



Study of Pulmonary Mycosis in a Tertiary Care Centre in a Coastal city of South India

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Abstract

Aim: Pulmonary mycosis is a critical health issue with increasing morbidity and mortality internationally, especially in developing nations. We aim to study patients with pulmonary mycosis presenting to respiratory and medicine department in a tertiary care centre from February 2012-2013.

Material and Method: This is a prospective study of patients with pulmonary mycosis in a tertiary care centre. 56 patients with confirmed fungal sub-culture have been included. Study was done with the objective of assessing the epidemiology, clinical profile, associated co-morbidities and culture isolate pattern of pulmonary mycosis.

Result: Mean age group of our patient was 52.36 ± 14.55 years. Pulmonary mycosis occurred in the setting of pre-existing lung disease in 64.28% of patients. Mycosis in naïve lung and with no immunocompromised condition was seen in 17.86% while 73.21% patients had an underlying lung disease or an immunocompromised status. Of the total patients, 23.21 % were diabetics, 5.35% had been having hematological malignancies, and 10.71% with autoimmune connective tissue disorders on steroids and 1.78% with retroviral disease. Our records suggest fungal culture isolates with prevalence of *candida albicans* (69.6%), *candida krusei* (12.5%), *candida glaberata* (10.7%), *candida tropicalis* (5%) and *aspergillus fumigatus* (5%).

Conclusion: Pulmonary mycosis is a challenging hassle in developing countries. Though, it is found usually in patients with underlying structural lung disease and immune-compromised hosts, a high index of clinical suspicion should be kept even in people with no obvious risk factors as primary pulmonary mycosis incidence in naïve lung is on rise. Our study also emphasizes the role of early bronchoscopy and lavage cultures for early diagnosis and more precise treatment for pulmonary mycosis.

Keywords: Pulmonary mycosis; diagnosis; culture isolate; risk factors.

Introduction

Pulmonary mycosis is a budding problem internationally. In a developing country, it remains more so a challenge due to increased fungal invasion in diseased lung secondary to tuberculosis or other immunocompromised state, lack of diagnostic facilities and financial constraints which in turn pose a challenge in proper diagnosis, follow up and treatment. With increasing scientific achievements, in addition to the equipment of better diagnostic techniques and advances for prompt microbiological analysis we have witnessed an increase in load of opportunistic fungal pathogens reported. More so these pathogenic organisms have been reported to be invaders of even naïve lung in immunocompetent patients causing primary pulmonary mycosis. Respiratory physicians have evidenced both allergic and non allergic manifestations of this ubiquitous organism. The increasing burden of the problem, need for its well timed treatment and control makes it integral for all clinicians and allied scientists to know more about these tiny but virulent pathogens of lung. Pulmonary mycosis has a great response to therapy and lesser mortality provided the treatment is initiated early. It is an emerging threat in our critical care units and respiratory wards.

Aim

- To look at the epidemiological, demographic and clinical details of patient diagnosed to have pulmonary mycosis in a tertiary care teaching hospital in a developing country.
- Assess the clinical, radiological & bronchoscopic profile of patients with pulmonary mycosis.
- Assess the association of pulmonary mycosis with co-morbid illnesses.
- Diagnose the specific fungal etiological agents for pulmonary mycosis and estimate the prevalence of infection by a specific fungal species.

Material and Method

In the present study, we describe a prospectively collected cohort of pulmonary mycosis identified using positive culture report in a tertiary care hospital over 1 year i.e. from February 2012-2013. In our study, we included patient with confirmed fungal culture positive report. In suspected cases, work up for pulmonary mycosis was done based on integrated approach with the help of clinical examination, radiological evidence and microbiological isolation of the fungi and other relevant tests. Clinical history and physical examination was done with emphasis on history of any underlying lung disease or co morbid condition. Based on this data we have classified patients as having primary mycosis with naïve lung and secondary to any respiratory or other immunocompromised state. The assessment of all these patients was made via clinical examination and other relevant investigations like complete blood count, blood sugar, sputum smear for acid fast bacilli (AFB), bronchoscopy & pleural fluid cytology wherever indicated. Radiological examination was done using chest radiograph and CT scan wherever indicated. Sputum examination was done for every case. Sputum samples showing less than 10 squamous epithelial cells and 25 or more polymorphonuclear leukocytes per low power field (100×) had been included in this study. The specimens of sputum were dispatched to the department of microbiology and all sputum specimens had been processed for Gram staining and pyogenic culture, acid-fast bacilli, and fungal culture. The appropriate samples have been cultured on plain Sabouraud's Dextrose Agar (SDA) and additionally on SDA containing chloramphenicol and cycloheximide. SDA slants were incubated at 37⁰C and examined weekly two times to look for growth of cream colored pasty colonies suggestive of *Candida* species. The slants were incubated for one week and discarded if no growth occurred by then. ESR, IgE testing and serology for *Aspergillus* sp was done wherever indicated. In suspected cases of pulmonary mycosis where sputum studies were inconclusive

and did no longer yield a definitive diagnosis, bronchoscopy was performed and bronchial lavage samples have been analyzed for AFB, cytology, pyogenic culture and sensitivity, KOH mount and fungal culture. In instances of pleural effusion with suspected pulmonary mycosis, pleural fluid analyses for AFB, pyogenic and fungal cultures have been performed. The records have been entered in MS Excel. Descriptive statistics, i.e., means, standard deviations, frequencies, and percentages, have been used to describe the study variables

Result

We have studied 56 patients with pulmonary mycosis. Of these 58.9% (33) were males and 41.1 % (23) were females (Figure-1). Mean age group of our patient was 52.36±14.55 years. History revealed that 37.2 % of patients were people who smoke or ex-smokers. Pulmonary mycosis occurred in the setting of pre- existing lung disease in 64.28% patients (Figure-2). Significantly 17.86% had primary pulmonary mycosis in setting of a naïve lung with no other immunocompromised status (Figure-3).

Respiratory mycosis is common in patients with immune-compromised state and in our cohort had set in 23.21% of uncontrolled diabetes, 5.35% have been secondary to malignancies especially hematological malignancies and 10.71% have been on long term steroid therapy and 1.78% had been in the setting of positive retroviral disease status.

Figure-1

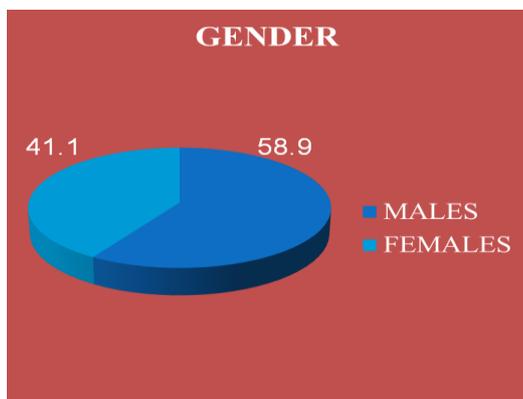


Figure-2

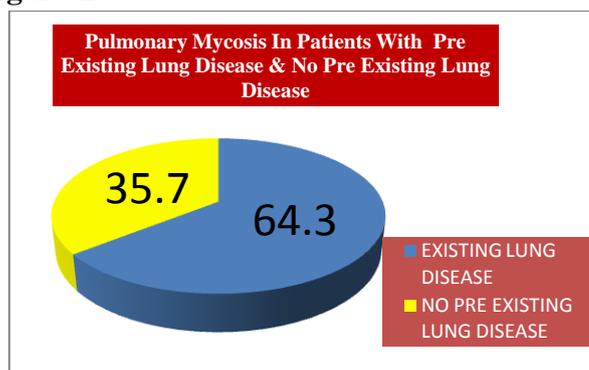
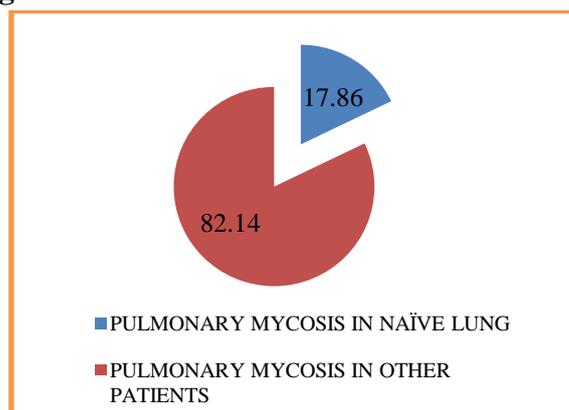
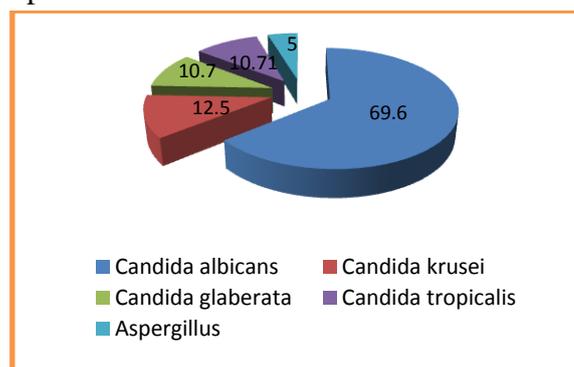


Figure-3



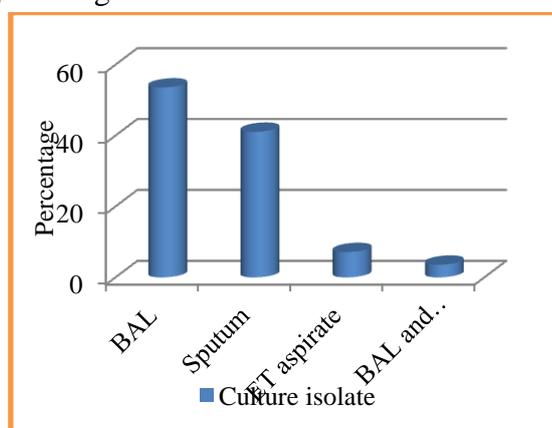
Our data suggests Candida as the most common isolated species. Candida albicans was isolated in 69.6%, followed by non albicans candida i.e. Candidakrusei (12.5%), Candida glabrata (10.7%), and Candida tropicalis (5%). Aspergillus fumigatus was isolated in 5% cases (Figure-4). In our cohort, 1.78 % patients with respiratory mycosis had concomitant active pneumonia and Klebsiella was the most common secondary organism isolated in our patients. Active tuberculosis was concomitantly proved by AFB positivity in 10.7 % (6) of the patients.

Figure 4. Fungal species isolated from different samples



These fungi had been isolated from sputum in 41.07 % of patients (Figure 5). In sputum culture negative patient's mycosis was isolated from bronchial lavage in 53.57 % and from ET aspirates in 7.14%. In one patient fungus was isolated from pleural fluid. 26.7% patients additionally had a fungal KOH mount positive suggestive of mycosis. Bronchoscopy was beneficial in making diagnosis in 50% of patients and bronchoscopic visualization showed copious secretion in 39.2% and gelatinous blob of secretions occluding lung segments in 32.14 % and the rest had inflamed bronchi. Serum IgE was done for 42.8% of our patients and the mean value was 1679.9 IU (normal value < 200). We had 3 (0.05%) patients with multiple fungal pathogens being isolated from different culture samples. One patient who had grown both *Candida albicans* and *Aspergillus fumigatus* and the other two patients had both *Candida albicans* and non *albicans* being isolated from their samples.

Fig-5. Fungal isolation rate from different samples



Discussion

Pulmonary mycosis is certainly an emerging problem with budding yeasts and molds frequently invading the lungs and posing a challenge in diagnosis and treatment.^{1,3} In our study, we attempted to find these organisms in clinically susceptible cases and studied in detail the demographic, clinical, microbiological, bronchoscopic findings and serological profile in patients in a tertiary care setup in a developing country. Pulmonary mycosis is often undiagnosed,

under diagnosed and rarely reported despite the fact that the disease is on rise in the current years. Worldwide only some studies are available describing clinical epidemiological, etiological, microbiological and bronchoscopic profile of patients with pulmonary mycosis. In our study, we found that pulmonary mycosis was seen in 58.9 % (33) of male and 41.1% (23) females. This is consistent with other researches wherein male predominance has been seen.^{3,4} This pattern can be attributed to the increasing percentage of smoking and the subsequent lung pathologies in males and increased outdoor exposure in men. From the available history from patients, we found that 37.2% of patients in our study were smokers or ex smokers. Possibly increase in underlying lung disease like emphysema due to smoking will also increase the chance of mycotic infection. However, there is shortage of information regarding the association of smoking with pulmonary mycosis. Fungus has traditionally been described as an opportunistic infection in diseased lung or immunocompromised state. Nowadays with alarming increase in the number of patients with immunocompromised conditions, increasing transplant rate and better life expectancy in immunocompromised people, certainly pulmonary mycosis is an emerging threat and is being encountered on increasing numbers.² Post-operative status, acute renal failure, neutropenia, malignancies long term steroids are some of the commonly listed risk factors for pulmonary mycosis.⁵⁻⁷ Taviani et al from Italy has shown pulmonary mycosis in association with lymphatic leukaemia.⁸ Consistent with those findings, in our cohort also, immunocompromised state like uncontrolled diabetes mellitus, malignancies and chronic steroid use was found in 41.05% patients with mycotic infection. 5.35% have been secondary to malignancies particularly hematological malignancies and 10.71% have been on long term steroid therapy. Preexisting lung ailment is a predisposing condition to pulmonary mycosis. This association of pulmonary mycosis with underlying lung disease

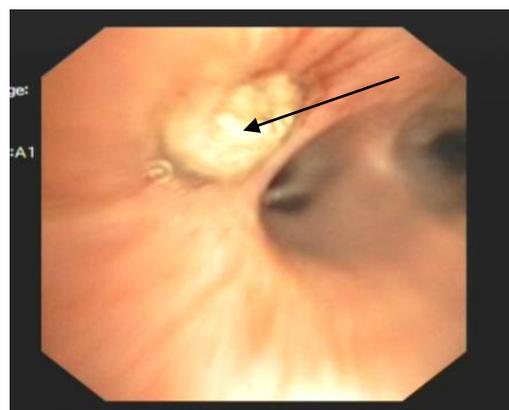
has been mentioned in various researches like Shimuzu et al series showing pulmonary mycosis with bronchogenic carcinoma, Tedder series from North Carolina showing pulmonary mycosis associated with lung abscess^{9,10} In our study we have found pulmonary mycosis in setting of preexisting lung disease like bronchiectasis, tuberculosis, asthma in 64.28% of patients. Co-existing chronic lung disease and structural lung diseases were by far the most common predisposing factor for pulmonary mycosis in our study. Mycotic infection is a crucial co-infection in active pulmonary tuberculosis patients. In those patients clinical and radiological manifestations depend on the degree of immunocompetence.^{11,12} Although active mycosis can be an independent marker of advanced immunosuppression, it could additionally act as a co-factor in accelerating and amplifying the clinical course of tuberculosis.¹² In our study, 10.7% have been found to have active pulmonary tuberculosis diagnosed via AFB positivity in sputum or bronchoalveolar lavage (BAL) sample. Bansod et al¹¹ in their study showed out of 500 pulmonary tuberculosis patients, 203 patients have been suffering from mycotic infection. The percentage of mycotic infections in pulmonary tuberculosis patients was turned out to be 46%. In their study, they found mainly four forms of fungi, i.e. aspergillus niger, a. fumigatus, histoplasma capsulatum and cryptococcus neoformans, which causes severe infection in lungs in patients suffering from pulmonary tuberculosis.¹² However in our observation, candida albicans was more frequently isolated from patients with active tuberculosis. Pulmonary mycosis in setting of co-existing tuberculosis may have crucial clinical implications. Often both these diseases can also masquerade each other and might result in non-diagnosis of the other. Also, as seen in many of our cases, persistence of respiratory problems in patients with pulmonary tuberculosis, who were put on optimal antitubercular treatment ultimately brought about the diagnosis of concomitant mycotic lung infections on further evaluation.

Generally it is assumed that mycotic pulmonary infections are seen in immune-compromised hosts & in those with underlying structural lung disease. An interesting finding in our study was the high prevalence of primary pulmonary mycosis. We discovered 17.86% patients in our study had pulmonary mycosis in background of naïve lung. It is alarming information as it shows that in our set up, physicians should suspect its presence even in immunocompetent hosts. Overuse of higher antibiotics by primary care physicians could be a cause for growing occurrence of primary pulmonary mycosis. Case reviews of candida pneumonia in immune competent host possibly due to aspiration has been reported however is not common.¹³ Also, primary pulmonary mycosis due to candida non-albicans & aspergillus species had been additionally reported in our study that is in contrary to the general norms. Our study underlies the importance of clinical suspicion for pulmonary mycosis even in people with no obvious risk factors. A high index of suspicion can alert the health care practitioner and aid in well-timed diagnosis and prompt initiation of treatment, as results with prompt initiation of treatment are encouraging. Most preceding researches have observed candida as the most common organism leading to pulmonary mycosis.¹⁴⁻¹⁸ However, differentiating between candida as oropharyngeal commensal or as a pathogen is a challenge. Mustafa et al in their article discuss the role of diagnostic criteria for candida pneumonia, which remains to be described. Because there is no pathognomonic clinical picture for candida pneumonia, diagnosis has relied for years on detecting the presence of candida in sputum or bronchoscopic specimens in a clinical set up.¹⁵ Richardson et al reported candida and aspergillus as most common reason for invasive fungal infection and additionally threw light on reemerging new fungal infections.¹⁶ A multicenter surveillance study performed in Quebec, Canada by Germain G. St et al in 1998 discovered the distribution of candida species to be as follows: C. albicans 54%, C. glabrata 15%, C. parapsilosis

12%, *C. tropicalis* 9% and *C. krusei* 3%.¹⁷ American thoracic society convened a working group on fungal infection and its relevance in pulmonary and critical care medicine. According to the compiled data from the latest worldwide researches *Candida albicans* is the commonest pathogenic fungus followed by *Candida glabrata*.¹⁸ Studies from distinctive parts of India has additionally proven *Candida albicans* as the most common culprit for pulmonary mycosis. Pukhan et al and Debasis et al showed isolation of *Candida tropicalis* as common non *albicans* from respiratory sample.^{14,18} Our data is consistent with present study and shows *Candida* as the most common isolated species. *Candida albicans* was the leading isolate in 69.6%, but among non *albicans* group, *Candida krusei* was more common in 12.5%, followed by *Candida glabrata* (10.7%) and *Candida tropicalis* (5%). *Aspergillus fumigatus* was isolated in only 5% cases. However, no new species or other mycotic infection was found in our cohort. This has major therapeutic implications as *Candida non-albicans* are generally refractory to empirical treatment with fluconazole, which is the first-choice empiric anti-fungal therapy. This study stresses on the value of fungal culture for organism identification and specific therapy thereafter for a good response. Since Echinocandins, the primary line of drugs for *Candida non-albicans* are very expensive, it emphasizes the role of bronchoscopy and lavage cultures for early diagnosis and more specific treatment for pulmonary mycosis. Bronchoscopic alveolar lavage (BAL) was useful in making diagnosis in 53.57% of patients of these patients. Saito and co-workers suggested that BAL had a sensitivity of 75% and a specificity of 100% for the diagnosis of *Candida pneumonia* in patients with acute leukemia and severe neutropenia.²³ Bronchoscopy for analysis was not done in all cases. In cases with high suspicion of pulmonary mycosis wherein sputum examination was inconclusive or patients were unable to expectorate or good quality sputum as per the microbiological criterion could not be obtained,

bronchoscopy & lavage were performed. On bronchoscopy, 39.2% had copious secretion or gelatinous bleb (Fig 3) and 32.14% had inflamed bronchi. Thick gelatinous blob of secretions occluding lung segments was one of the characteristic bronchoscopic finding in our study and invariably cultures isolated fungi in these cases. This bronchoscopic finding has previously not been widely recognized and reported. We conclude that bronchoscopy and BAL can be useful aids in isolation of fungus in clinically suspect patients with sputum negativity. Since bronchoscopic lavage cultures are more representative samples, with a better specificity, there can be a much wider role for early bronchoscopies in patients with suspected pulmonary mycosis.

Fig 6. Bronchoscopy showing thick gelatinous bleb.



Role of serum IgE in pulmonary mycosis has been studied and raised IgE in pulmonary mycosis was also seen in study done by Ray et al at CMC Vellore.²⁴ In our study, we found the mean serum IgE value as 1679.9 which is significantly higher than normal range. More prospective studies need to be carried out to evaluate the position of serum IgE as a predictive or prognostic marker in pulmonary mycosis. There were isolated case reviews in past with isolation of concomitant multiple mycotic organisms inflicting systemic fungal infection during the same course of illness especially in leukemic patients.²⁵ We had 3(0.05%) patients with multiple pulmonary fungal pathogens being isolated. One patient who had

grown both candida albicans and aspergillus fumigatus and other two of the patients had both candida albicans and non albicans being isolated from their sample. Multiple fungal species poses challenge to the clinicians in their management.

Conclusion

Pulmonary mycosis is a challenging problem. It poses significant threat in coming times. Indeed well timed suspicion, proper diagnosis and prompt treatment can decrease its morbidity and mortality significantly. Our data shows increasing prevalence of pulmonary mycosis and its different faces in a developing country. Our study is an indicator towards the upsurge in the incidence of primary pulmonary mycosis that's an alarming prospect. The role of early bronchoscopy and its usefulness in a more accurate and well timed diagnosis can't be undermined. More prospective researches on various aspects of pulmonary mycosis is the need of the hour to amplify our horizon of knowledge about the prevalence, presentation, diagnosis and treatment of various mycosis which are invading the lungs at an alarming rate in developing countries as well.

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