Original Research Article

Spectrum of fungal infections in patients with COVID-19

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Abstract

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been sweeping across the globe. Based on a retrospective analysis of SARS and influenza data from China and worldwide, we surmise that the fungal co-infections associated with global COVID-19 might be missed or misdiagnosed. Although there are few publications, COVID-19 patients, especially severely ill or immunocompromised, have a higher probability of suffering from invasive mycoses. Aspergillus and Candida infections in COVID-19 patients will require early detection by a comprehensive diagnostic intervention (histopathology, direct microscopic examination, culture, (1, 3)-b- D-glucan, galactomannan, and PCR-based assays) to ensure effective treatments. We suggest it is prudent to assess the risk factors, the types of invasive mycosis, the strengths and limitations of diagnostic methods, clinical settings, and the need for standard or individualized treatment in COVID-19 patients. We provide a clinical flow diagram to assist the clinicians and laboratory experts in the management of aspergillosis, candidiasis, mucormycosis, or cryptococcosis as comorbidities in COVID-19 patients.

Keywords: COVID-19, SARS-CoV-2, Fungal co infection, Aspergillosis, Candidiasis.

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus2 (SARS-CoV-2), is a new viral respiratory infection first reported in Wuhan (Hubei province), China, at the end of 2019[1], later spread globally to cause the pandemic. Although infection can vary from asymptomatic to mild upper respiratory infection, it can also lead to a severe pneumonia with acute respiratory distress syndrome (ARDS), requiring critical care and mechanical ventilation[2]. SARS-CoV-2 infection leads to both innate and adaptive immune responses, which include a local immune response, recruiting macrophages and monocytes that respond to the infection, release cytokines, and prime adaptive T and B cell immune responses. In most cases, this process is capable of resolving the infection. However, in some cases, which present as severe COVID-19 infections, a dysfunctional immune response occurs, which can cause significant lung and even systemic pathology[3]. The diffuse alveolar lung damage and dysregulated immune response in severe COVID-19 pneumonia makes these patients vulnerable to secondary infections[4]. Viral, bacterial, and fungal co-infections have been reported in COVID-19 patients, and the early diagnosis of these co-infections is important in order to allow for the institution of appropriate antimicrobial therapy[5].

Materials and methods

It is a case series study, conducted in a tertiary centre Basaveshwara medical college and hospital from March 2021 to June 2021. Total of 850 covid-19 positive patients were screened for fungal infection by history, clinical examination and laboratory diagnosis. Total 100 patients were diagnosed to be having fungal infection and included in the study. Socio demographic parameters like age, sex, BMI, were taken. Patient pre-existing co-morbidities were noted, clinical examination including vital parameters and systemic examination was done. Patients were categorized into three categories based on the severity of covid-19 infection and fungal infection. Diagnosis of fungal infection was made by clinical general physical examination, imaging like CT scan thorax, MRI brain and MRI Para nasal sinuses. Patients were categorized based on the severity of disease and pattern of involvement. Majority of the patients were treated medically and few patients requiring surgical invention. **Discussion**:Most common fungal infections encountered in patients with COVID-19 infection are Candidiasis, Aspergillosis and Mucormycosis.Yeast species belonging to the Candida genus, including Candida albicans, Candida glabrata, Candida parapsilosis, Candida tropicalis, and Candida krusei, are the most prevalent fungal species inhabiting various mucosal surfaces, such as the skin and the respiratory, digestive, and urinary tracts[6]. Although being commensal within the human host, Candida species are equipped with virulence attributes, enabling them to invade when opportunities arise and cause various infections in humans, especially when the immune system is impaired[7]. Superficial infections, such as skin disorders; mucosal infections, including oropharyngeal or vulvovaginitis candidiasis; and invasive candidiasis are established clinical entities of candidiasis[8]. Candida is among the most frequently recovered pathogen in the intensive care unit (ICU), a_ecting between 6% and 10% of patients, and some studies have noted an increasing trend for candidemia[9]. Mucormycosis is an angioinvasive disease caused by fungi of the order Mucorales like Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia. The prevalence of mucormycosis in India is approximately 0.14 cases per 1000 population, about 80 times the prevalence in developed countries[10]. COVID-19 infection has been associated with fungal infections. Mucormycosis is more often seen in immunocompromised individuals & complications of orbital & cerebral involvement are likely in diabetic ketoacidosis and with concomitant use of steroids. The most common risk factor associated with mucormycosis is diabetes mellitus in India[11]. In

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the background of the COVID-19 pandemic, only a limited number of cases of mucormycosis have been reported, but there are no known documented cases of sudden-onset visual loss with incidental COVID-19 infection in a newly detected non-ketotic diabetic[12].

Risk Factors

The first group includes common risk factors predisposing ICU patients to invasive candidiasis. These include diabetes mellitus, renal failure requiring hemodialysis, abdominal surgery, triple lumen catheters, parenteral nutrition, receipt of multiple antibiotics, length of ICU stay >7 days, and prior abdominal infections[13].

Diagnosis

The diagnosis of candidemia and other forms of invasive candidiasis remains challenging, which is mostly due to the low number of yeast cells in circulation or infected tissue[14], a requirement of an invasive procedure for diagnosing deep-seated candidiasis, and the use of non-fungal-specific media to culture clinical samples[14]. While culture remains the gold standard, approximately 50% of the invasive candidiasis are not identified by blood culture, and the application of non-culture diagnostics—i.e., beta-D-Glucan (BDG) and mannan antigen testing, and molecular platforms such as PCR and T2 Candida panel—are recommended to improve the diagnosis[14].

Results

Total 100 patients were diagnosed to be having fungal infection and included in the study. Out of which 72(72%) were males and 28(28%) were females (GRAPH-1).

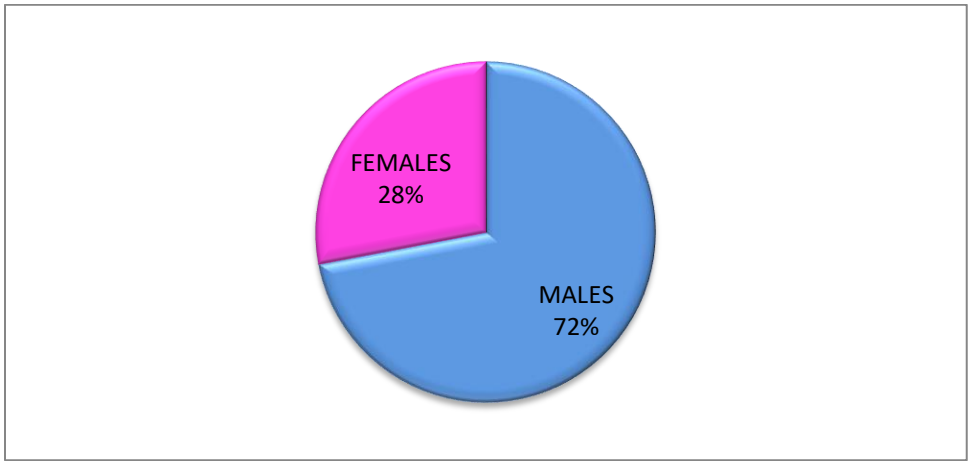

Fig 1: Sex-wise distribution of the sample size.

Candida infection was noted in 46 (46%) patients, Aspergillosis was noted in 36 (36%) patients and mucormycosis was noted in 18 (18%) patients (GRAPH-2).

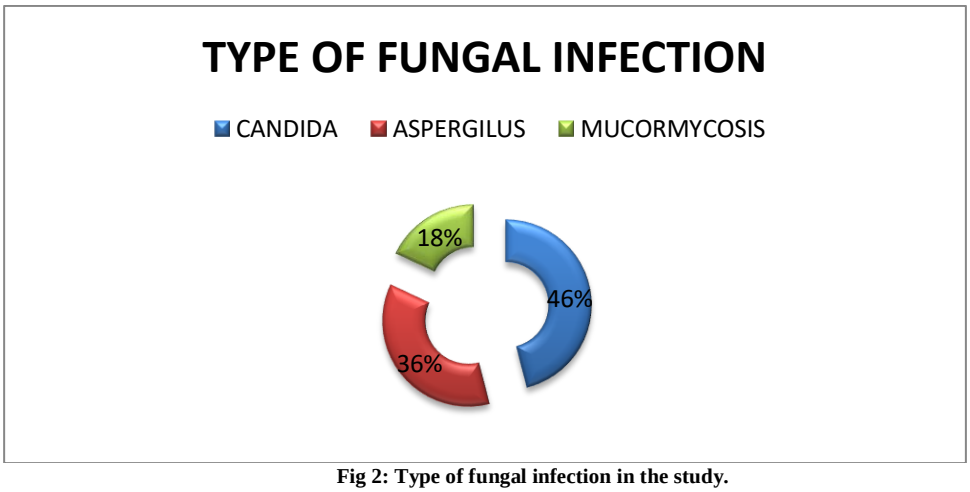

Fig 2: Type of fungal infection in the study.

50(50%) patients were having mild disease, 22(22%) patients were having moderate disease and 28 (28%) patients were having severe disease (GRAPH-3).

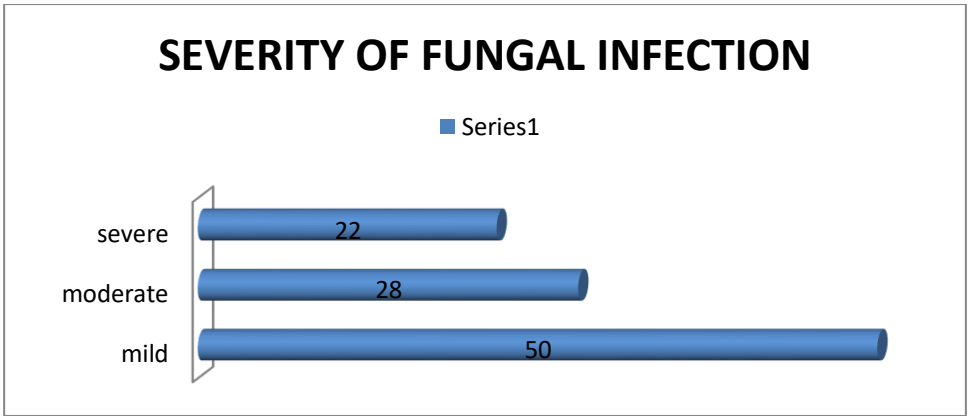

Fig 3: Classification of sample based on severity.

46 (46%) patients were having oro pharyngeal candidiasis, 36 (36%) patients were having pulmonary cavitatory lesion and 12 (12%)patients were rhino mucormycosis, 06(6%) patients were having rhino-cerebro-ocular mucormycosis and 04 (4%) patients were having cerebral mucormycosis (GRAPH-4).

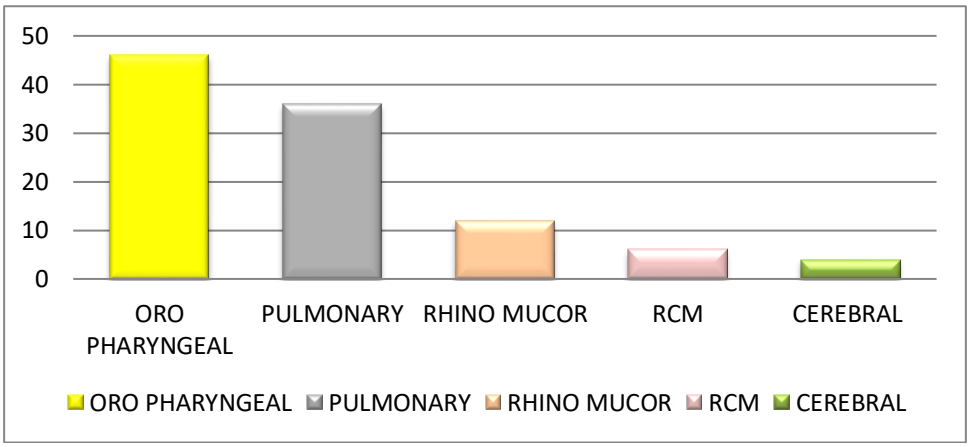

Fig 4: Patten of involvement.

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