



## CANDIDEMIA: A POST COVID CO-INFECTION

## Microbiology

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## ABSTRACT

**Background:** Candida species are major constituents of the human mycobiome and the main cause of invasive fungal infections, with a high mortality rate and recognized as a complication of severe COVID-19. The present study is an attempt to identify the etiological agents in blood samples of critically ill Covid positive patients so that timely interventions can be helpful to reduce morbidity and mortality in such patients. **Material and method:** This retrospective observational study was conducted at Tejas Microdiagnostics during 30 April 2021 to 30 June 2021. A total of 126 Covid positive patients requiring admission in SRN Hospital, Prayagraj were included. Blood specimen collected in FA and FAN bottles were sent for culture and antibiogram to Tejas Microdiagnostics within eight hours of admission. **Results:** Blood culture of 89 (70%) patients was positive while 37 (30%) patients did not show any growth. Fungi were isolated in 24(26.96%) cases while bacterial growth was identified in 65(73.04%) cases. *Candida tropicalis* was the most predominant species while *Aspergillus fumigatus* and *Penicillium* were isolated among dimorphic fungi. Mortality was observed in 15% cases. **Conclusion:** Our study illustrates the predominance of *Candida tropicalis* from blood samples of Covid positive patients. This statistics may be the tip of the iceberg. The reason for such a high incidence can be the wide spread use of empirical antibiotics and steroids which may increased the risk of fungal infections in patients with COVID-19. Isolation and identification of pathogens are prudent and may reduce the morbidity and mortality of the patients.

## KEYWORDS

Fungemia, Candida, infection, COVID-19.

## INTRODUCTION

Infection with SARS-CoV-2 can lead to Coronavirus disease 2019 (COVID-19), where respiratory symptoms may include cough, breathing difficulties, and in severe cases, result in acute respiratory distress syndrome (ARDS) [1, 2]. In the beginning of the COVID-19 pandemic, superinfections have been rarely reported (3), reports about secondary fungal infections as complications of severe COVID-19 are on the rise. In COVID-19 patients with ARDS, COVID-19 associated pulmonary aspergillosis [3-5] and COVID-19 associated candidiasis [6-7] have been described to complicate the clinical course. Although the exact pathogenesis of these co-infections remains unclear, there are several immunological mechanisms that can facilitate the development of fungal diseases. The burden of COVID-19 patients with co-infections and their etiologic agents is paramount for the optimal management of COVID-19 patients resulted in unprecedented deaths worldwide [8]. Therefore, the present study is an attempt to isolate and identify the etiological agents in blood samples of critically ill Covid positive patients so that timely interventions can be done to reduce morbidity and mortality in such patients.

## MATERIAL AND METHOD

This study was designed as a retrospective observational analysis in patients diagnosed with positive RTPCR on nasopharyngeal swab from Moti Lal Nehru Medical College, Prayagraj and admitted to Covid ICU from 1st October 2020 to 15th MAY, 2021 at SRN Hospital, Prayagraj. The patients were followed during the hospital stay and their outcomes were noted. Inclusion criteria comprised of age >18 years (male or female), without any previous underlying cause with SOFA score >1. After obtaining informed consent, clinical data and laboratory investigations were collected and noted.

Blood samples for culture were collected within 8 hour of admission to ICU aseptically via central line in FA and FAN bottles for the isolation of aerobes, anaerobes and fungus along with other laboratory parameters and sent to Tejas Microdiagnostics, Prayagraj.

These three inoculated bottles were further incubated in BactAlert 3D system following standard protocols. The isolated pathogens were reexamined microscopically to ensure the staining and morphologic characteristic of organism. Further identification was done at species level by the Vitek-2 system.

## RESULT

Out of 126 Covid positive patients, blood culture of 89 (70%) patients were found positive while samples of 37 (30%) patients did not show

any growth after the incubation of 7 days at 37°C Out of 89 culture positive blood samples 24 (26.96%) patients showed positive growth for fungus while blood culture of 65 (73.04%) patients were positive for bacterial pathogens. Among 26.96% of fungi, percentage of different *Candida* species was illustrated in Figure -1.

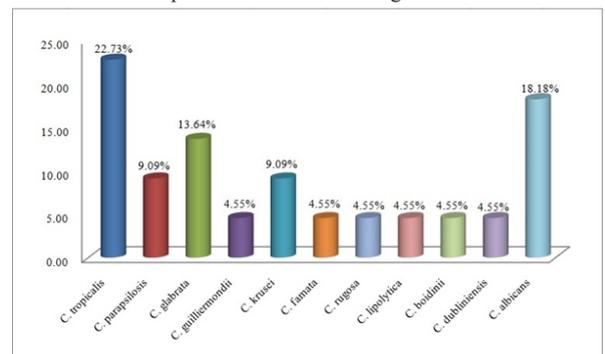


Figure 1: Various species of *Candida* isolated from the blood samples of Covid positive patients.

Among the different species of *Candida*, *Candida tropicalis* was the most predominant isolated species from the blood samples of Covid positive patients. Percentage of different dimorphic fungi was illustrated in Figure -2.

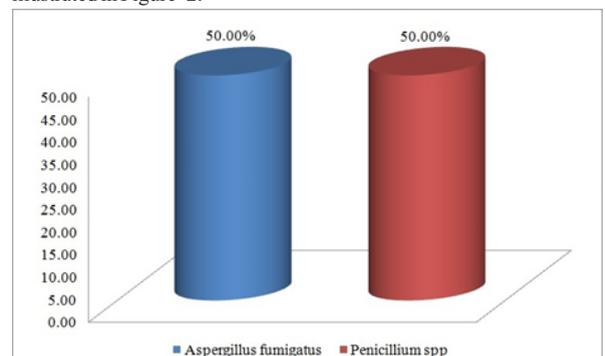


Figure 2: Various species of dimorphic fungi was isolated from the blood samples of Covid positive patients.

Both the genera of dimorphic fungi were isolated in equal proportion. The demographic features of positive & negative blood cultures of Covid positive patients are depicted in table 1.

**Table 1: Demography of Positive & Negative blood cultures of Covid positive patients.**

S.No	Demography		Positive Blood Culture	Negative Blood Culture
1	Mean Age ± SD (Range) in years		64.6 ± 16.42	50.87 ± 16.91
2	Gender	Male	33 (55%)	24 (53.3%)
		Female	27 (45%)	21 (46.67%)

As the data revealed average mean age is 64.6 ± 16.42 with male predominance. The description of Laboratory parameters of positive & negative blood cultures of Covid positive patients are depicted in table 2.

**Table 2: Description of Laboratory parameters of Positive & Negative blood cultures of Covid positive patients.**

S. No	Laboratory Parameter	Positive Blood Culture		Negative Blood Culture		Statistical significance	
1	TLC	15405	6751.02	11080	4269.36	-2.172	0.03
2	FBS	185.39	109.91	133.39	71.45	-1.594	0.12
3	HbA1C	7.47	2.75	6.75	1.6	-0.904	0.37
4	CRP	84.45	50.65	49.37	31.91	-2.351	0.02
5	Serum ferritin	878.54	544.44	928.79	679.72	0.243	0.8
6	D dimer	2.753	1.874	1.461	1.076	-2.386	0.02
7	Serum procalcitonin	9.31	10.87	4.02	4.52	-1.768	0.08

**DISCUSSION**

COVID-19 induces a plethora of immunological reactions affecting the innate and adaptive immune responses, which are critical to the clinical course and outcome of patients. Severe COVID-19 can result in excessive cytokine release or immunosuppression, with substantial morbidity and mortality mostly in older patient populations [1, 9-10]. Recent reports indicate an increased rate of fungal co-infections during COVID-19. With incomplete understanding of the pathogenesis and without isolation of the pathogens, secondary infections may be detrimental to the prognosis.

In our study fungal pathogen was attributed to central line source. Similar findings were also observed by a study from Oman [11] and Hughes et al. [12], they reported candidemia and the source was a central venous catheter. We isolated both bacteria and fungi from the blood stream. Chen and colleagues 6 also reported both bacterial and fungal co-infections.

Most frequent causative agent of blood stream fungal infections were caused by yeasts with *Candida* species. *C. tropicalis* were more predominant as a single pathogen; however, other major *Candida* species— *C. glabrata*, *C. parapsilosis*, *C. albicans*, *C. rugosa*, *C. Famata*, *C. guilliermondii*, *C. lipolytica*, *C. boidinii*, *C. dubliniensis* and *C. krusei* and accounting for 91.6% while filamentous fungi (moulds) such as *Aspergillus* and *Penicillium*, were much less common, and together represent about 8.4% cases. Elsevier reported four fungal pathogens from three studies [13-15], namely *Candida albicans*, *Candida glabrata*, *Aspergillus flavus* and *Aspergillus fumigatus*. Recently, Verweij et al. [16], reported that *Aspergillus* species as co-pathogens are commonly identified in COVID-19 patients and are an important cause of mortality.

We believe that this study is important considering its early detection and reporting of various *Candida* species and dimorphic fungi in blood stream of Covid positive patients. And this may be the reason of low mortality (15%) in our patients.

**CONCLUSION**

Our study illustrates that 26.96% fungal pathogens were isolated from 89.8% positive blood cultures samples of Covid positive patients. This statistics may be the tip of the iceberg. The reason for such a high incidence can be the wide spread use of empirical antibiotics and steroids which may increased the risk of fungal infections in patients with COVID-19. Isolation and identification of such infections is prudent and may reduce the morbidity and mortality of the patients

**REFERENCES**

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet (London England)* (2020)

395:497–506. doi: 10.1016/s0140-6736(20)30183-5

2. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* (2020) 579:270–3. doi: 10.1038/s41586-020-2012-7

3. Garcia-Vidal C, Sanjuan G, Moreno-García E, Puerta-Alcalde P, Garcia- Pouton N, Chumbita M, et al. Incidence of co-infections and superinfections in hospitalized patients with COVID-19: a retrospective cohort study. *Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis* (2020) 27(1):83–8. doi: 10.1016/j.cmi.2020.07.041

4. Arastehfar A, Carvalho A, van de Veerdonk FL, Jenks JD, Koehler P, Krause R, et al. COVID-19 Associated Pulmonary Aspergillosis (CAPA)-From Immunology to Treatment. *J Fungi (Basel Switzerland)* (2020). doi: 10.3390/jof6020091

5. White PL, Dhillon R, Cordey A, Hughes H, Faggian F, Soni S, et al. A national strategy to diagnose COVID-19 associated invasive fungal disease in the ICU. *Clin Infect Dis Off Publ Infect Dis Soc America* (2020). doi: 10.1093/cid/ciaa1298

6. Al-Hatmi AMS, Mohsin J, Al-Huraizi A, Khamis F. COVID-19 associated invasive candidiasis. *J Infect* (2020) S0163–4453(20)30539-9. doi: 10.1016/j.jinf.2020.08.005

7. Antinori S, Bonazzetti C, Gubertini G, Capetti A, Pagani C, Morena V, et al. Tocilizumab for cytokine storm syndrome in COVID-19 pneumonia: an increased risk for candidemia? *Autoimmun Rev* (2020) 19:102564. doi: 10.1016/j.autrev.2020.102564

8. Arastehfar A, Carvalho A, Nguyen MH, Hedayati MT, Netea MG, Perlin DS, Hoengl M. COVID-19-Associated Candidiasis (CAC): An Underestimated Complication in the Absence of Immunological Predispositions? *J Fungi* 2020, 6, 211; doi:10.3390/jof6040211

9. Gao YM, Xu G, Wang B, Liu BC. Cytokine storm syndrome in coronavirus disease 2019: A narrative review. *J Internal Med* (2020) 289(2):147–61. doi: 10.1111/joim.13144

10. Remy KE, Mazer M, Striker DA, Ellebedy AH, Walton AH, Unsinger J, et al. Severe immunosuppression and not a cytokine storm characterizes COVID-19 infections. *JCI Insight* (2020):1–15. doi: 10.1172/jci.insight.140329

11. Al-Hatmi AMS, Mohsin J, Al-Huraizi A, Khamis F. COVID-19 associated invasive candidiasis. *J Infect.* 2021;82(2):e45–e46. doi:10.1016/j.jinf.2020.08.005

12. Hughes S, Troise O, Donaldson H, Mughal N, Moore LSP. Bacterial and fungal coinfection among hospitalized patients with COVID-19: a retrospective cohort study in a UK secondary-care setting. *Clin Microbiol Infect.* 2020;26(10):1395-1399. doi:10.1016/j.cmi.2020.06.025

13. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: Descr Study. *Lancet.* 2020;395:507–513

14. Wang Z., Yang B., Li Q., Wen L., Zhang R. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. *Clin Infect Dis.* 2020;71(15):769–777.

15. Yang X., Yu Y., Xu J., Shu H., Xia J., Liu H. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single- centered, retrospective, observational study. *Lancet Respir Med.* 2020;8(5):475–481.

16. Verweij PE, Gangneux JP, Bassetti M, Brüggemann RJM, Cornely OA, Koehler P. Diagnosis COVID-19-associated pulmonary aspergillosis. *Lancet Microbe.* 2020;1(2):e53–e55.