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PULMONARY FUNGAL INFECTIONS IN PATIENT WITH COVID-19

Pathology

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ABSTRACT

Background: The incidence of pulmonary fungal infections in patients with COVID-19 disease is not well described. Isolation and identification of these infections may improve patient's outcome. Therefore, the objective of the study is to find out the incidence of pulmonary fungal co-infections and to isolate and identify the fungal pathogens in COVID positive patients.

Methods: This retrospective observational study was conducted at Tejas Microdiagnostics during 30 April 2021 to 30 June 2021. A total of 59 patients with severe COVID-19 infection requiring admission in SRN Hospital, Prayagraj were included in the study. Sputum specimen was sent for culture and sensitivity to Tejas Microdiagnostics within eight hours of admission for the evaluation of fungal infections.

Results: Out of 59 COVID positive cases, 53 cases were identified with fungal infections. The mean age of patients with infections was 61.29 + 7.84 years with males being about 73.6% and females about 26.4%. The pulmonary fungal infection comprised of Candida glabrata (13.21%), Candida tropicalis (33.96%), Candida albicans (9.43%), Candida cruzi (15.09%), Candida parapsilosis (18.87) Mucour (3.77%), Penicillium (1.89%), Rhizopus (1.89%) Aspergilluss fumigatus (1.89). Mortality was observed in 7.5% cases.

Conclusion: Our study illustrates that 89.8 % COVID positive patients were infected with pulmonary fungal infections. 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.

KEYWORDS

Fungus, Pulmonary, infection, COVID-19.

INTRODUCTION

Since coronavirus disease 2019 (COVID-19) was first recognized in December 2019, it has resulted in the ongoing worldwide pandemic [1]. COVID-19 primarily presents as a respiratory tract infection with symptoms varying from mild flu-like illness to acute respiratory distress syndrome (ARDS) [2, 3]. Critically ill patients, especially the patients who were admitted to the intensive care unit (ICU) and required mechanical ventilation, or had a longer duration of hospital stays, even as long as 50 days, were more likely to develop fungal co-infections [4].

Pulmonary infections in COVID-19 patients are not well described and raised an important knowledge gap. Furthermore, other infectious and non-infectious complications have been described in hospitalized COVID-19 patients strongly associated with underlying COVID-19 infection such as pneumothorax, myocarditis, and even device-related secondary infections (e.g., central venous catheter, foley catheter) [5-7].

Lung involvement with fungal pathogens often deprived of an early specific treatment because of delay in diagnosis. Most of the COVID-19 patients did not have a sputum fungal evaluation at the start of their treatment [8]. In severe COVID-19 patients with a broader spectrum of antibacterial medications, parenteral diet and invasive examinations, or in patients with persistent neutropenia and other immune disability causes, the risk of *Candida* infection may increase dramatically [9], and moreover, it is very difficult to differentiate between different invasive fungal species radiologically especially in COVID scenario, as all of them show overlapping radiological features among themselves and with COVID. Therefore, the objective of the study is to find out the incidence of pulmonary fungal co-infections and to isolate and identify the fungal pathogens in COVID positive patients.

METHODS

It was a retrospective observational study, conducted in Tejas Microdignostics, Prayagraj during 30 April 2021 to 30 June 2021. A sputum specimen of 59 COVID positive patients, admitted in COVID ICU Swaroop Rani Nehru Hospital, M.L.N. Medical College, a tertiary care centre for COVID-19, were sent to Tejas Microdiagnostics within eight hours for fungus culture and sensitivity testings. We reviewed the patient's demographics, COVID-19 test results, and treatment modalities of COVID-19 infection. In all the cases data related to the age, sex, occupation, personal habits etc were noted. Care was particularly taken to record the presence of superficial mycotic infections on other parts of the body.

Each specimen was divided into two parts; one was taken for direct microscopic examination after 10% KOH solution treatment and second was inoculated on Sabouraud Dextrose agar (M286) and Sabouraud Cycloheximide Chloramphenicol agar (M664). Cultures were routinely incubated at $21^0 - 37^0$ c and examined daily for up to 4 weeks. The identification of individual diamorphic fungi was based on standard methods such as microscopy, morphology, colonial characterization and pigment production, rate of growth and biochemical test while yeast identification was done by Vitek-2 (Biomeurix, France)

RESULTS

Out of 59 laboratory and radiology diagnosed cases of COVID-19, 53 cases were found culture positive for different fungi. The mean age of patients with infections was 61.29 $\pm$ 7.84 years with males being about 73.6% and females about 26.4%. Their base line data are summarized (Table 1).

Table 1: Demographic And Baseline Parameters Of Patients.

S.N.	Parameters	Values
1	Age	61.29 $\pm$ 7.84 years
2	Gender	Males 73.6%. Females 26.4%
3	Diabetes	35.8%
4	Hypertension	26.4%
5	Chronic Kidney Disease	11.4%
6	Heart Disease	5.7%
7	Others	20.75%

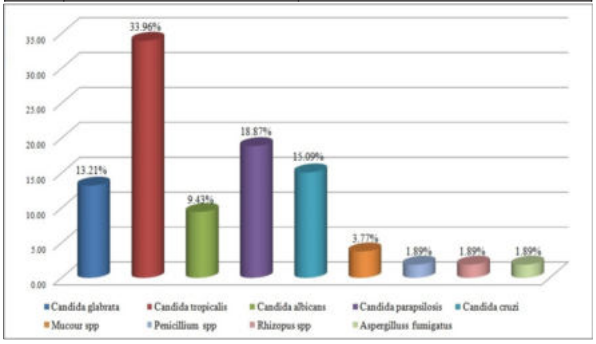

Figure 1: Incidence of Fungal pathogens in patients with COVID-19.

Out of 53 (89.3%) culture positive cases, dimorphic fungi were isolated in 9.4% cases while *Candida* and its different species were isolated in 90.6% cases. When the data was further analyzed *Candida glabrata* (13.21%), *Candida tropicalis* (33.96%), *Candida albicans* (9.43%), *Candida cruzi* (15.09%), *Candida parapsilosis* (18.87*) Mucour* (3.77%), *Penicillium* (1.89%), *Rhizopus* (1.89%) *Aspergilluss fumigatus* (1.89) were observed (Figure 1). *Candida species* accounted for majority of the isolates and more so in the recent years.

DISCUSSION

Our study revealed incidence of 89.3% fungal co infections in COVID positive patients however, Chen et al. reported 5% cases [10], Yang et al recorded 5.8% [4] and a German study found 26.3% in patients with COVID-19 disease [11]. The high incidence of fungal infection in our study may be due to the unfortunate combinations of co morbidities with COVID-19 disease and sputum was sent religiously to the lab.

In our study the mean age of patients with fungal infections was 61.29 ± 7.84. Our data were consistent with most of the published studies [8].The occurrence of fungal infections in our study was predominantly in males73.6% while female showed fungal positivity only 26.4%. Roopek et al reported male predominance [8].

We identified following fungal species from the sputum specimen of the COVID positive patients eg *Candida glabrata* (13.21%), *Candida tropicalis* (33.96%), *Candida albicans* (9.43%), *Candida cruzi* (15.09%), *Candida parapsilosis* (18.87*) Mucour* (3.77%), *Penicillium* (1.89%), *Rhizopus* (1.89%) and *Aspergilluss fumigatus* (1.89). Out of the 26 observational studies14.3% studies had no description of fungal isolates [12] while a study repotred single case of *Aspergillus flavus*, and *Candida glabrata* while three cases of C.albicans [10]. Yang et al. found *A. flavus*, *A. fumigatus* and *C.albicans* [4]. This study is a largest study till date from Uttar Pradesh. Also worth mentioning is the fact that fungal isolates have not been reported till this date in patients with COVID-19 disease. Mortality was observed in 7.5% cases.

It is hypothesized that uncontrolled hyperglycaemia is frequently seen as a result of corticosteroid use. Acidosis causes a low pH, which is ideal for fungus to grow [13] COVID-19 frequently causes endothelialitis, endothelial damage, lymphopenia, thrombosis and a decrease in CD4+ and CD8+ levels, putting the patient at risk for opportunistic fungal infection [14]. For mucormycosis, free iron is a great resource. Hyperglycaemia causes transferrin and ferritin to be glycosylated, which lowers iron binding and allows for more free iron. Furthermore, a rise in cytokines, particularly interleukin-6, increases free iron via raising ferritin levels due to increased synthesis and reduced iron transport in COVID-19 patients [15] In the setting of diminished WBC phagocytic activity, mucor formation is encouraged by high glucose, low pH, and free iron [16].

CONCLUSION

It was a challenge for the clinicians to distinguish between bacterial and fungal infections clinically in a dreaded disease like COVID. This diagnostic uncertainty has contributed an overuse of antibiotics in patients with COVID-19 viral illness. Secondly steroid was also one of the parts of the treatment and these were the reasons of high incidence of fungal infections in patients with COVID-19. Hence, isolation and identification of such infections is prudent and may reduce the morbidity and mortality of the patients.

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