of the cases of chronic pulmonary aspergillosis in patients of a tertiary care hospital in South Punjab, Pakistan.

Materials and Methods

Study Design and Setting

It was a cross-sectional study which was retrospective and undertaken in the Department of Pulmonology, Nishtar Medical University Hospital, Multan, Pakistan. Nishtar Medical University is a teaching tertiary care hospital, which is a referral center to patients of South Punjab and other localities. The sample involved patients who came to the pulmonology outpatient department in the period of April 2024 through May 2025.

Ethical Approval

The Institutional Review Board (IRB) of Nishtar Medical University, Multan (Approval No: 14482/NMU) gave the study ethical approval. The IRB waived the necessity of written informed consideration since this was a retrospective study that did not require it, as it was founded upon reviewing medical records. The study did not violate patient confidentiality and anonymity.

Study Population

All the patients who were suspected to have chronic pulmonary aspergillosis (CPA) and those patients with confirmed chronic pulmonary aspergillosis (CPA) who were diagnosed between the study period were assessed. Patients with medical records that had clinical suspicion of CPA were reviewed and those who met the diagnostic criteria were selected as the final analysis.

Sample Size

Out of the total number of 51 patients who were included in the analysis, they were included in the study period. Given that CPA is a relatively rare occurrence and this research was conducted in retrospective based on case records, all the eligible patients who reported to the study throughout the study period were incorporated to increase the statistical power and provide a holistic data analysis.

Case Definition of Chronic Pulmonary Aspergillosis

Chronic pulmonary aspergillosis (CPA) diagnosis was determined using a complex of clinical signs, radiology, and microbiological or serological data adjusted to the international standards of diagnosis. CPA was viewed as present when patients had complete chronic respiratory symptoms like cough, haemoptysis, weight loss, or dyspnea lasting more than three months and radiologic signs on high-resolution computers tomography (HRCT) of the chest with signs of cavitary lesions, fungal balls (aspergilloma), fibrosis, or pleural thickening. Besides that, *Aspergillus* infection was to be confirmed microbiologically or serologically, e.g. positive *Aspergillus*-specific IgG antibodies or the presence of *Aspergillus* species in sputum culture.

Inclusion Criteria

The inclusion criteria of the study were that patients met the eligibility criteria. These were patients of 18 years or older with a clinical suspicion or proven diagnosis of chronic pulmonary aspergillosis (CPA). The condition was that the potential patients should be having high-resolution computed tomography (HRCT) imaging of the chest which can be radiologically assessed. Further, at least one diagnostic test that confirmed *Aspergillus* infection was needed, such as serological tests of the presence of *Aspergillus*-specific IgG antibodies or fungal culture findings. The final analysis was only conducted on patients who had complete clinical records in the hospital database.

Exclusion Criteria

The study excluded patients who had unfinished clinical or diagnostic records which could influence proper analysis of data. Patients who have history of invasive pulmonary aspergillosis were also left out as this would guarantee the inclusion of only chronic cases of pulmonary aspergillosis in the study. Secondly, patients who were diagnosed with acute fungal infections or pulmonary fungal diseases, which were caused by organisms other than *Aspergillus* were excluded. The study also excluded patients who were treated with antifungal therapy to treat malignancy-related invasive fungal infection to eliminate any possible confounding factors.

Data Collection

The data were retrospectively retrieved by use of hospital medical records through structured data collection form. The variables extracted to the research were the demographic variables which were the age and gender and the clinical history items such as past pulmonary tuberculosis, history of sputum infections, history of antifungal medications and history of thoracic surgery. Data on underlying comorbidity were also taken, such as asthma, chronic obstructive pulmonary disease (COPD), diabetes mellitus, hypertension, bronchiectasis, allergic bronchopulmonary aspergillosis (ABPA), and chronic kidney disease. The radiological images were compared to high-resolution computed tomography (HRCT) scans of the chest to determine typical characteristics of chronic pulmonary aspergillosis, such as aspergilloma (fungal ball), cavities, bronchiectasia, pulmonary fibrosis, and consolidation.

Serological Testing

The serology test was carried out to identify *Aspergillus*-specific immunoglobulin G (IgG) antibodies in patients suspected of having chronic pulmonary aspergillosis. The analysis of serum samples was done by immunoassay methods which are in the hospital diagnostic laboratory. Those who were identified as supportive evidence to the diagnosis of CPA consisted of detection of *Aspergillus* fumigatus and *Aspergillus* flavus IgG antibodies. A positive IgG was taken to be an indicator of previous or current exposure to *Aspergillus* species and was used in combination with clinical presentation and radiologic observations.

Microbiological Testing

Microbiological assessment was conducted on sputum fungal culture of the samples collected on patients. The samples were subjected to processing and culture on the right fungal growth media in the microbiology laboratory to determine *Aspergillus* species. Fungal isolates were identified by morphology of the colonies and microscopic analysis. Microbiological evidence that was important in the diagnosis of chronic pulmonary aspergillosis included the presence of *Aspergillus* species in the sputum culture.

Statistical Analysis

Statistical Package of Social Sciences (SPSS version 24.0) was used to analyze the data. Continuous variables like age were put in a form of mean stability deviation (SD) and median with interquartile range (IQR). Frequencies and percentages were used to summarize categorical variables (underlying diseases, radiological findings, and microbiological results). The Chi-square test or Fisher exact test were used in case of evaluating the associations between clinical characteristics, radiological patterns, and microbiological findings. A p-value of below 0.05 was taken as significant.

Results

Demographic Characteristics of the Study Population

The study included 51 suspected or confirmed chronic pulmonary aspergillosis (CPA) patients. Average age of the patients was 47.1 ± 15.9 years and median age of the patients was 48.0 years (IQR: 35.8-60.0) and the age range of 21-72 years this meant that CPA was affecting a very wide range of adults. In terms of treatment history, there were 35 (71.4%) patients who had not taken any antifungal therapy before presentation and 16 (28.6%) patients who had an antifungal therapy of four months or more (Table 1).

Table 1. History of antifungal therapy among patients with chronic pulmonary aspergillosis (n = 51)

Antifungal therapy history	Frequency (n)	Percentage (%)
No prior antifungal therapy	35	71.4
≥ 4 months antifungal therapy	16	28.6
Total	**51**	**100**

Underlying Comorbidities and Predisposing Conditions

Diagnosis of underlying pathology indicated that the most common predisposing factor to CPA was a history of pulmonary tuberculosis (TB), which had been treated before and was there in 29 individuals (56.9%). Other comorbidities were also reported frequently; asthma occurred in 23 patients (45%), diabetes mellitus in 15 patients (29.4%), and allergic bronchopulmonary aspergillosis (ABPA) in 10 patients (19.6%). Other comorbidities were hypertension in 7 patients (13.7%), chronic obstructive lung disease (COPD) in 6 patients (11.7%), bronchiectasis in 5 patients (9.8%), chronic kidney disease and ischemic heart disease in one patient respectively (1.9%). The results indicate that structural lung damage especially the post-tuberculosis pulmonary sequelae is the biggest risk of developing CPA (Table 2).

Table 2. Underlying comorbidities and predisposing conditions among CPA patients (n = 51)

Underlying condition	Frequency (n)	Percentage (%)
Treated pulmonary tuberculosis	29	56.9
Asthma	23	45.0
Diabetes mellitus	15	29.4
Allergic bronchopulmonary aspergillosis (ABPA)	10	19.6
Hypertension	7	13.7
Chronic obstructive pulmonary disease (COPD)	6	11.7
Bronchiectasis	5	9.8
Chronic kidney disease	1	1.9
Ischemic heart disease	1	1.9

Serological Findings

Aspergillus fumigatus IgG and *Aspergillus* flavus IgG Serological tests of *Aspergillus*-specific IgG antibody revealed that 27 (53) and 24 (47) patients were positive of *Aspergillus fumigatus* IgG and *Aspergillus* flavus IgG, respectively. The findings suggest that *A. fumigatus* was the most commonly identified serological species of CPA patients, but *A. flavus* also had a significant percentage of patients. Figure 1 depicts the distribution of *Aspergillus* IgG serology in the CPA patients.

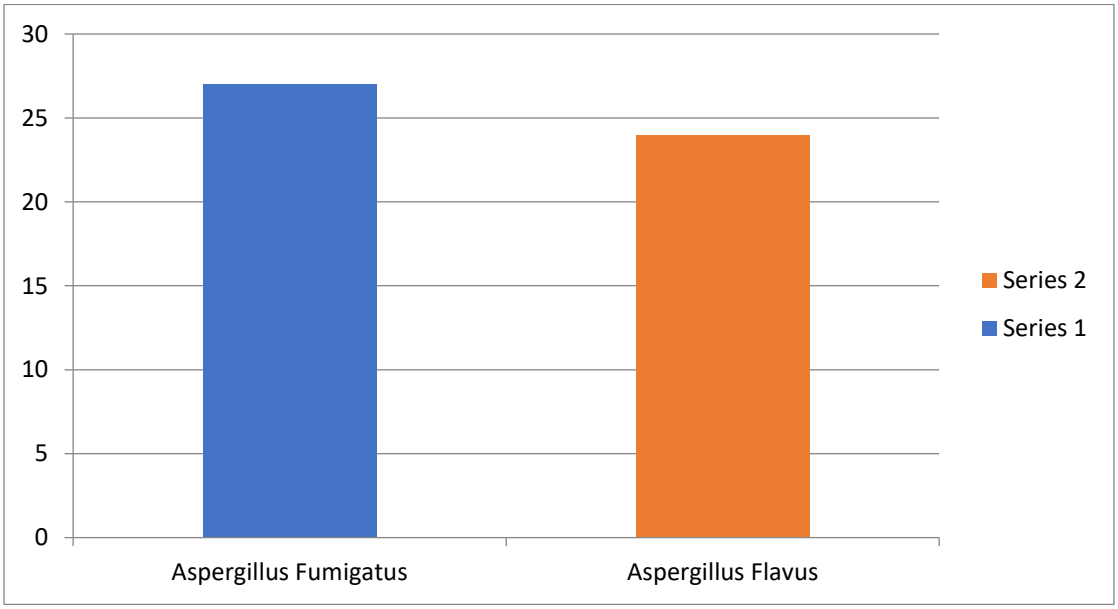

Figure 1. Distribution of *Aspergillus* IgG Serology

Microbiological Findings

The results of fungal culture of 22 patients (43% of the total) were provided in sputum. *Aspergillus* species were found in all the cultured samples amongst these patients. The most frequently isolated species was *Aspergillus* niger (was identified in 10 patients (45.5%), *Aspergillus flavus* (in 9 patients (41%)) and *Aspergillus fumigatus* (in 3 patients (13.5%)). Despite the fact that the number of cases where fungal cultures were available were limited, these results prove that the presence of several species of *Aspergillus* appeared among patients of CPA. Figure 2 provides the distribution of fungal isolates.

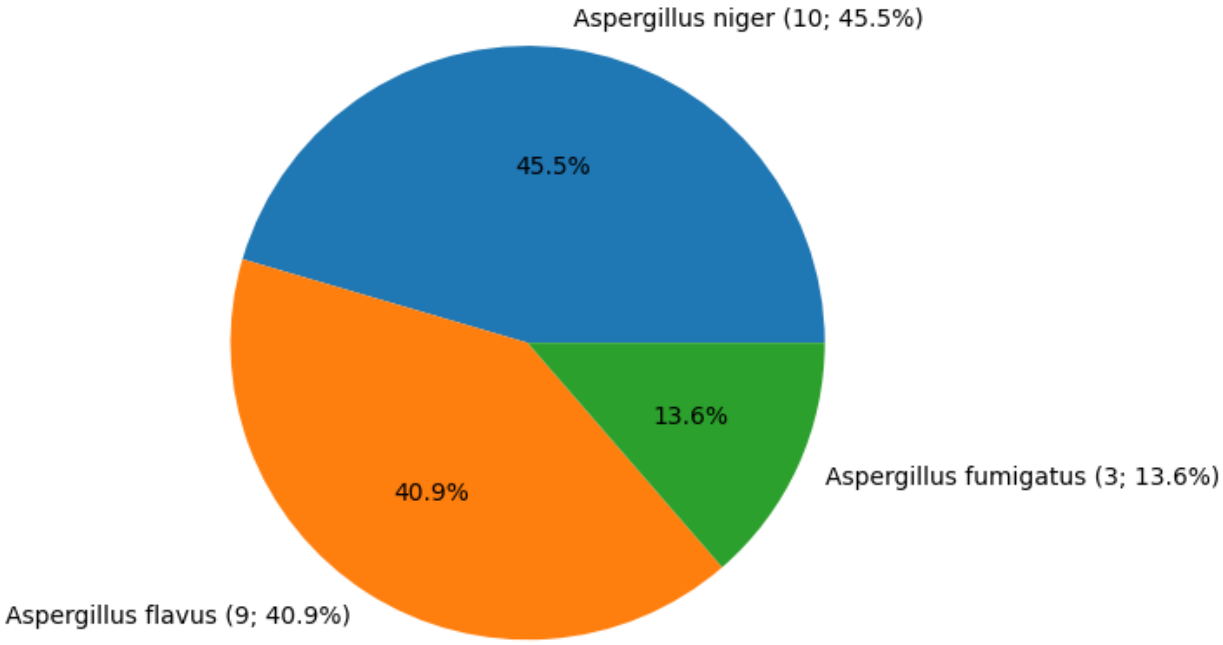

Figure 2. Distribution of *Aspergillus* species isolated from sputum cultures among patients with chronic pulmonary aspergillosis (n = 22). *Aspergillus niger* was the most frequently isolated species (45.5%), followed by *Aspergillus flavus* (40.9%) and *Aspergillus fumigatus* (13.6%).

Radiological Findings

Computer tomography was performed on the chest with high resolution (HRCT) showing a number of radiological patterns typical of chronic pulmonary aspergillosis (CPA). The radiologic finding that was most common was aspergilloma (fungal ball) as it was identified in 28 of the participants (55%), showing that cavity related fungal colonization was prevalent in this cohort. Additional radiological abnormalities descriptions were bronchiectasis (14/27.5%), pulmonary fibrosis (10/19.6%), cavitary lesions (7/13.7%), pulmonary consolidation (2/4%). These results indicate that aspergilloma was the most popular radiological presentation of CPA patients, next by bronchiectatic and fibrotic pulmonary outcomes. Figure 3 shows the radiological pattern distribution of CPA.

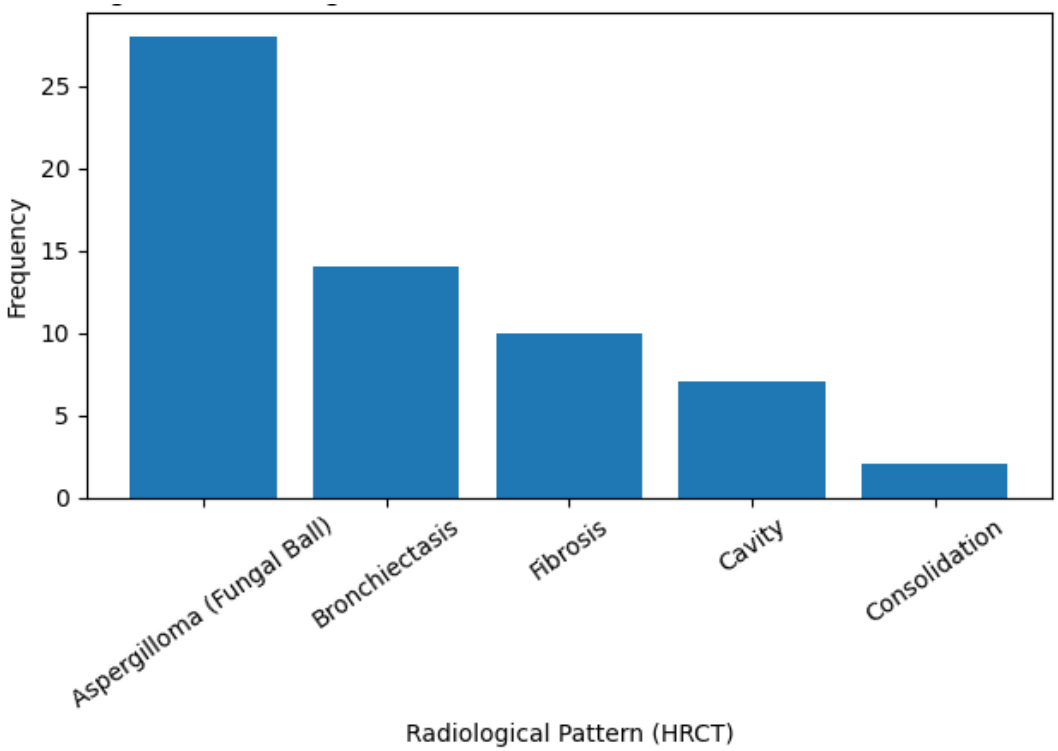

Figure 3. Radiological distribution of chronic pulmonary aspergillosis (CPA) patterns observed on high-resolution computed tomography (HRCT) among study participants (n = 51). Aspergilloma (fungal ball) was the most frequently observed radiological finding, followed by bronchiectasis, fibrosis, cavitary lesions, and consolidation. Due to the descriptive nature of the study and the limited sample size, the analysis primarily focused on descriptive statistics including frequencies and percentages. No inferential statistical comparisons were performed between variables.

Discussion

Chronic pulmonary aspergillosis (CPA) is a chronic fungus which occurs mainly in patients with underlying structural lung defects. The current paper measured the clinical presentation, underlying risk factors, radiology and microbiology among the patients diagnosed with CPA in a tertiary care hospital in South Punjab, Pakistan. The results indicate a strong connection of pulmonary tuberculosis and other chronic respiratory illnesses to the occurrence of CPA and the importance of the joint radiological, microbiological, and serological research to accurately diagnose the pathology. In the present research, the past treated tuberculosis (TB) in the lung was found to be the most prevalent underlying condition related to CPA. This fact aligns with the evidence provided by epidemiological studies carried out in different parts of the world to show that TB is the most significant risk factor in the development of CPA [12]. The presence of structural lung damage due to TB especially residual cavities and fibrosis creates an ideal environment of colonization and growth of *Aspergillus* species. A number of studies have found that a significant percentage of patients who eventually undergo the TB treatment, also develop CPA as a chronic pulmonary complication [19, 20]. This close relationship between TB and CPA can be especially applicable to the country like Pakistan where tuberculosis is still high. Along with tuberculosis, other underlying comorbidities that were identified in this study were asthma, diabetes mellitus, allergic bronchopulmonary aspergillosis (ABPA), and chronic obstructive pulmonary disease (COPD). The conditions have been cited as significant risk factors of CPA because of having been associated with a reduced immune response and lung tissue damage (Bassetti et al., 2021).

Specifically, diabetes mellitus has been linked to susceptibility to fungal infections because of poor host immunity and changes in inflammation [21]. Likewise, problems of chronic respiratory illness, including COPD and bronchiectasis, have been demonstrated to raise the risk of CPA due to the chronic inflammation of the airways and structural lung alterations [15]. Radiological imaging is central in diagnosing and assessment of CPA. Aspergilloma (fungal ball) was the most frequent radiological diagnosis in the current study, referred to by HRCT, and bronchiectasis, pulmonary fibrosis, cavitary lesions, and consolidation. The results are in line with earlier reports stating the presence of cavitary lesions and fungal balls as typical radiological manifestations of CPA [22]. It is believed that high-resolution computed tomography is the most sensitive imaging modality to identify these abnormalities and identify CPA among other chronic pulmonary diseases [13]. The relatively large percentage of aspergilloma in the current study can be due to the large number of patients who had a history of tuberculosis in the history because fungus balls normally form inside existing pulmonary cavities that are created following TB infection. In this research, IgG antibodies that were specific to *Aspergillus* were also a significant diagnostic tool and were detected by serological testing. *Aspergillus fumigatus* IgG positive was a bit order of magnitude higher than *Aspergillus* flavus IgG positive among the study subjects. The presence of the *Aspergillus* IgG antibodies is also a primary diagnostic marker that is commonly recommended in cases of CPA and is a part of international diagnostic recommendations [17]. A number of studies have indicated that the *Aspergillus* IgG assays have high diagnostic sensitivity and specificity especially when used in conjunction with radiological and microbiological evidence [16, 18]. Thus, clinical settings with a potential low sensitivity of fungal culture may benefit greatly by using serology to enhance the accuracy of diagnoses. *Aspergillus niger* was predominant in our study in the microbiological examination of sputum cultures followed by *Aspergillus flavus* and *Aspergillus fumigatus*. In spite of A. fumigatus being typically stated as the most prevalent causative species of CPA on pain of the planet, the problem of species distribution due to geographical differences has been recorded [14]. The abundance of particular species of *Aspergillus* in various populations may be affected by environmental factors, climatic conditions, and the ecology of particular fungi in their areas. Hence, the bias of *A. niger* in this study could be due to local environmental pattern of exposure in South Punjab. CPA is a significant yet unacknowledged public health issue worldwide. It is estimated that about three million people across the globe are afflicted with CPA with a significant percentage developing the disease after a pulmonary tuberculosis [12]. The mortality rates related to CPA are still high, and one-year mortality rates were found to be about 7-15 percent and five-year mortality was found to be over 50 percent in certain cohorts [23]. In spite of such a heavy load, CPA is often mistaken with recurrent or treatment-resistant tuberculosis, especially in places with fewer resources where sophisticated diagnostics is not easily accessible [15]. The early identification of CPA and the right antifungal treatment is thus critical in enhancing clinical outcomes. The general implications of the present research are that it adds to the ever-expanding list of literature on the significance of early diagnosis and control of CPA, especially in areas where tuberculosis is widely prevalent. Better diagnostic measures such as regular HRCT scan and *Aspergillus* IgG of patients with persistent respiratory symptoms after TB treatment can help in the early diagnosis and minimize the morbidity and mortality caused by the disease.

Study Limitations

The limitations in this study are quite a number and would be put into consideration when interpreting the findings. Firstly, the retrospective design restricted the access to full diagnostic information of all patients especially the microbiological culture data. Second, the researchers have carried out the study in one tertiary care center, and this could be a weakness regarding the applicability of the results to other individuals. Third, in the diagnosis, more sophisticated methods like the use of molecular identification of *Aspergillus* species were not used

and this could have compromised the accuracy of species identification. Lastly, the sample size used was relatively small and, therefore, it might have been constraining the possibility of conducting more complex statistical analyses.

Future Perspectives

More multicenter studies involving larger sample sizes should be conducted in the future to gain a better insight into the epidemiology and risk factors of CPA in Pakistan. Diagnostic accuracy can be further improved by using sophisticated diagnostic methods, such as molecular identification of fungi and improved serological tests. Also, CPA screening in patients who have persistent respiratory symptoms following tuberculosis therapy can be used to diagnose this disease at an earlier stage and enhance patient prognosis. More studies should also be conducted so as to assess the efficacy of various antifungal therapies and long-term managements of CPA.

Conclusion

Chronic pulmonary aspergillosis is a significant complication of underlying pulmonary disorders, especially in the past treated tuberculosis. Pulmonary tuberculosis was found to be the leading underlying condition of CPA, [Asthma and diabetes mellitus came in second and third place respectively]. The radiological appearances of Aspergilloma were the most common findings on HRCT and *Aspergillus* fumigatus IgG positivity was also a common finding on serologic tests. Microbiological analysis showed that there is a regional difference in distribution of *Aspergillus* species with *Aspergillus* niger commonly isolated. The results provide a significant implication that to properly diagnose CPA, clinical evaluation, HRCT scan, microbiological tests, and serological tests should be accompanied. Early diagnosis and prompt antifungal therapy are crucial to minimise morbidity of the disease and positively change clinical outcomes especially in areas where pulmonary tuberculosis is high.

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