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Spectrum of Respiratory Pathogens, especially Filamentous Fungi causing Lower Respiratory Tract co-infections in cases of Pulmonary Tuberculosis

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Abstract
This study was conducted in a tertiary care hospital in Western India[1] To determine the spectrum and prevalence of pathogens in lower respiratory tract co-infections, in Pulmonary TB cases, with special emphasis on the filamentous fungi.[2] To find out the relative risk of acquiring these infections in patients having TB-HIV co infection as compared to the patients having pulmonary TB without HIV.
Methodology: *Lower respiratory specimens from 167 cases of pulmonary TB, admitted with respiratory complications were subjected to bacterial and fungal microscopy, cultures and identification. Giemsa Staining was done for detection of Pneumocystis carinii cysts.*
Results: *[1] Fungal pathogens found in 14.37% cases, out of which, 9.6% were candida sp. and 4.2% were fungal moulds while, Pneumocystis carinii cysts detected in 0.6%. [2] The moulds isolated were Fusarium sp.-- 1.8%, Aspergillus fumigatus-- 1.2%, Mucor sp.-- 1(0.6%) and Trichosporon sp.—1 (0.6%). [3] Bacterial pathogens found in 57.48% cases (44.3% mono-bacterial, 13.2% multibacterial coinfection), most common ones being, Klebsiella sp., and Pseudomonas sp. [5] Bacterial and fungal coinfection found in 10.18% cases. [6] TB and HIV co infection found in 4.2% cases and the relative risk of acquiring a respiratory filamentous fungal infection in patients having PTB+HIV co infection found to be 2.1, as compared to those having PTB without HIV. Thus, knowledge of the pathogen spectrum and prevalence of respiratory co-infections with TB (in a particular region), is essential for maintaining a high index of suspicion for the same, and for better patient management.*
Keywords: *Tuberculosis, Oppurtunistic Fungi, Filamentous Fungi, Moulds, TB –HIV coinfection.*

Introduction

India has the highest burden of TB in the world, an estimated 2.1 million cases annually. This accounts for approximately one fifth of the global incidence of TB (about 9 million cases annually). Since a majority of the cases of TB in India are due to reactivation of latent infection (which occurs when the immune status of the individual deteriorates), so, Tuberculosis patients have a poor immune status and on prolonged antimicrobial therapy, hence fungal infection occurs in early stage of TB infection [3]. Also, the synergistic growth promoting association of certain fungi and Mycobacterium increases their significance in pulmonary tuberculosis patients[1]. The major opportunistic fungal pathogens include: *Candida* species causing candidiasis, *Aspergillus* species causing

aspergillosis, *Mucor* species causing mucormycosis and *Cryptococcus neoformans* causing cryptococcosis[10].

This problem is complicated even further, by the "Dual Epidemic" of TB and HIV co infection, which is rampant in the developing world where the burden of both these diseases is very high. In 2013 of the estimated 9 million people who developed TB an estimated 1.1 million (13%) were HIV positive.

Pulmonary TB remains the most important cause of sub acute and chronic respiratory morbidity in India, which most often leaves behind a scarred pulmonary parenchyma, vulnerable to fungal colonization, for instance, TB of the lung can be seen as a predisposing factor for colonizing aspergillosis in case with aspergilloma[1]. Also, It has been shown that the polysaccharide fraction of *C.albicans* enhances the growth and reduces the generation time of tubercle bacilli [9], suggesting a synergistic growth promoting association between MTB and certain fungi. To make matters worse, immunocompromised status of the host, which is even more severe in cases of TB-HIV co infection, renders these patients highly vulnerable to respiratory (opportunistic) infections, which complicate the management of the underlying disease (TB and/or HIV), and increase the morbidity and mortality in these patients. Since, the number of patients at risk, is very high in India, the need of the hour is to have some sort of guidelines for screening and prophylaxis of such opportunistic infections in the target population. However, such national guidelines cannot be formulated without having the basic prevalence data of such infections in the population at risk. But, unfortunately, there are hardly any Indian studies addressing this issue, and a lot needs to be done in this regard.

Objectives

The present study was carried out with the primary objective of determining the spectrum of pathogens and the prevalence of each of them, in lower respiratory tract infections, in known cases of Pulmonary TB, with special emphasis on the filamentous fungi, in Western India. It also aimed to find out the relative risk of acquiring these infections in patients having TB-HIV co infection as compared to the patients having pulmonary TB without HIV.

Materials and Methods

- **Study Site:** The present study was carried out in the Dept. of Microbiology, SSG Hospital and Medical College Baroda, Vadodara, Gujarat. (A tertiary care govt. hospital in Western India).
- **Study Design and Duration:** This was a cross-sectional study carried out over a period of 4 months, at the above site.
- **Study Population:** The study population includes patients of all ages and sexes who were known cases of pulmonary TB (confirmed by sputum microscopy for AFB and/or Gene Xpert RIF), currently on AKT drugs under DOTS (RNTCP), who were admitted to the chest/pulmonary ward of the above hospital, with lower respiratory tract complications or exacerbation of symptoms of pulmonary TB, irrespective of their HIV status.
- **Sample Size:** A total of 167 non- duplicate, lower respiratory tract specimens from these patients were analyzed, which included, 109 expectorated sputum samples, 32 pleural fluid samples, & 26 Inter Costal Drain (ICD) fluid samples.

Sample Inclusion Criteria

The quality of the sputum samples was assessed microscopically (under 10x objective), using the Bartlett's grading criteria. Those found inappropriate for processing were rejected and a freshly expectorated sputum sample collected aseptically, was requested.

Candida, when detected in sputum samples, were considered pathogenic only after confirming the presence of pseudohyphae, correlating with the clinical condition and drug intake history of the patient and noting the time of collection of sample from the patient. Also, a repeat freshly expectorated sputum sample, after performing oral toilet, was requested to rule out the presence of candida as oral commensals, however these repeat samples were

not included in the study (since, only non-duplicate samples were used, so as to avoid skewing of data).
Repeat samples were requested for all specimens, in which fungal hyphal elements were seen in KOH mount, and both sets of specimens were put up for fungal culture simultaneously, so as to eliminate the possibility of the fungus being an environmental contaminant. However, this was used only for the confirmation of the diagnosis, but, the duplicate samples were not included in the study, to avoid skewing of data.

- **Sample Processing**

A. Direct Microscopy

Gram's Staining was performed for each specimen, and the slides were observed for the presence of bacterial pathogens and yeast like cells with pseudohyphae. Further, all respiratory fluid specimens were centrifuged at 3000 rpm for 10-15 minutes (for concentrating the fungal elements, if any), and KOH mounts were prepared from the sediment (4 KOH mounts were prepared per sample), and observed for the presence of fungal hyphal elements. Giemsa Staining (using a 1:20 dilution) was done for detection of Pneumocystis carinii cysts in induced sputum samples or Broncho Alveolar Lavage (BAL) samples, the smears being prepared from the sediment after concentration by centrifugation, as described above (4 smears per specimen). All samples were processed within half an hour of collection (immediately on receipt in the laboratory).

B. Culture and Isolation

All samples were cultured on BHI agar, Mac Conkey's agar and Blood agar, for bacterial isolation. The specimens in which fungal hyphae were seen in 1 or more KOH mounts, were set up for 2 sets of fungal culture on SDA plates with 2mg/ml of gentamicin, 1 set being incubated at room temperature (25-27°C), and the other set at 37±2°C, for upto 21 days.

C. Identification of the cultured Isolates

Bacterial isolates were identified by motility, gram staining, and biochemical identification from culture.

While, for fungal isolates (SDA plates), after the appropriate period of incubation, the growth form**,** rate of growth, surface of the colony, and obverse and reverse coloration on SDA plates were noted. LPCB mounts were prepared for the moulds isolated and they were identified based upon their distinctive microscopic morphological features and their colony characteristics. In the case of fungal cultures, positive results of mycological examinations were accepted only if the two parallel sets of media (from the original and repeat specimen) showed growths of the same fungus. Cases failing these criteria were regarded as environmental contaminants.
The candida sp. isolates (which had been considered pathogenic and not a part of oral commensal flora, as per the sample inclusion criteria), were subjected to the germ tube test, inoculation on CHROM agar (HiMedia Pvt. Ltd.) and slide culture on CornMeal Agar with Tween80. These isolates were identified as *C.albicans* if they were germ tube positive, showed apple green coloured growth on CHROM agar and the production of pseudohyphae and chlamydospores on slide culture. The remaining isolates were classified as candida non-albicans and species identification was done on the basis of the results of slide culture and colour production on CHROM agar and sugar assimilation tests.

Results

Out of a total of 167 samples (109 sputum, 32 pleural fluid, & 26 ICD fluid), from cases of pulmonary TB, showing worsening of symptoms or development of pulmonary complications:
At least one additional infectious etiological agent (bacterial and/or fungal) was isolated in 103 (61.7%) samples, while no infectious etiology (except MTB and/or HIV) could be detected in 64 (38.3%) of the samples. Out of these 103 positive samples, bacterial pathogens were isolated from 96 (93.2% n=103; 57.5% n=167) specimens, while fungi were isolated from 24 (23.3% n=103; 14.4% n=167) specimens, and 17 (16.5% n=103; 10.18% n=167) specimens showed bacterial and fungal co infection.

Fungal isolates were found in 24 (14.37% n=167; 23.3% n=103) cases, out of which, 16 were candida sp., and 7 (4.2% n=167; 29.2% n=24) were filamentous fungi while, Pneumocystis carinii cysts were detected in 1(0.6% n=167; 4.2% n=24) sample *[Table 1]*. Out of the 16 candida isolates, the highest prevalence was of *C.albicans* 10 (6% n=167; 41.67% n=24; 62.5% n=16), while the remaining 6 were Candida nonalbicans 6 (3.6% n=167; 25% n=24), which were presumptively identified as *C.tropicalis*, *C.glabrata*, and *C.krusei* having 3,2 and 1 isolates respectively. *[Table 1, Fig 1(a)]*. The most common respiratory fungal pathogen co infecting PTB patients, was found to be *C.albicans [Table 1]*.

The fungal moulds (filamentous fungi) isolated were *Fusarium sp.*-- 3 (1.8% n=167), *Aspergillus fumigatus*-- 2 (1.2% n=167), *Mucor sp.*—1 (0.6% n=167) and *Trichosporon sp.*—1 (0.6% n=167). *[Tables 1, 2, Figt 2(b)]*. The most common clinical presentations in PTB cases having fungal LRTIs were hydropneumothorax and pleural effusion.

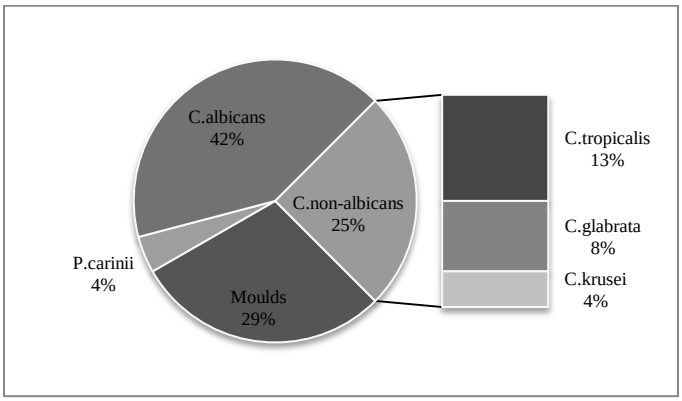

Fig. 1(a) Distribution of Yeasts

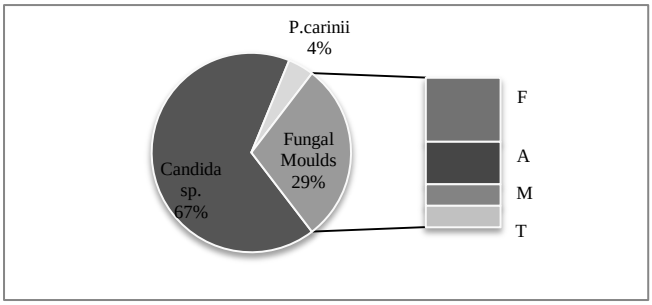

Fig. 1(b) Distribution of Filamentous Fungi

[F- Fusarium sp.(13%), A- Aspergillus fumigatus (8%), M- Mucor sp. (4%), T- Trichosporon sp. (4%)]

Table 1 Fungal Pathogens

Genera	No (% Preval) n=167	Genera	No (% Preval) n=167
YEASTS	**16(9.6%)**	**MOULDS**	**7(4.2%)**
C.albicans	0 (6)	*Fusarium*	3 (1.8)
C.tropicalis	3 (1.8)	*A. fumigatus*	2 (1.2)
C.glabrata	2 (1.2)	*Mucor sp.*	1 (0.6)
C.krusei	1 (0.6)	*Trichosporon sp.*	1 (0.6)
Other Fungi	**1 (0.6%)**		
P.carinii cysts	1 (0.6)		

(Total cases with fungal pathogens = 24/167 = 14.37%)

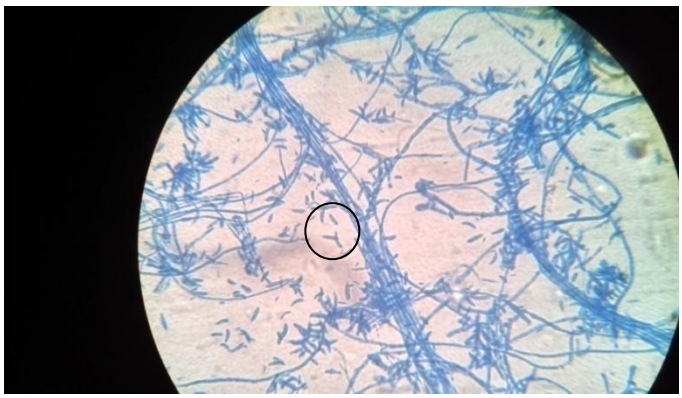

Fig. 2 LPCB mount of *Fusarium sp.* (400x) *(showing fusiform to crescentic macroconidia (3-4 celled)—circled and fusiform (1-2 celled) microconidia.)*

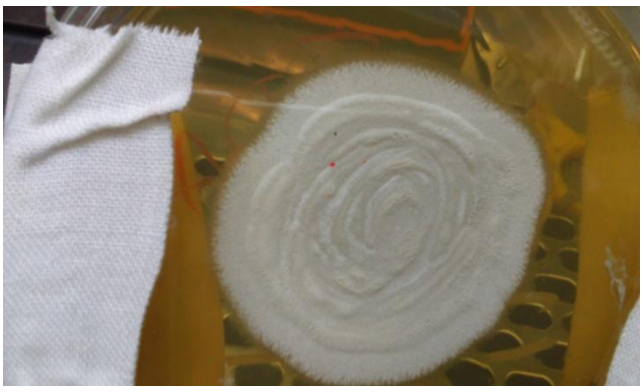

Fig. 3(a) Colony of *Trichosporon sp.* on SDA *(off-white coloured, having a dull, wrinkled surface, with a mycelial fringe)*

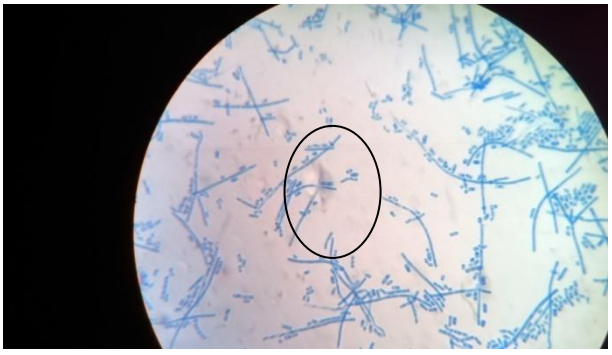

Fig. 3(b) LPCB mount of *Trichosporon sp*.

(showing abundant hyphae and arthroconidia. The circled area shows fragmentation of the hyphae into arthroconidia.)

A Bacterial Pathogen(s) was/were found in 96 (57.48% n=167) of the cases. Out of these, a single bacterial isolate was found in 74 (44.3% n=167) cases, while multibacterial infection was found in 22 (13.2% n=167) cases. The bacterial species isolated were, *Klebsiella sp.*—31 (18.56%), *E.coli*—29 (17.36%), *Pseudomonas sp.*—21 (12.57%), *Acinetobacter sp.*—17 (10.18%), *Streptococcus & Enterococcus sp.*—6 (3.6%), and *S.aureus*—2 (1.2%), (where n=167, for each). *[Table 2, Fig 4]*

Table 2 Bacterial Pathogens

Genera	No (% Preval) n=167
Gram Negative Bacilli	**98**
Klebsiella sp.	1 (18.56)
E.Coli	9 (17.36)
Pseudomonas	1 (12.57)
Acinetobacter sp.	7 (10.18)
Gram Positive Cocci	**08**
Streptococcus & Enterococcus sp.	6 (3.6)
S.aureus	2 (1.2)

(Total cases with bacterial pathogens = 96/167 = 57.5%)

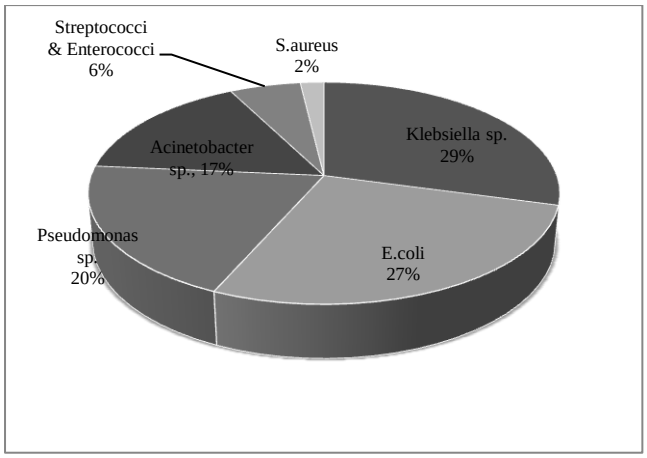

Fig. 4 Distribution of Bacterial Pathogens

Age and Sex Distribution: The maximum cases of pulmonary infections by filamentous fungi were found in the later middle age group, i.e., 35- 50 yrs, followed by the older age group, i.e., 51- 65 yrs. No pulmonary fungal infections were found in the extremes of age. This may be due to the fact that, both, the levels of exposure (that is highest in 20-50 yrs age groups), and the immune status (that declines as we move towards the extremes of age), play an equally important role in acquiring of respiratory fungal infections, and thus, considering both factors together, the age group of 35- 50 yrs may be the most vulnerable. Also, all the above cases were males.

Bacterial and fungal co infection was found in 17 (10.18%) cases, out of which, the fungal isolate was *candida sp.* In 13 cases (7 *C.albicans* & 6 *C.nonalbicans*), while 4 were moulds. Thus, out of the 7 moulds isolated, more than 57% of them showed co infection with a bacterial pathogen (other than MTB), while out of the 16 candida isolates, 13 (81%) showed co infection with a bacterial pathogen (other than MTB).

TB and HIV coinfection was found in 7 (4.2% n=167) cases, and in this group, the number of fungal pathogens was significantly higher (28.57%, $p<0.05$), which was more than double than in those having TB without HIV. A respiratory infectious pathogen (other than MTB), was found in 71.43% of the TB+HIV co infected cases, which was significantly higher ($p<0.05$) than that found in cases of PTB without HIV (61.25%). *[Table 3]*.

The predominance of fungal pathogens increases significantly and becomes nearly equal to that of bacterial pathogens (which were, otherwise nearly 4 times more common than fungal infections), in the absence of HIV. The *relative risk (RR) for acquiring a lower respiratory tract fungal infection, in cases having pulmonary TB and HIV co infection, as compared to those having TB without HIV, is 2.1*, while relative risk of acquiring any respiratory infection (bacterial or fungal) is 1.2. [as calculated from *Table 3*] Thus, if a patient with pulmonary TB also acquires HIV infection, then his/her risk of being infected with a respiratory fungal pathogen, more than doubles, than those without HIV.

Table 3 Lower respiratory pathogens in cases of Pulmonary TB with and without HIV

Sr. No	Parameter (Type of infectious agent)	PTB without HIV (n = 160)	PTB with HIV (n = 07)
1	Pathogen present	98 (61.25%)	5 (71.43%)
1a	Single fungus	22 (13.75%)	2 (28.5%)[a]
1b	Single bacteria	72 (45%)	2 (28.5%)
1c	Multibacterial	21 (13.12%)	1 (14.29%)
1d	Fungus + Bacteria	17 (10.62%)	0
2	No pathogen	62 (38.75%)	2 (28.5%)

The fungi isolated from the TB+HIV co infected group *Pneumocystis carinii* and *Candida krusei*, were not found in the group not infected by HIV, suggesting that, due to severe immunosuppression in the hosts, the spectrum of fungal pathogen is also altered in this group.

Discussion

In the present study, out of a total of 167 samples from cases of pulmonary TB, admitted to the hospital with pulmonary complications:

Atleast one infectious etiological agent (bacterial and/or fungal) was isolated in 61.7% samples, while no infectious etiology (except MTB and/or HIV) could be detected in 38.3% of the samples. Out of these positive samples, bacterial pathogens were isolated from 57.5% specimens, while fungi were isolated from 14.4% specimens. The latter finding was in agreement with a study conducted by J. Mowna *et al*, at Sri Sathya Sai Medical College, Kanchipuram dist. who found the prevalence of fungal pathogens to be 15.5%[4]. Bacterial and fungal co infection was found in 10.18% cases in the present study, which was comparable to a study by E.N. Mwaura *et al*, at Nairobi, Kenya, in which bacterial and fungal co infection was found in 11.6% of the cases[2].

Out of the cases infected with fungal pathogens, yeast (candida) infections were seen in 9.6% of the cases, while, 4.2% were infected with filamentous fungi. The most common respiratory fungal pathogen co infecting patients with pulmonary TB, was found to be *C.albicans* (6%), a finding that was corroborated by studies by E.N. Mwaura *et al*, at Nairobi, Kenya[2], and J. Mowna *et al*, at Sri Sathya Sai Medical College, Kanchipuram dist.[4] It has been shown that the polysaccharide fraction of *C.albicans* enhances the growth and reduces the generation time of tubercle bacilli [8,9]. This might be the reason for the high prevalence of *C.albicans* in TB patients. Although *C.albicans* was the most common co infecting fungal respiratory pathogen with MTB, but its prevalence in the present study was found to be much lower than the above 2 studies. This may be due to the fact that we have been extremely cautious in reporting candida as a pathogen in sputum samples, since, the isolation of *Candida* from cultures of sputum, endotracheal aspirates and bronchoscopic samples, may only represent colonization of the tracheobronchial tree and invasive lung infection by *Candida* species is rare in non immunocompromised subjects [20]. The criteria for the diagnosis of pulmonary candidiasis are still controversial. It is now well established that *Candida* colonization is uniform throughout the different lung regions, and that the presence of *Candida* in respiratory samples, independently of quantitative cultures, is not a good marker of *Candida* pneumonia in critically ill, non-neutropenic, non-AIDS patients [20].

Candida non albicans were found to be pathogenic in 3.6% of the cases, which was comparable to the findings of E.N. Mwaura *et al*, at Nairobi, Kenya[2] (4%), and J. Mowna *et al*, at Sri Sathya Sai Medical College, Kanchipuram dist.[4] (4.5%). Most of the non- albicans strains observed during the study did not show the formation of pseudohyphae, and hence were deemed non pathogenic (i.e., not causing tissue invasion, and thus, the low prevalence of pathogenic non albicans strains. This finding was corroborated in the study by E.N. Mwaura *et al*, at Nairobi, Kenya[2]. Out of the pathogenic non albicans strains, *C.tropicalis* was the commonest, found in 1.8% cases, which was also noted by J. Mowna *et al*, at Sri Sathya Sai Medical College, Kanchipuram dist.[4], but with a slightly higher rate of prevalence (3%). *C.krusei* which is normally a commensal member of the oral flora, was found to be pathogenic in TB+HIV co infection.

Filamentous fungal pathogens were found in 4.2% of the cases. This was much higher than that found by Yahaya H., *et al.*, in Kano, Nigeria (1.6%) [1].This indicates that TB patients in our part of the world might be as a higher risk of pulmonary fungal infections, than their counterparts elsewhere. However, the prevalence found in our study was lesser than another study in southern India [4] which found it to be 15.7%. This might have two possible explanations: Firstly, the other comparable Indian study included all patients on DOTS/ AKT therapy

(both hospitalized as well as non hospitalized), whereas the present study included only those patients, whose symptoms were severe enough to warrant hospitalization. Secondly, our approach to diagnosis of the fungal infection, was to perform fungal culture only for those specimens where microscopy was positive for fungal elements. This may have resulted in marginally lower rates of detection.

The demographic profile of the filamentous fungal pathogens in the present study, was as follows: Maximum cases of pulmonary infections by filamentous fungi were found in the later middle age group, i.e., 35- 50 yrs, followed by the older age group, i.e., 51- 65 yrs. No pulmonary fungal infections were found in the extremes of age. This was comparable to the findings of Yahaya H., *et al.*, Kano, Nigeria[1], who found the maximum prevalence between 21- 50 yrs. This may be due to the fact that, both, the levels of exposure (that is highest in 20-50 yrs age groups), and the immune status (that declines as we move towards the extremes of age), play an equally important role in acquiring of respiratory fungal infections, and thus, considering both factors together, the age group of 35- 50 yrs may be the most vulnerable. All the above cases were males (in the present study), a finding again probably related to the levels of exposure (since men traditionally perform more outdoor activities like farming, etc in India). Thus, males seem to be having a significantly higher risk of acquiring respiratory fungal infections. This finding was corroborated by other comparable studies.[1,4]

The fungal moulds detected were:

1. *Fusarium sp.* in 1.8% cases, comparable to the findings of Yahaya H., *et al.*, in Kano, Nigeria (1.5%) [1].
2. *Aspergillus fumigatus* in 1.2% cases, in agreement with the findings of Yahaya H., *et al.*, Kano, Nigeria (1%) [1] and E.N. Mwaura *et al*, Nairobi, Kenya[2] (1.7%)
3. *Mucor sp.* in 0.6% cases, comparable to the findings of Yahaya H., *et al.*, in Kano, Nigeria (0.3%) [1]
4. *Trichosporon sp.* in 0.6% cases, which was lesser than that found by E.N. Mwaura *et al*, in Nairobi, Kenya[2] (2.3%), while none of the previous Indian studies have reported this fungus as a respiratory pathogen in cases of pulmonary TB. This may be attributed to the variation in geographical distribution of the fungus.

Pneumocystis carinii cysts were detected in the induced sputum samples of 0.6% of the cases, all of which were already co infected by HIV, leading to very severe immunosuppression.

TB and HIV co infection was found in 4.2% of the cases, and in this group, the predominance of fungal pathogens increased significantly and their prevalence became nearly equal to that of bacterial pathogens (which were, otherwise nearly 4 times more common than fungal infections, in the absence of HIV). The relative risk (RR) for acquiring a lower respiratory tract fungal infection was found to be 2.1 in the presence of HIV co infection, i.e., for a TB patient the risk of acquiring a fungal LRTI more than doubled if he/she gets infected by HIV, due to severe immunosuppression. (However, the number of such patients was small in this study. A larger sample size for the TB-HIV co infected group would be preferable). Also the fungal pathogen profile was altered in this group, and some unusual fungal pathogens like *Pneumocystis carinii* and *C.krusei* (which were not seen in TB patients without HIV), were also found.

Conclusion

Pulmonary TB remains the most important cause of sub acute and chronic respiratory morbidity in India, which most often leaves behind a scarred pulmonary parenchyma, vulnerable to fungal colonization. Thus, in the setting of a weakened immune system, these patients are rendered vulnerable to Opportunistic Fungal infections, which are significant co-infecting respiratory pathogens complicating the management of pulmonary TB.

Respiratory fungal infections were found in 14.4% of the cases. However, the actual prevalence may be

much higher, since, culturing the fungus from a patient's respiratory fluids (which was performed here), although a cheap and simple method is much less sensitive, than molecular methods of diagnosis. Fungal and bacterial (other than MTB) co infection was found in 10.18% cases.

The most common fungal respiratory pathogen co existing with MTB is *Candida albicans*, possibly due to the synergistic growth promoting association between the two.

Filamentous fungi were found in 4.2% of the cases, which was higher than in some other parts of the world. The spectrum of pathogenic filamentous fungi found in this study included, *Fusarium sp., Aspergillus fumigatus, Mucor sp., and Trichosporon sp.* Male patients were at a significantly greater risk of acquiring filamentous fungal infections, as compared to females. Maximum risk was in the later middle age- group, i.e., from 35- 50 yrs, followed by, the 51- 65 yrs age group.

TB and HIV co infection was found in 4.2% of the cases, and in this group, the predominance of fungal pathogens increased significantly and their prevalence became nearly equal to that of bacterial pathogens (which were, otherwise nearly 4 times more common than fungal infections, in the absence of HIV). The relative risk (RR) for acquiring a lower respiratory tract fungal infection was found to be 2.1 in the presence of HIV co infection, i.e., for a TB patient the risk of acquiring a fungal LRTI more than doubled if he/she gets infected by HIV, due to severe immunosuppression. Also the fungal pathogen profile was altered in this group, and some unusual fungal pathogens like *Pneumocystis carinii* and *C.krusei* (which were not seen in TB patients without HIV), were also found.

Considering that India is home to one-fifth of the TB patients in the whole world, and the significant number (approx. 14-15%, as found in this study) of these cases being co infected by opportunistic fungal respiratory pathogens, which greatly increase the rates of morbidity and mortality, it is surprising that there are no national guidelines under RNTCP for regular screening and/or prophylaxis of these infections, in pulmonary TB patients! Also, there are hardly any large- scale Indian studies to support such decisions. Thus the need of the hour is to carry out several such large-scale Indian studies determining the pathogen spectrum and prevalence of such co morbid infections in these patients, so as to raise the index of suspicion both, amongst the clinicians as well as laboratory personnel, so as to minimize missing or delays in diagnosis and hence provision of prompt and optimal treatment to the patient, and also to help in the formulation of a national policy.

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