

Candida co-infection in pulmonary TB patients in Asia: A Narrative Review

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Abstract

Tuberculosis is an infectious disease that causes the second most deaths in the world after COVID-19. Progress of TB disease and prolonged treatment with antibiotics or immunosuppressive agents makes TB patients immunocompromised and become susceptible to fungal infections. The coexistence of pulmonary TB and fungal infections will affect the treatment and increased mortality. With the narrative review method, this study aims to discover the prevalence of TB and candida fungus co-infection in Asian countries. *Candida albicans* species is the most common in co-infections with TB and *Candida* fungi.

Keywords: Tuberculosis, Coinfection, Fungal, Candida

INTRODUCTION

Tuberculosis is an infectious disease that causes the second most deaths in the world after COVID-19. TB disease comes from *Mycobacterium tuberculosis* (1). Without treatment, the death rate from TB is high (around 50%) (2). Meanwhile, with treatment according to WHO recommendations, the cure rate for TB sufferers reaches 85%. TB treatment is carried out using anti-TB drugs for 4-6 months.

Progress of TB disease and prolonged treatment with antibiotics or immunosuppressive agents makes TB patients immunocompromised and become susceptible to fungal infections (3). Up to 1 million people recovered from TB develop concomitant fungal infections which are often misdiagnosed as relapsed

TB (4). The fungal *Candida* spp. colonise the oral cavity as commensals but becomes pathogenic in immunocompromised individuals. *Candida albicans* has emerged as a potentially pathogenic fungus rather than innocuous mucosal commensal in patients with broncho-pulmonary diseases (5). Although *Candida albicans* continues to dominate species in pulmonary candidiasis, many others non-*albicans* *Candida*, are increasingly infecting humans, some are linked to specific groups of factors also others are associated to particular patients types (6). The coexistence of pulmonary TB and fungal infections will affect the treatment and increased mortality (7). Previously, there had been several studies regarding *Candida* fungal infections in TB patients. This study aims to collect and summarize various literature related to the discovery of *Candida* fungal infections in pulmonary TB patients.

METHOD

This research is a literature review with a narrative review design. The data used for this literature review is secondary data in the form of research journals related to the topic. The research journal that will be used as a source for this narrative review is an English-language journal and published within 10 years, namely between 2013-2023.

RESULT

The first literature, was a study regarding fungal co-infection with TB patients in India. This research was published in 2013, where results were obtained from 75 tuberculosis patients positive for Ziehl Neelsen staining, 30 patients (40%) were positive for *Candida* fungal co-infection with *Candida albicans* is the most common isolate observed in 50% of the patients, followed by *C. tropicalis* (20%) and *C. glabrata* (20%). *Candida* co-infection was found in 62.5% female patients, while it was observed in only 29.4% of the male patients. There was no significant difference in the mean age of the patients with and without *Candida* co-infection (5). The advantage of this literature is that acid-fast stem staining was carried out to eliminate the exclusion criteria in this study. This study shows that there is a significant difference in results between women and men positive for *candida* co-infection. The weakness of this journal is that researchers do not explain the control variables that can influence the discovery of fungi in sputum samples such as storage and room temperature or sample quality.

The second literature is a 2014 study which also came from India. The results of this study were, from 107 sputum positive pulmonary tuberculosis patients, fungal *Candida* coinfection was found in 19 samples (17.7%). Among these 19 samples, two samples showed dual infection (two different species of *Candida* in the same sample). So the total number of *Candida* isolated was 21. *Candida albicans* was the

predominant species causing secondary infection. Out of 21 *Candida* isolates, 14 were identified as *C. albicans* (66.7%), two samples were *C. tropicalis* (9.5%), two samples were *C. krusei* (9.5%) and two samples were *C. parapsilosis*. And *C. glabrata* was isolated from one sample (4.8%). In this study there is no gender specific prevalence of fungal infections among TB patients. This study also did not include age as a research variable (8). The strength of this research is that it compares the types of TB patients (category 1, category 2, and XDR TB) who experience fungal co-infection. The weakness of this research is that it does not explain the control variables that can influence the discovery of fungi in sputum samples. Apart from that, this study also did not include a variable for the average age of patients positive for fungal coinfection.

The third literature used in this narrative review is research on fungal co-infections conducted in Iran in 2007-2017 with publication year 2018. This research include not only *Candida* spp., but also *Aspergillus* spp. Amongst the positive tuberculosis patients, 16/130 cases (12.3%) had the coinfection of *Mycobacterium tuberculosis* with fungal microorganisms. And 6/12 (37.5%) had the coinfection of *Candida* spp. the most occurrence coinfection of *Candida* spp. was reported in the age groups of 21-30. The coinfection of TB with fungal infections in males (15.4%) was higher than in females (14.7%) (9). The advantage of this research is that it carries out a sputum staining examination to determine the presence of *Mtb* bacteria as an effort to eliminate exclusion criteria and differentiate types of TB patients.

The fourth and final literature used in this narrative review is research in 2020 in Indonesia. The strength of this research is that it divides the sample into previously treated case patients and new cases. Where previously treated case patients had a higher percentage of fungal co-infections (86.8%) compared to new TB cases (71.2%). There were 147 positive samples coinfecting with *Candida* spp. of 193 patients. *Candida albicans* remains the most common fungal coinfection with a percentage exceeding 50%. proportion of fungal positive culture in women was higher, compared to men (86% vs 69.2%) and showed a significant difference. with the average age of previously treated cases patients being 48 years old and new cases being 43 years old (7).

DISCUSSION

The results from the first literature were that *Candida albicans* was the most common isolate observed in 50% of the patients with co-infection. The prevalence of *Candida* coinfection was found to be higher in women. The average age of *Candida* co-infected patients was 47.77 with a standard deviation of approximately 20.43. (5)

The results of the second study showed that *Candida albicans* was the predominant species causing co-infection among pulmonary tuberculosis patients. In this study there is no gender specific prevalence of fungal infections among TB patients. This study does not show the average age of TB patients with fungal coinfection but shows that the prevalence of fungal infection is more common in patients having low BMI when compared to those with normal or high BMI and this difference was found to be statistically significant. (8)

The third literature not only describes the incidence of *Candida* coinfection but also describes coinfection from *Aspergillus* species. The results of this research on *Candida* fungi showed that non-*albicans* spp. were the most common species among *Candida* spp. with the most prevalence was in the age group of 41-50 years. This study obtained results of fungal coinfection with a higher prevalence in men. (9)

The results of the fourth study were, *Candida albicans* is the most common fungal species in pulmonary TB patients (54.05%). The prevalence of fungal coinfections was found to be higher in women. The average age of patients with fungal coinfection was 44.18 with a standard deviation of approximately 16.82. (7)

CONCLUSION

Of the four literatures used in this research, three literatures found that *Candida albicans* was the most common fungal species in TB co-infection. This literature has not been able to prove that gender factors influence the incidence of fungal co-infections, but in two of the four literatures used as references, it was found that women had a higher prevalence. Based on the age factor, TB and fungal co-infections were mostly found in patients with an average age of over 40 years

REFERENCES

1. Global tuberculosis report 2023. Geneva: World Health Organization; 2023. Licence: CC BY-NC-SA 3.0 IGO.
2. Behr MA, Edelstein PH, Ramakrishnan L. Is Mycobacterium tuberculosis infection life long? BMJ. 2019;367:l5770 (<https://doi.org/10.1136/bmj.l5770>).
3. V.S. Rathod, J.S. Raut, S. Mohan Karuppayil, Antifungal drug susceptibility of Candida albicans isolates from pulmonary tuberculosis patients, Int. J. Pharm. Pharm. Sci., Suppl. 5 (2012) 323–326.
4. S.A. Naz, P. Tariq, A study of the trend in prevalence of opportunistic Candida coinfections among patients of pulmonary tuberculosis, Pak. J. Bot. 36 (2004) 857–862.
5. Kali A, Charles MVP, Joseph NM, Umadevi S, Kumar S, Easow JM. Prevalence of Candida coinfection in patients with pulmonary tuberculosis. AMJ 2013, 6, 8, 387-391. <http://dx.doi.org/10.4066/AMJ.2013.1709>
6. Trofa, D., Gacser, A., and Nosanchuk, J. D. (2008). Candida parapsilosis, an emerging fungal pathogen. Clinical Microbiology Review; 21:606- 25
7. Soedarsono S, Prasetyo YD, Mertaniasih NM. Fungal isolates findings of sputum samples in new and previously treated cases of pulmonary tuberculosis in Dr. Soetomo Hospital Surabaya, Indonesia. Int J Mycobacteriol 2020;9:190-4.
- 8 Mathavi S, Shankar R, Kavitha A, Sasikala G, Priyadharsini I. A Study On Prevalence Of Pulmonary Candidiasis Among Tuberculosis Patients And Use Of Chromagar In Identification Of Candida Species. JDDT [Internet]. 15May2014 [cited 19Nov.2023];4(3):118-21. Available from: <https://jddtonline.info/index.php/jddt/article/view/821>
- 9 Siami, Azad Khaledi. Tuberculosis Status and Coinfection of Pulmonary Fungal Infections in Patients Referred to Reference Laboratory of Health Centers Ghaemshahr City during 2007-2017. Ethiop J Sci.2018;28(6):683. doi:<http://dx.doi.org/10.4314/ejhs.v28i6.2>