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Research article

## PREVALENCE AND FUNGAL PROFILE OF PULMONARY ASPERGILLOSIS IN IMMUNOCOMPROMISED AND IMMUNOCOMPETENT PATIENTS OF A TERTIARY CARE HOSPITAL

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### ABSTRACT

**Background:** *Aspergillus* is a fungus which may present an array of pulmonary manifestations, depending on the patient's immunological and physiological state. Although the incidence of pulmonary aspergillosis occurs primarily in immunocompromised patients but the incidence is also rising in immunocompetent individuals, especially in developing countries. **Aim:** The objective of the study was to determine the prevalence and predisposing factors of pulmonary aspergillosis along with species identification. **Materials and Methods:** One hundred and three patients admitted to the Department of Chest and Tuberculosis and in the Department of Medicine from Jan 2012 to Jan 2013 were included in this study. The patients were epitomized on the basis of clinical signs and symptoms, physical examination, chest radiography, CT scans, histopathological examination, bronchoscopy and fungal examination including potassium hydroxide mount, fungal culture of sputum and bronchoalveolar lavage. Species identification was done by colony characteristics, slide culture and Lactophenol Cotton blue mount. **Results:** Out of the 103 patients, (63 males and 40 females) *Aspergillus species* has been isolated from 17 (16.5%) males and 07 (6.79%) females. Various predisposing factors of pulmonary aspergillosis have been identified in which pulmonary tuberculosis, chronic smoking and environmental exposure to asbestos, cement its tops the list. Many of the patients had multiple predisposing factors. *Aspergillus* species were isolated in 24 (23.3%) cases. *Aspergillus fumigatus* was the predominant species isolated in 13 (54.16%) cases followed by *Aspergillus flavus* in 07 (29.16%) cases, *Aspergillus niger* in 03 (12.5 %) and *Aspergillus terreus* in 1 (4.16%) cases. **Conclusion:** It is concluded that the prevalence of pulmonary Aspergillosis is quite high in immunocompromised individuals and low in immunocompetent individuals. An adequate and efficient evaluation of the etiological agents has a crucial role in the management of such patients.

**Keywords:** Aspergillus, Tuberculosis, Sputum, Immunocompromised.

### INTRODUCTION

In recent years fungal infections are one of the important cause of pulmonary infections.<sup>1</sup> *Aspergillus* primarily affects the lungs, causing a variety of manifestations, including allergic bronchopulmonary aspergillosis (ABPA), aspergilloma, and invasive

aspergillosis. Invasive pulmonary aspergillosis is an increasingly common fungal infection with high morbidity and mortality in immunocompromised patients. The incidence and clinical impact of these infections is on the rise in the developed countries,

which is possibly related to increased number of immunocompromised patients, owing to improved survival from AIDS, malignancies and more intensive cytotoxic therapy, organ transplantation and better treatment and prophylaxis for other fungal infections.<sup>2</sup> Immunocompromised individuals are susceptible to pulmonary aspergillosis, but invasive aspergillosis is extremely uncommon in individual's with intact immunity. Immunocompetent persons seldom develop this infection and do so only in the presence of other pulmonary and systemic abnormalities such as fibrotic lung disease,<sup>3</sup> suppurative infection<sup>4</sup> or treatment with corticosteroids.<sup>5</sup> Pulmonary aspergillosis shows a variable inimitable pattern of lung disease that primarily depend on the patient's immune status. Preexisting lung diseases acts as a significant predisposing cause for pulmonary aspergillosis.<sup>6,7</sup> Pulmonary aspergillosis is generally presented as a wide range of pulmonary manifestations, from aspergilloma with a comparatively benign course, to invasive pulmonary aspergillosis, which can be terminal. Pulmonary aspergillosis is one of the main causes of pulmonary infections and creates a complicated diagnostic challenge due to lack of pathognomonic clinical features. The diagnosis of aspergillosis is frequently missed as the diagnostic tests for their detection is not done in routine diagnostic laboratories and/or is not suspected by the physician.

Therefore, the present study aims to a) detect the prevalence of pulmonary aspergillosis in immunocompromised and immunocompetent individuals. b) To study the various predisposing factors. c) Isolation and differentiation of *Aspergillus* species from clinical specimens of patients suffering from pulmonary infections.

## METHODS

This study was conducted on 103 patients with different chronic pulmonary infections admitted in the wards of Department of Chest and Tuberculosis, and Department of Medicine between the period of January 2012 to January 2013. The cases are the patients with various chronic pulmonary infections of more than one year on whom bronchoscopy, radio imaging was done. This work has been approved by the Institutional Ethical Committee.

Data were collected regarding age, sex, detailed medical history (immunosuppressive conditions like

pulmonary tuberculosis, Diabetes mellitus, AIDS etc, chronic smoking and environmental exposure to asbestos, cement etc smoking), physical examination (vital signs, cyanosis, pallor, clubbing etc), chest radiography, Computed Tomography (C.T) scan, bronchoscopy etc. A complete blood picture and histopathological examination were done. We have considered the infections/diseases as a prime risk factor in patients with multiple risk factors.

The sputum and bronchoalveolar lavage was homogenized and direct microscopy was performed by using 10% KOH mount. It was inoculated on one set of Sabouraud's Dextrose Agar (SDA) [HIMEDIA, MUMBAI] plain and SDA with Chloramphenicol (0.05 mg/mL) [HIMEDIA, MUMBAI] and also on Czapek Dox agar [HIMEDIA, MUMBAI]. The inoculated SDA were incubated at 25°C and at 37°C. The colony morphology of obverse as well as reverse was studied.<sup>8</sup> Tease Mount Preparation (TMP) of the mould isolated was prepared in Lacto Phenol Cotton Blue (LPCB) for identification detailed morphology including hyphae, phialides, vesicles and spores. The confirmation of fungal species was done by slide culture.<sup>9</sup>

Statistical analysis: The data were analyzed by using SPSS version 17. The descriptive analysis and chi square test were applied. The results obtained were presented by using appropriate tables and charts.

## RESULTS

A total of 103 patients {63 (61.16%) males and 40 (38.83 %)} of various age groups with indications of chronic pulmonary infections were admitted in the wards of the Hospital during the study period as shown in **Table 1** and **Table 2**. The chi square test is appropriate at 5% level which shows no significance among culture positive males and females while significant in age group > 40 years (Elderly).

*Aspergillus species* have been isolated from 17 (16.5%) males and 07 (6.79%) females. The elderly patients (>40 years) had a higher incidence of pulmonary aspergillosis in males as well as females.

There are 17 culture positive cases among immunocompromised and 07 cases among immunocompetent cases. Based on the data of the clinical history, the various risk factors like pulmonary tuberculosis, diabetes mellitus, HIV infection, chronic smoking, recurrent respiratory tract infections, Bronchial Asthma, Pleural effusion, environmental

exposure to asbestos, cement and other chemicals are documented in Figure 1.

*Aspergillus fumigatus* was the predominant species isolated from 13 (54.17%) cases significant by chi

square test, followed by *Aspergillus flavus* which was isolated in 7 (29.17%) cases, 3 (12.5%) cases of *Aspergillus Niger* and 1 (4.7 %) case of *Aspergillus terrus* as depicted in Table 3 and figure 2.

**Table 1: Distribution of culture positive and culture negative patients on the basis of sex.**

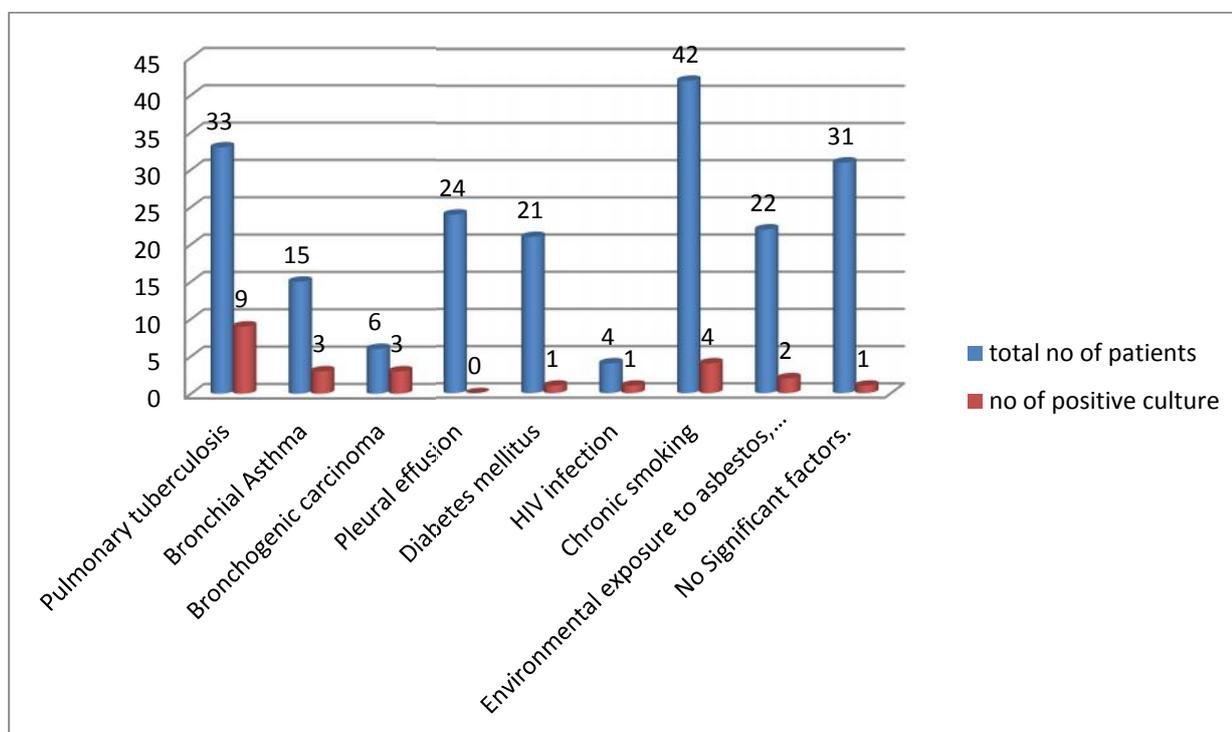
SEX	Culture Positive Patients	Culture Negative Patients	Total	P value
MALE	17	46	63	$\chi^2 = 1.231$ P= 0.2671
FEMALE	07	33	40	
TOTAL	24	79	103	

**Table 2: Age group of culture positive and culture negative patients.**

Age Group	Culture Positive	Culture Negative	Total	P value
0-20 YRS	01	23	24	$\chi^2 = 6.92$ P= 0.0314*
21-40 YRS	08	24	32	
>40 YRS	15	32	47	
TOTAL	24	79	103	*Significant

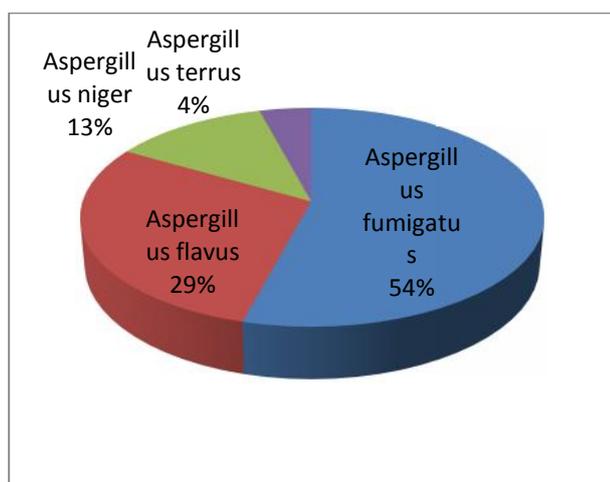
**Table 3: The incidence of *Aspergillus* species isolated among patients of chronic lung disease.**

SPECIES	No. of Positive Cultures	Percentage	P value
<i>Aspergillus fumigatus</i>	13	54.17%	$\chi^2 = 6.92$ P= 0.0314*
<i>Aspergillus flavus</i>	07	29.17%	
<i>Aspergillus niger</i>	03	12.5%	
<i>Aspergillus terrus</i>	01	4.7 %	



**Fig 1: The various risk factors in the patients that may be associated with pulmonary aspergillosis**

Note: various patients had multiple risk factors.



**Fig 2: Percentage of *Aspergillus* species in culture positive patients.**

## DISCUSSION

*Aspergillus* species are common saprobic in the soil, and their vegetative spores are ever present. Generally, only immunocompromised patients or the individuals who suffer from other chronic lung conditions are susceptible. Recently, reports of invasive pulmonary aspergillosis in immunocompetent patients have increased in the clinical literature.<sup>10,11</sup>

Immunocompetent patients are generally asymptomatic and only incidentally they are found to have aspergillosis.<sup>12-14</sup> Though, the rare cases of pulmonary aspergillosis in patients with intact immune system have been documented.<sup>11</sup> In recent time, reports about invasive pulmonary aspergillosis in COPD patients and apparently non-immunocompromised patients<sup>15-22</sup> have been reported.

In our study, the prevalence of pulmonary aspergillosis was 23.3%. The prevalence was higher than Henderson *et al*<sup>23</sup> who reported an incidence of 11%, Pepy *et al*<sup>24</sup> reporting 8% and Campbell and Clayton 8.2 % respectively.<sup>25</sup> This might be due to the more exposure of the patients to the predisposing factors and environmental conditions favouring the growth of the fungus.

Among the risk factors pulmonary tuberculosis, chronic smoking, bronchial Asthma, bronchogenic carcinoma was seen. Multiple risk factors were also found in patients admitted. Risk factors such as COPD, systemic corticosteroid therapy, non-haematological malignancy, chronic renal disease, liver failure, diabetes mellitus, near-drowning, HIV infection, etc have been described in earlier studies.<sup>26-</sup>

<sup>29</sup> The incidence of aspergillosis was more common in

males as compared to females, more in adults as compared to children which may be due to increased exposure to risk factors. Our study showed a higher incidence of Aspergillosis among immunocompromised individuals and low in immunocompetent individuals. More recently, reports have described

patients with normal immunity and invasive or semi-invasive infections caused by *Aspergillus* species, most commonly *Aspergillus fumigatus*, involving the chest wall<sup>30</sup>, brain, middle ear<sup>31</sup>, and lung<sup>10,14</sup>.

Methods of prompt diagnosis of pulmonary aspergillosis are based on isolation of *Aspergillus* in culture, serological methods and histopathological examination which is an invasive method, for which both clinicians and patients may be reluctant to undertake. The culture was positive in 24 (23.3%) samples. *Aspergillus fumigatus* was the predominant species isolated in 13 (54.17%) cases which is in line with the findings of Bordane *et al* and Shahid *et al*.<sup>32, 33</sup>

The other species isolated were *Aspergillus flavus*, *Aspergillus niger* and *Aspergillus terreus* in 7 (29.17%), 3 (12.5%), and 1 (4.7 %) cases respectively.

## CONCLUSION

Finding of *Aspergillus* species in respiratory tract samples in the patients should not be routinely discarded as colonization, even if the patients are immunocompetent<sup>[27]</sup>. It is concluded from the present study that the prevalence of pulmonary Aspergillosis in immunocompromised as well as immunocompetent patients is rising in our country; hence, any patient of chronic lung infection not responding to regular antibiotic therapy should be investigated for infection by *Aspergillus*. Any indication of aspergillosis, by positive sputum culture, serological tests, should compel the physician to initiate anti-fungal treatment.

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