



POST COVID-19 FUNGAL INFECTIONS ASSESSMENT AMONG PATIENTS ATTENDING A TERTIARY CARE HOSPITAL

Microbiology

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ABSTRACT

Introduction: Invasive fungal infections have been significantly increasing worldwide due to increase in immunocompromised population and also due to advancement in medical management. It's a known fact that zygomycosis is a most lethal opportunistic invasive fungal infection especially among patients with predisposing factors. So we aimed to study different fungal pathogen along with zygomycosis fungi prevalent in this area among COVID-19 patients.

Materials And Methods: Patients who were diagnosed as COVID-19 before admission either by microbiological or radiological investigations were considered and among those who was suspected of fungal infections were included in this study. All specimens were processed immediately by KOH mount and fungal culture.

Results: Majority of the cases were in the age group of 41 - 50 years which was accountable up to 45.8% followed by 71-80 years age group, it was 12.5%. Out of 24 fungal isolates, 15 (62.5%) were Rhizopus, 7 (29.1%) were Mucor and remaining 2 (8.3%) were Aspergillus.

Conclusion: Early diagnosis by KOH mount or radiological investigations will definitely support clinician to start prompt management as early as possible to avoid severe progression of disease and to reduce the mortality rate of COVID-19 patients.

KEYWORDS

Post Covid-19, Fungal infection

INTRODUCTION

Most of the patients affected by SARS CoV2 recover completely within a few weeks. But some patients continue to experience symptoms; those were referred as Post COVID-19 patients and that condition is referred as POST-COVID-19 syndrome.

Patients experience many post COVID-19 symptoms such as malaise, muscle and joint pains, intermittent fever, chest pain, mood disturbances, SOB, cough etc. and still researches are going on to find out many more symptoms.

SARS CoV2 is a virus responsible respiratory illness and caused COVID-19 pandemic. This virus belongs to coronaviridae which has notable variants of B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.617.2 (Delta), originated from Wuhan, Hubei Province in China. World Health Organization declared the outbreak a public health emergency of international concern on 30 January 2020 and a [pandemic on 11 March 2020 [1].

COVID-19 can also present in some patients with co-infections and super infections. The reason behind co-infections or super infections in COVID-19 patients is inconclusive; even very few studies have been published. Questions have been arising about widespread and irrational use of antibiotics in health care settings and animal husbandry [2].

In India, fungal superinfections were noted among post COVID-19 patients during second wave of pandemic; Rhino-Orbital Mucormycosis co-infections has shown a rise in COVID-19 patients [3].

Invasive fungal infections have been significantly increasing worldwide due to increase in immunocompromised population and also due to advancement in medical management. Major risk factors for mucormycosis include immunocompromised state, diabetes mellitus, on corticosteroid therapy for prolonged time, prolonged stay in hospitals especially Intensive care units [4]. Transmission of Mucormycosis is by the inhalation of spores which are widely distributed in soil, debris and damp places.

Diagnosis of fungal infections is quite challenging for lab doctors, because isolates can be pathogens or commensals or colonizer. Various diagnostic modalities helps to diagnose fungal infections including KOH, Calcoflor white, fungal culture, GMS for tissue specimens, MRI, HRCT. After diagnosing the fungus, correlating with clinical picture is an important aspect for accurate management.

It's a known fact that zygomycosis is a most lethal opportunistic

invasive fungal infection especially among patients with predisposing factors. So we aimed to study different fungal pathogen along with zygomycosis fungi prevalent in this area among COVID-19 patients.

The objectives of the study are

- i) To know the incidence of fungal infections in post covid patients
- ii) To know the age and sex distribution among post covid fungal infected patients
- iii) To study the predominant fungal pathogens affecting COVID-19 patients

MATERIALS AND METHODS

This is a prospective, descriptive, cross-sectional study conducted on 110 samples of SARS CoV2 affected patients suspicious of fungal infections at Department of Microbiology, Government Medical College, Ongole. Patients or Patient attenders were clearly explained about the study and its usefulness; informed consent was taken from them. Patients who were diagnosed as COVID-19 before admission either by microbiological or radiological investigations were considered and among those who was suspected of fungal infections were included in this study. Patients on antifungal medications were excluded from the study.

All patients were advised to undergo endoscopic procedure as soon as clinician suspected of fungal etiology. During endoscopic procedure tissue bits were collected from nasal cavities or sinuses at Department of ENT and those samples were sent in a leak proof, sterile, universal container with normal saline immediately to microbiological laboratory for analysis of fungi.

All specimens were processed immediately at Microbiology department by 10% KOH mount and fungal culture after receiving at lab. Microscopy examination of KOH mount was observed for fungal hyphal filaments and other fungal elements [Fig 1]. Culture samples were inoculated on two sets of Sabouraud dextrose agar and incubated at 25°C and 37°C.

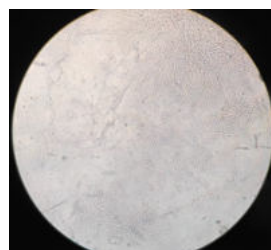


Fig 1. KOH Microscopic Examination Showing Fungal Elements

Fungal cultures were followed until growth occurs or till 28 days. Those cultures which showed positive were identified by macroscopic and microscopic characteristics [Fig 2]. Data was collected and entered in to spread excel sheet to analyse the results. Descriptive quantitative variables were presented as numbers, percentages.



Fig 2. LPCB Mount Of Fungal Culture Showing Rhizopus Morphology

RESULTS

A total of 110 samples of post covid-19 patients suspicious of fungal infections were processed for fungal culture and sensitivity, among them all were above the age of 31 years. Out of 110 studied population, 24 (21.8%) were confirmed fungal infected patients. Predominant number of clinically suspected patients with confirmed fungal positive culture was noted in the age group of 71-80 years.

Among covid-19 associated fungal infected patients majority of the cases were in the age group of 41- 50 years which was accountable up to 45.8% followed by 71-80 years age group, it was 12.5%, 16.6% were 61-70 years, 16.6% were 51-60 year and 8.3% were 31-40 years of age (Table 1).

Table 1. Fungal Culture Positives In Relation To Age

Age in years	No. of fungal suspected cases	No. of fungal positive cases (%)
10-20	2	0 (0)
21-30	5	0 (0)
31-40	12	2 (16.6)
41-50	43	11 (25.5)
51-60	21	4 (19.04)
61-70	17	4 (23.5)
71-80	10	3 (30)

Male predominance was noted. Out of 24 fungal culture positive cases, 15 (62.5%) were males and 9 (37.5%) were females (Table 2).

Table 2. Fungal Culture Positives In Relation To Sex

Sex	No. of fungal suspected cases	No. of fungal positive cases (%)
Female	48	9 (18.7)
Male	62	15 (31.2)

Out of 24 fungal isolates, 15 (62.5%) were Rhizopus, 7 (29.1%) were Mucor and remaining 2 (8.3%) were Aspergillus (Fig 3&4).

Fig 3. Fungal isolates of post covid patients

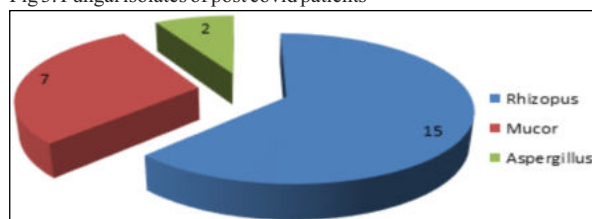


Fig 4:- Showing Fungal Culture of Mucorales

DISCUSSION

The US Centers for Disease Control and Prevention (CDC) defines super infections as “an infection following a previous infection especially when caused by microorganisms that are resistant or have become resistant to the antibiotics used earlier”, while a coinfection is one occurring concurrently with the initial infection, the difference being purely temporal [5].

COVID-19 disease has been rampant throughout the world and devastating the human lives. SARS CoV2 cause severe disease which may require oxygenation, mechanical ventilation and prolonged hospitalization, in few cases even complications may arise, including fibrosis of lungs, hospital acquired infections, opportunistic pathogens invasion. Secondary infections in covid-19 patients might be due to bacterial, fungal and viral; these infections affect mostly patients who are intensive care during hospitalization. Fungal co-infections among covid-19 patients has been reported by various studies [6,7].

Fungal infections, also known as mycosis can affect any organ in the body and also it causes high mortality rate approximately equivalent to tuberculosis and three times more than that of malaria [8]. Comorbid illness such as diabetes mellitus, cancer, immunosuppressed patients, irrational use of broad spectrum antibiotics, patients on corticosteroids or prolonged hospitalization or IV drug abuse, transplantation patients are more susceptible to contract fungal infections. Covid-19 condition is a immunosuppressive, invasive, severe respiratory disease which may require prolonged hospitalization and other invasive procedures such as mechanical ventilation, ECMO etc; in such cases there is a greater chance for fungal pathogens to invade SARS CoV2 affected patients.

Fungal infection invades human body either through breaches in skin or through orifices by its spores. After interaction with the receptors of cells causes cell damage and few fungi can even spread to result in organ and systemic infection. In Immunocompetent people, the polymorphonuclear phagocytes and other immune cells eliminate the spread of fungal infection to deeper tissues. In India, Mucormycosis is emerging among SARS CoV2 patients which are significant health problem, causing high morbidity and mortality [9]. Among covid-19 patient immune dysregulation occurs which results in reduction of T lymphocytes numbers, CD4+T cells and CD8+T cells, may alter innate immune system [10]. Mucormycosis, also known as zygomycosis that belongs to the subphylum Mucoromycotina and order Mucorales; mucorales fungi is a habitat of soil, plants, decaying fruits and vegetables, air, and even the mucus of healthy people.

Among SARS infected patients, fungal infections incidence was reported 14.8% to 33% in few studies [11,12] and it is also responsible for high mortality of 25-73.7% among COVID-19 affected patients, which is a critic determinant of post covid-19 infections [13]; with this it's been clear now how important to consider as a significant public health problem.

In the present study, among covid-19 associated fungal infected patients majority of the cases were in the age group of 41- 50 years which was accountable up to 45.8% followed by 71-80 years age group, it was 12.5%. Out of 24 fungal culture positive cases, 15 (62.5%) were males and 9 (37.5%) were females. Ahmet Dilek et al [14] found 76% were males.

Out of 24 fungal isolates, 15 (62.5%) were Rhizopus, 7 (29.1%) were Mucor and remaining 2 (8.3%) were Aspergillus. A Study from Germany documented that 26.3% were invasive aspergillosis cases among critically ill patients with moderate to severe ARDS [15]. A Study from Netherlands 19.4% was presumed to be infected by invasive pulmonary aspergillosis among ICU patients [16]. El-Kholy NA et al [17] did a study on invasive fungal sinusitis among COVID-19 infected patients by using CT, MRI and H&E investigations in their institution, on confirmation by histologically acute invasive rhino sinusitis cases revealed 77.8% of Mucor species, 30.6% of Aspergillus species and remaining 8.3% of patients were infected with both Mucor and Aspergillus. Wael F Ismaiel et al [18] reported 44.4% of Rhizopus oryzae, 33.3% of Aspergillus fumigatus and 11.1% of Absidia and Mucor and 11.1% of other fungal infections among post-COVID-19 patients. A Multi-centric study from Bangalore, India noted 16 Mucormycosis cases, 1 case of Aspergillosis and 1 Mixed fungal infection on Covid-19 patients with uncontrolled diabetes [19]. Sen M et al [20] did a study in 2021 who observed 6 rhinoorbital

mucromycosis in covid-19 patients, all those patients underwent endoscopic sinus debridement and two among them underwent orbital exenteration.

Mucorales is a rare fungal infection usually, but it is a deadly fungus which can affect sinus, orbital, brain, lungs, intestines, skin, soft tissues and can be life-threatening in immunocompromised patients. Mucorales and other fungal infections involved in causing Acute invasive fungal rhinosinusitis has been evolved during this covid-19 pandemic period especially in India. By keeping the view of aggression of Mucorales and hyalophycomycetes in mind, clinicians should be scrupulous in early diagnosis of these fungi by radiology and laboratory support and also needs to immediate surgical debridement together with vigorous medical management to save human lives.

CONCLUSION

In this study we conclude that Mucorales are most common fungi infecting post covid-19 infected patients and *Aspergillus* is also quite common to report in acute invasive fungal rhino sinusitis clinical entities among SARS CoV2 infected patients. Early diagnosis by KOH mount or radiological investigations will definitely support clinician to start prompt management as early as possible to avoid severe progression of disease and to reduce the mortality rate of COVID-19 patients.

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