Section A-Research paper

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Fungal co-infections in COVID19 patients

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Abstract

Background: As the COVID-19 infection may induce significant and persistent lymphopenia, the risk of acquiring secondary fungal infections was increased in the midst of this pandemic.

Common fungal pathogens in severe COVID19 patients are Aspergillus spp. and Candida spp. but infections Mucormycosis may be found. **Material And Method:** Data was analysed retrospectively from mycology laboratory at Microbiology department, Dr. V. M. Government Medical College, Solapur during MAY 2021 to SEP 2021. Samples from suspected cases of COVID 19 associated fungal infections were considered only in this study. After receiving, samples were subjected to 10% KOH mount and each sample was cultured on two Sabouraud dextrose agar slant of which one was kept at 25°C and other at 37°C and observed for fungal growth till 3 weeks. Depending on whether isolate was a Yeast or mould standard microbiology technique including germ tube, LPCB stain etc. were used to identify fungus. **Result:** Total 701 samples of suspected COVID-19 associated fungal infections were analysed, of which Out of 88 fungal culture positive patients 54(61.34%) were male and 34(38.66%) were female. In our study out of 701 COVID 19 patients KOH positive and culture positive percentage were 30.67% and 12.55% respectively. sensitivity and specificity of culture in comparision with KOH is 40.93% and 100% respectively. In all (n=701) samples 613 were negative for fungal growth while remaining had maximum Rhizomucor species(51.13%), followed by Candida (18.18%) Aspergillus spp. (15.90%) and while 14.77% of other fungal isolates includes Fusarium, Chrysonilia & Bipolaris.

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Introduction

At end of 2019, Influenza like illness with Corona virus disease 2019 (COVID19) outbreak was seen which soon spread across globe as pandemic.(1) Diagnosis of this diseases is done by RT-PCR method.(2)The second wave and third wave of this disease has led to panic in

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many countries, including India.[3] Studies in China confirms coinfection with different bacteria, viruses and fungi in laboratory-confirmed COVID19 cases.[1]

In the pandemic it was found that secondary fungal infection seen commonly in the COVID-19 patients[3]. As understood so far, COVID19 infection may induce significant and persistent lymphopenia, increasing the risk of various opportunistic infections[1]. Heavy doses of steroids are given to COVID19 patients which weakens immune system making patient susceptible to Mucormycosis. Also steroids can cause blood sugar levels to increase ultimately becoming challenging in patients with uncontrolled diabetes, making conditions favourable for fungal (especially Mucorales) infection.[3] Common fungal pathogens in severe COVID19 patients are Aspergillus spp. and Candida spp. but infections Mucormycosis may be found [4]. Mucormycosis is a neglected infection which should be considered in the patients with COVID19, in the same way as COVID19 associated pulmonary aspergillosis.[5]

COVID19 patients admitted in ICU may have ventilator support with longer duration of hospital stay and immune suppression, so likely to develop fungal infection. [4] Also chance of fungal infection rise in infections during the middle and latter stages of this disease, especially severely ill ones.[4]

Patients have chance of invasive fungal infection in severely ill patients which might be fatal in some cases, so early diagnosis by comprehensive diagnostic intervention (Direct microscopic examination, culture) is very important.[4]

Increasing awareness of possibility of fungal coinfection in COVID 19 will help for rapid diagnosis and treatment.[6]

Hence for optimal management of COVID19 patients, understanding burden of secondary fungal infection is important.This information will to refine empiric antimicrobial management for patients to improve outcome.[7]

Bacterial and fungal infections in COVID-19 patients have not be adequetly diagnosed and reported.[3] So our study is with aim to report fungal infection coinfection in COVID19 patients.

Material and Method

Data was analysed retrospectively from mycology laboratory at Microbiology department, Dr. V. M. Government Medical College, Solapur during May 2021 to September 2021. Nasal swab samples from suspected cases of fungal infection from COVID 19 positive patients were considered in this study. Samples were processed according to below mentioned flow chart.

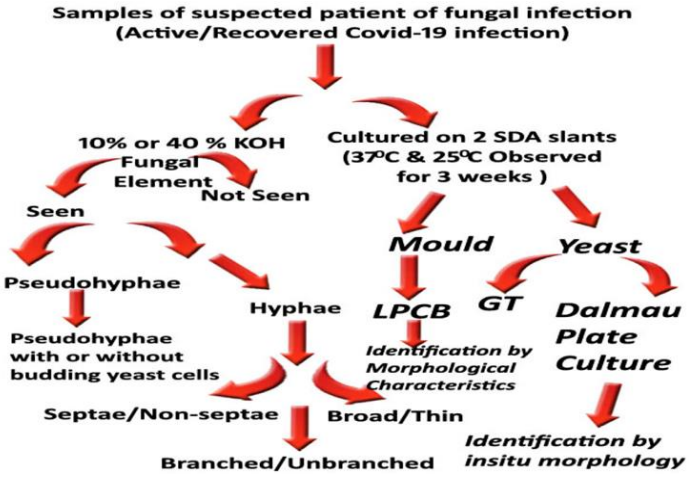

Figure 1

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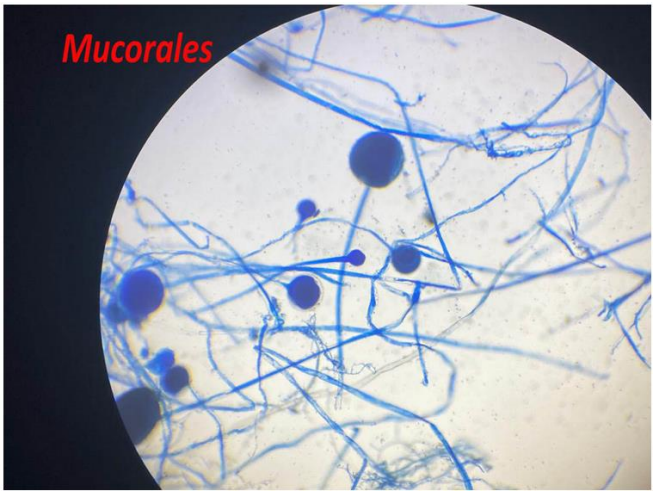

Figure 2

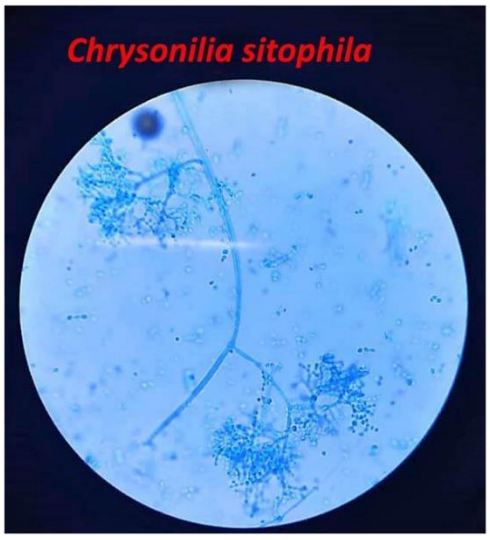

Figure 3

Figure 4

Results

A total 701 COVID-19 positive patients suspected of fungal infections, admitted between May 2021 to September 2021 were included in this study. Out of 701 patients, 215 (30.67%)

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patients were positive in KOH test and 88 (12.55%) patients revealed fungal growth in culture.

Out of 88 fungal culture positive patients 54(61.34%) were male and 34(38.66%) were female.

Table 1: Distribution of specimen according to KOH & Culture positivity

CULTURE Result	**KOH Result**	**POSITIVE**	**NEGATIVE**	**TOTAL**
POSITIVE		88	00	88
NEGATIVE		127	486	613
TOTAL		215	486	701

Table 2: Distribution according to Age and Sex in COVID 19 positive patients with fungal growth.

Age group in years	**Genders**	**Male**	**Female**	**Total**
< 20		1 (1.81%)	0	1(1.14)
20-40		10 (18.2%)	8 (21.73%)	18(20.45%)
41-60		24 (43.63%)	15 (43.5%)	39(44.32%)
>60		19 (36.36%)	11 (34.77%)	30(34.09%)
Total		54 (100)	34 (100)	88 (100)

Maximum number of patients who acquired fungal infections were in the age group of 41-60 years(44.32%) followed by patient aged >60 years(34.09%).

Table 2: Distribution of various fungi isolated from COVID 19 patient.

Different isolated fungi in COVID 19 patients.	**Total**
Rhizomucour	45(51.13%)
Candida	16(18.18%)
Aspergillus	14(15.90%)
Other	13(14.77%)
Total	88 (100)

The most frequently isolated fungi were *Rhizomucour* (51.13%) followed by *Candida species* (18.18%) and *Aspergillus* (15.90%). Other isolated fungi were *Fusarium spp., Crysionilia sitophila* and *Bipolaris.*

Discussions

In our study out of 701 COVID 19 patients KOH positive and culture positive percentage were 30.67% and 12.55% respectively. So sensitivity and specificity of culture in comparision with KOH is 40.93% and 100% respectively.

Sensitivity of fungal culutre method in studies of Barrie et al[8] is 41.7% which is equivalent to our study while Malwadi et al shows 50% sensitivity which is littlebit high in compare to our study.

Opportunistic mycoses are serious complication in viral infection, particularly associated with COVID-19. In our study fungal infection was observed 12.55% in COVID-19 positive patients.

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Fungal co-infection in COVID19 patient was observed by Chong et al.[9] 6.3% which is less than our observation, Calvo.et al.[2] have mentioned 22.8% which is almost double of our observation.

Risk of fungal infection in COVID-19 increases because of its effect on the patient's immune system and also treatments for COVID-19 like steroids etc can decreases immunity further. [6]

In our study we observed fungal culture positivity was more common in male (61.34%) as compared to female (38.66%), which is almost similar to Sadat et.al.[10] which reports fungal culture positivity in male is 72.9 % and 25.9% in female. Also Kumar.et.al.[11] documented fungal culture positivity with male predominance as 78.9% in male and 21.1% in female. This is may be because in India specifically in this study region, outdoor jobs are commonly performed by male. So exposure to infective air is more common in male.

In present study most common age group affected was between 41 to 60 years (44.32%) followed by > 60 years (34.9%). So, overall fungal co-infection in COVID 19 patients above 41 year of age group is commonly affected. Similarly fungal infetion in elderly age group was observed in the study of Sadat et.al.[10] they also reported 66.2% fungal coinfection occurs in more than 50 years age group patients. This might be because fungal infection is seen more commonly in older age groups because of decreased immunity but in our study most common age group is middle age (41 to 60) along with older age greater than 60. In our study most commonly isolated fungus was Mucorales (51.13%) followed by Candida species. (18.18%). Study Kumar et.at.[11] also reported predominant isolate as Mucorales (81.2%) but much higher than our study.

Silvia et.al.[12] in his study reported Candida species (21.4%) as second common isolate which is quite similar to our studies (18.18%) .

Our study shows Aspergillus species (15.90%) as third common isolate. While studies of Silva et. al.[12] & Song et. al.[4] shows most common isolate as Aspergillus in 39.1% & 26.3% respectively among COVID 19 patients.

Conclusion

- The manifestation of different fungal infections in COVID-19 patients appears to be consequences of COVID 19 further influenced by immunosuppressive treatments, mechanical ventilation, catheterization, diabetes, old age, etc
- Fungal infection is predominant in COVID 19 positive male.
- Common isolation of angio-invasive and fatal Mucormycosis from COVID -19 patient have raised concern for clinicians. Mucormycosis should be highly suspected in COVID 19 patient if slightest symptoms or sign appears, as it might be fatal within few hours. So sample should be collected immediately after clinical suspicious and processed for KOH immediately. Along with suspicion of mucor we have to consider other fungus for diagnosis.
- **Limitation of study-** This study does not include clinical data which corelate with some underlying disease (e.g Diabetes) in cases of Mucorales or previous lung pathology (e.g T.B) in case of aspergillus.

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