ORIGINAL RESEARCH PAPER
Volume - 11 | Issue - 10 | October - 2022 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PREVALENCE OF FUNGAL COINFECTIONS AMONG COVID 19 PATIENTS IN A TERTIARY CARE HOSPITAL

Microbiology

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ABSTRACT

Coronavirus disease 2019 (COVID-19), caused by Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been an emergency global public health events.COVID-19 patients, especially severely ill or immunocompromised, have higher probability of suffering from fungal coinfections. The study aims to investigate the prevalence of fungal coinfections among patients with confirmed severe acute respiratory syndrome coronavirus 2(SARS-CoV-2).A prospective study was undertaken in the Department of Microbiology, Government Medical College, and Amritsar for a period of 6 months from May 2021 to October 2021. A total of 216 confirmed cases of COVID 19 disease were enrolled for the study. Various clinical samples obtained were processed by direct microscopic examination in 10% KOH solution, Gram stain, Calcoflour white staining and culture on Sabouraud dextrose agar media. Identification of fungi was done by lacto Phenol Cotton Blue, Germ tube test and Candida CHROM agar for species identification.Out of 216 cases, 138 were culture positive. Candida species were predominant isolates with Candida albicans (49%) being the major species followed by Aspergillus species (21.7%), Mucorales (19%) and mixed growth (1%). Predominantly males were affected in the age group of 46-55 years. Most common risk factor was hypertension (42%).An increasing prevalence (63.8%) of fungal coinfections has been reported among COVID 19 patients resulting in poor patient outcome and high mortality rates. Therefore, awareness of high risk of occurrence of fungal infections is crucial to downgrade any delay in diagnosis and treatment to support the prevention of complications related to these infections.

KEYWORDS

COVID-19, Coinfections, Candida, Aspergillus, Mucorales.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), an etiological agent of coronavirus disease 2019 (COVID-19), has arisen from Wuhan, China, in late 2019, it has swept globally to pandemic proportions resulting in catastrophic healthcare and economic threats[1,2].

Globally, till now 603,164,436 confirmed cases of COVID 19, including 6,482,338 deaths have been reported as per WHO. The main confounders of the deadly turnaround of events in India are dense population of more than 1.3 billion, poor socioeconomic status of majority of the people, overcrowding, inadvertent use of corticosteroids for treating mild to moderate infections, failure to follow norms of COVID appropriate behaviour, over the counter availability of drugs and prevailing epidemic of diabetes mellitus type-2[3].

SARS-CoV-2, is an enveloped, novel, single-stranded positive sense RNA beta coronavirus of the family Coronaviridae[2].The virus utilizes the human angiotensin-converting enzyme 2 (ACE2) receptors located on cells in many organs/tissues, to gain entry and trigger a range of clinical manifestations. The clinical manifestations range from a self-limiting illness to more severe complications, including acute respiratory distress syndrome, sudden cardiac death, liver dysfunction, and multi-organ failure, particularly due to SARSCoV-2's high human-to-human transmission rate via respiratory droplets[4].

Severe COVID-19 disease provides an ideal environment of hypoxia, new onset or steroid-induced hyperglycaemia, metabolic acidosis, diabetic ketoacidosis, increased ferritins and decreased phagocytic activity of white blood cells due to immunosuppression which increases the susceptibility to bacterial and fungal infections in patients with predisposing factors of diabetes, mechanical ventilation and cytokine storm[5,4,1] leading to blindness, pulmonary embolism, pneumonia, acute increased mortality and morbidity. Therefore, the present study was aimed to evaluate prevalence of fungal Coinfections among COVID 19 patients in a tertiary care hospital in North India.

MATERIAL AND METHODS

A prospective study was undertaken in the Department of Microbiology, Government Medical College, and Amritsar for a period of 6 months from 1st May 2021 to 31st October 2021. A total of 216 confirmed cases of COVID 19 disease were enrolled for the study. Various clinical samples like sputum sample, tissue sample, nasal swab, pus swab, nasal secretions, tracheal aspirate and pleural fluid were received in the Department of Microbiology. These samples were processed for direct examination of fungal elements in 10% KOH solution, under low power as well as high power microscope. Each sample was tested using Calcoflour white staining method under fluorescent microscope. This was followed by culture on Sabouraud dextrose agar media with chloramphenicol and gentamycin drugs at 25◦C and at 37◦C for 4 weeks. The presence of fungal elements in KOH mount was confirmed by growth on SDA. If growth was seen on SDA medium, the morphology of fungal isolates was further studied by using the Lacto Phenol Cotton Blue (LPCB) for identification of fungi. The growth was observed for the following-rate of growth, morphology of colony, texture and surface pigmentation.

Gram staining was done for presumptive identification of yeast and yeast like cells. The Various Candida species were identified by Germ tube tests and Candida CHROM agar.

RESULTS

Out of 216 samples, 130 were nasal swabs, 50 sputum samples, 22 tissue samples, 6 pleural fluid samples, 5 nasal secretions, 2 pus swabs and 1 tracheal aspirate. Maximum samples were received from Medicine department (137), followed by from Intensive care unit (55), Gynaecology ward (10), Ear nose and throat department (7) and Surgery department (7).

On KOH examination, budding yeast cells were seen in 80 samples, acute branching with thin hyaline septate hyphae were seen in 29 samples while broad aseptate hyphae with right angle branching were seen in 26 samples. Calcoflour white staining method showed synchronous results with KOH preparation.

On culture, 138 samples were found to be positive for fungal culture while 78 samples were found to be negative for culture as in Table 1.

Table - 1 Fungal Isolates

Sr.NO	Fungal isolates obtained	Number	Percentage
1)	Candida species		
(i)	Candida albicans	68	49%
(ii)	Candida parapsilosis	10	7.2%
(iii)	Candida krusei	1	0.7%
(iv)	Candida tropicalis	1	0.7%
2)	Aspergillus species		
(i)	Aspergillus fumigatus	15	11%
(ii)	Aspergillus flavus	8	6%
(iii)	Aspergillus Niger	5	4%
(iv)	Aspergillus terreus	1	0.7%
3)	Mucorales		
(i)	Mucor	4	3%
(ii)	Rhizopus	22	16%
4)	Mixed growth	2	1%
5)	Lab contaminants	1	0.7%
	Total	138	

Major fungal isolates were Candida (80), followed by Aspergillus (29) and Mucorales (26). Mixed growth was observed in 2 cases. Among Candida species, Candida albicans (68) was predominant followed by Candida parapsilosis (10). Aspergillus fumigatus (15) was the most common Aspergillus species followed by Aspergillus flavus (8). 22 of these patients reported with symptoms of acute respiratory distress and 7 reported with nonspecific symptoms. Rhizopus was major isolate in case of Mucorales. Furthermore, 26 cases were confirmed to be suffering from mucormycosis. 20 of these patients presented with rhino-oculo-cerebral manifestations, 4 patients presented with pulmonary symptoms and 2 presented with uncommon symptoms. Hypertension was the most common risk factor 58(42%), followed by Diabetes mellitus 40(29%), invasive respiratory support 24(17%) & corticosteroid/Antibiotic overuse 16(12%) in patients suffering from fungal infections as in table 2.

Table -2 Risk Factors

Sr. no	Risk factor	N=138	Percentage
1	Hypertension	58	42%
2	Diabetes mellitus	40	29%
3	Invasive respiratory support	24	17%
4	Corticosteroid/Antibiotic overuse	16	12%
	Total	138	

Maximum number of patients 53(38.4%) were seen in age group of 46-55 years , followed by 36-45 years 47(34%), 56-65 years 17(12.3%). Fungal infections were more frequent among males (73) than females (65) as in table 3.

Table -3 Distribution Of Age And Gender In Culture Positive Patients

Sr.NO	Age group (in years)	Male	Female	Percentage
1	15-25	3	3	6(4.3%)
2	26-35	5	3	8(5.7%)
3	36-45	25	22	47(34%)
4	46-55	30	23	53(38.4%)
5	56-65	8	9	17(12.3%)
6	66-75	1	4	5(3.6%)
7	76-85	1	1	2(1.4%)
	Total	73	65	138

DISCUSSION

Severe acute respiratory syndrome coronavirus 2, had been armed by special abilities to spread and dysregulate the immune mechanisms. Several studies had addressed the probability of occurrence of fungal co-infections, particularly candidiasis and invasive pulmonary aspergillosis in COVID-19 patients[6].

In the present study, prevalence of fungal confections among COVID-19 patients was found out to be 63.8%.

Fungal confections were common in the age group of 46-55 years among males. Patients were within age range of 15-85 years with median age of 50 years. The findings of this study are comparable to study done by Bineeta Kashyap et at[7], Madhulika Mistry et al[8], Carolina Garcia-Vidal[9], and P. Lewis White et al[10]. Various factors accounting for fungal confections include increased prevalence of medical comorbidities, high-density housing, stigma, and barriers to accessing medical care.

Hypertension (42%) was the predominant confounding factor among COVID 19 patients in the present study, followed by diabetes mellitus (29%), invasive respiratory support (17%) and corticosteroid/ antibiotic overuse (12%). A highly complex interplay of the risk factors, use of steroids for treatment of COVID 19, along with markedly lower absolute number of T lymphocytes, CD4+T and CD8+T cells among COVID 19 patients results in severe immunosuppression allowing the colonization of various fungi. Our findings were consistent with the findings of Mohammadreza Salehi et al[6], Guan W-J et al[11] and Arnaud Fekkar et al[12].

Candida species was predominantly isolated with Candida albicans being the most common fungal species followed by Aspergillus species. Among Aspergillus species, Aspergillus fumigatus was predominant fungal species among COVID 19 patients as aforementioned in this study which coincides with the study done by Mohammadreza Salehi et al[6] and Chih Cheng Lai et al[13].

Rhizopus was found in 22 cases with Rhizopus arrhizus being predominant species, followed by Mucor in 4 and mixed growth in 2 of 138 cases, which is similar to the study done by Martin Hoenigl et al[14] and Moorthy et al[4]. It has been documented that immune dysfunction, diabetic ketoacidosis and raised free iron levels are all favourable factors for the growth and development of Mucorales among COVID 19 patients.

CONCLUSION

As COVID 19 continues to spread worldwide, it is important to continue to consider Coinfections including fungi especially in the at risk groups like with cardiovascular disease, diabetes mellitus and antibiotic overuse. In the present study prevalence of fungal confection among COVID 19 patients, was found to be high. Therefore, assessment of risk factors, type of invasive mycosis are important principals for early detection of fungal pathogens for reducing mortality and morbidity.

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