

EXPONENTIAL RISE IN INCIDENCE OF MUCORMYCOSIS IN THE MONTH OF APRIL AND MAY 2021

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Abstract

Introduction: The coronavirus disease 2019 (COVID-19) infection occurs due to acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may be associated with mild disease to life-threatening pneumonia. The incidence of opportunistic fungal infections is dramatically increased in COVID-19 patients with diabetes, mechanical ventilation and cytokine storm. The present prospective study has focused on summarizing the fungal infections reported in COVID-19 positive or post-COVID patients. **Aims:** To estimate the age and sex wise incidence and clinical presentation of mucormycosis in Post-COVID patients and to diagnose the mucormycosis as early as possible. **Methods:** A present study consists of 554 newly diagnosed cases of mucormycosis over a period of two months i.e. from 1st April, 2021 to 31st May, 2021. Out of them 531 cases of routine histopathological examination were processed in autotechnicon and stained with H & E stain. The 21 cases of rapid diagnosis for mucormycosis were studied by KOH, LPCB preparation and H & E stained smear examination. **Results:** A total of 554 cases of mucormycosis were diagnosed during last two months. The incidence is highest in May 2021 (90.76 %) after the second wave of COVID-19 infection. The highest incidence was identified in 6th decade of life with 34.52% followed by 5th decade (22.51%). The most common complaint was Headache (36.82 %). The other complaints were eye swelling and eye pain (17.15 %), facial swelling (9.93 %) and facial pain (9.57 %). Decreased vision or loss of vision was also noted. The most commonly involved site is bilateral nasal cavity (77.44 %). The incidence is also higher in known case of diabetes. **Conclusion:** COVID-19 is associated with a significant rise in incidence of secondary infections, particularly fungal infection – mucormycosis.

Keywords: Mucormycosis, Rapid diagnosis

Introduction:

The coronavirus disease 2019 (COVID-19) infection caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may be associated with a wide range of disease patterns, ranging from mild to life-threatening pneumonia.¹The pandemic coronavirus disease-2019 (COVID-19) resulted in more than 25 million confirmed cases worldwide, including over 850,000 associated deaths (<https://covid19.who.int/>). The important risk factors associated with severity and mortality in COVID-19 are

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older age, hypertension, chronic obstructive pulmonary disease (COPD), diabetes and cardiovascular disease.² Patients with severe COVID-19 infection requiring intensive care may also be challenged to battle against other coexisting infectious agents, such as other respiratory viruses (e.g. influenza), gram-positive and gram-negative bacteria and fungi (both yeasts and filamentous fungi). Corroborating this statement, we have witnessed increasing reports on the co-occurrence of respiratory viruses, like influenza epidemics/pandemics, and secondary invasive fungal infections, resulting in poor patient outcome and, consequently, high mortality rates. Therefore, this critical reality demands urgency for special focus on different aspects of this disease.³

Since most of the hospitalized COVID-19 patients are under severe medication care, as in ICU who are intubated or required mechanical ventilation, are potentially vulnerable for acquiring hospital infections. In this type of patients, broad-spectrum antibiotics were prescribed in 75% of COVID-19-infected patients.⁴

Relevantly, the incidence of opportunistic fungal infections is dramatically increased in COVID-19 patients with predisposing factors (e.g., diabetes, mechanical ventilation and cytokine storm). In fact, researchers around the world have been faced with many challenges regarding identification and diagnosis of fungal infections. As a result, early diagnosis and appropriate antifungal strategies for treatment have attracted attention to deal with it on a global scale. Moreover, the treatment of fungal infection is very costly and can be translated into a considerable impact on the economy of the health care systems across the globe.

With all this information, the present prospective study has focused on summarizing the fungal infections reported in COVID-19 positive or post COVID patients.

Aims and objectives:

- To estimate the age and sex wise incidence of mucormycosis in Post-COVID patients
- To find out incidence of various clinical presentations and site of involvement in patients with mucormycosis
- To diagnose the mucormycosis microscopically in Post-COVID patients as early as possible.
- To estimate the exponential rise in mucormycosis in Post-COVID patients

Materials and methods:

The present study consisted of 554 newly diagnosed cases of mucormycosis over a period of two months i.e. from 1st April, 2021 to 31st May, 2021; to know the age and sex wise incidence of mucormycosis in COVID or Post-COVID patients in tertiary care teaching hospital. Each of the 554 cases diagnosed as mucormycosis was studied in detail regarding detailed clinical history including age, sex, chief complaint, sites of involvement and physical examination. Radiological investigation was carried out. Tissue biopsy was received in normal saline for rapid diagnosis and in 10% neutral buffered formalin for routine histopathological examination. KOH Preparation and LPCB Preparation was prepared from fresh tissue received in normal saline and wet preparation is examined under microscope. The smears were prepared from fresh tissue received in normal saline, fixed with 95 % ethyl alcohol, stained by Haematoxylin and eosin stain and examined under microscope. The tissue, which was received

in 10% neutral buffered formalin, was fixed for overnight. Routine tissue was processed using autotechnicon and stained with H & E stain. PAS stain was performed as & when required. Microscopic diagnosis of mucormycosis was performed.

Results

A total of 554 newly diagnosed cases of mucormycosis in COVID and Post-COVID patients over a period of two months, i.e. from 1st April, 2021 to 31stMay, 2021 were studied in detail. Out of them 21 cases were examined for rapid diagnosis by wet preparation using KOH & LPCB method and smear examination. The remaining 533 cases were examined by routine histopathological examination.

Table 1 shows month wise incidence of mucormycosis in COVID and Post-COVID patients. It shows incidence is highest in May, 2021 (90.79 %).

Table 1: Month wise incidence of mucormycosis in COVID and Post-COVID patients

Month	Routine Histopathological examination	Rapid Diagnosis	Total	Percentage (%)
Apr-21	42	9	51	9.21
May-21	491	12	503	90.79
Total	533	21	554	

Table 2 shows, age and sex wise incidence of mucormycosis during biopsy examination. It suggests that the highest incidence was identified in 6th decade of life with 34.52% (184 cases) followed by 5th decade (22.51%). Our youngest patient was infant girl, while oldest patient was 82-year-old male. The number of cases significantly increases in old age group. Incidence is higher in male compare to female with M: F ratio of 2.29:1.

Table 2: Age and Sex wise incidence of Mucormycosis during Biopsy examination

Age group (years)	Male	Male percentage	Female	Female percentage	Total	Percentage
0-10	0	0	1	0.62	1	0.19
11-20	2	0.54	0	0	2	0.38
21-30	14	3.77	4	2.47	18	3.38
31-40	50	13.48	13	8.02	63	11.82
41-50	75	20.22	45	27.78	120	22.51
51-60	123	33.15	61	37.65	184	34.52
61-70	85	22.91	24	14.81	109	20.45
71-80	20	5.39	14	8.64	34	6.38
81-90	2	0.54	0	0	2	0.38
Total	371		162		533	

Table 3 shows, age and sex wise incidence of mucormycosis during rapid diagnosis by smear examination. It suggests that the highest incidence was identified in 6th decade of life with 47.62 % (10 cases) followed by 5th decade (23.81 %). Our youngest patient was 38-year-old male, while oldest patient was 73-year-old female. Incidence is higher in male compare to female with M: F ratio of 2.5:1.

Table 3: Age and Sex wise incidence of Mucormycosis during rapid diagnosis

Age group (years)	Male	Male (%)	Female	Female (%)	Total	Total (%)
31-40	2	13.33	0	0	2	9.52
41-50	5	33.33	0	0	5	23.81
51-60	5	33.33	5	83.33	10	47.62
61-70	2	13.33	0	0	2	9.52
71-80	1	6.67	1	16.67	2	9.52
Total	15		6		21	

Table 4 shows chief complains of patients, it shows the most common complaint was Headache (36.82%) followed by Eye swelling/ Eye pain (17.15%). Due to mucor ophthalmic involvement is also common, which may lead to decreased vision (0.72%) or loss of vision (0.90%). The most common involvement is nasal sinusitis or pansinusitis (13.51%) which may lead to headache, facial swelling, facial numbness, nasal discharge or nasal blockage. The incidence is also higher in known case of diabetes (31 cases). In 4 cases history of hypertension is also present. History regarding chronic renal disease or rheumatoid arthritis was not reported in any case.

Table 4: Chief complaints of patients

Complain	Routine Histopathological Examination			Rapid Diagnosis	Total	Percentage (%)
	Male	Female	Total			
Headache	138	61	199	5	204	36.82
Nasal Obstruction	8	3	11	4	15	2.71
Eye Swelling/Eye pain	77	17	94	1	95	17.15
Facial Pain	34	14	48	5	53	9.57
Facial Swelling	41	13	54	1	55	9.93
Nasal Blockage	32	12	44	1	45	8.12
Loss Of Vision	4	1	5	0	5	0.90
Decreased Vision	4	0	4	0	4	0.72
Facial Numbness	3	2	5	2	7	1.26
Palatal Erosion	0	3	3	0	3	0.54
Nasal Discharge	1	0	1	0	1	

Table 5 shows site wise incidence of mucormycosis. Bilateral Nasal cavity was most

commonly involved (77.44%), followed by maxillary involvement (20.94%). Eye ball was also received in the section, which was almost 4.15%.

Table 5: Site wise incidence of Mucormycosis

Site	Routine Histopathological Examination			Rapid Diagnosis	Total	Percentage (%)
	Male	Female	Total			
B/L Nasal Cavity	287	121	408	21	429	77.44
Maxilla	82	34	116	0	116	20.94
Eye Ball	12	11	23	0	23	4.15

Microscopic examination was carried out after H & E stain. The aspetate or minimally septate, broad, ribbon-like hyphae (10-20 μmeters) with right angle branching which was differentiated from aspergillus. Aspergillus shows septate hyphae (2.5 -4.5 μmeters) with acute angle branching with presence of fruiting bodies. Both invade the blood vessels.

Figure 1: Mucor - hyphae in KOH &LPCB preparation (Left upper inset LPCB & Right upper inset KOH preparation)

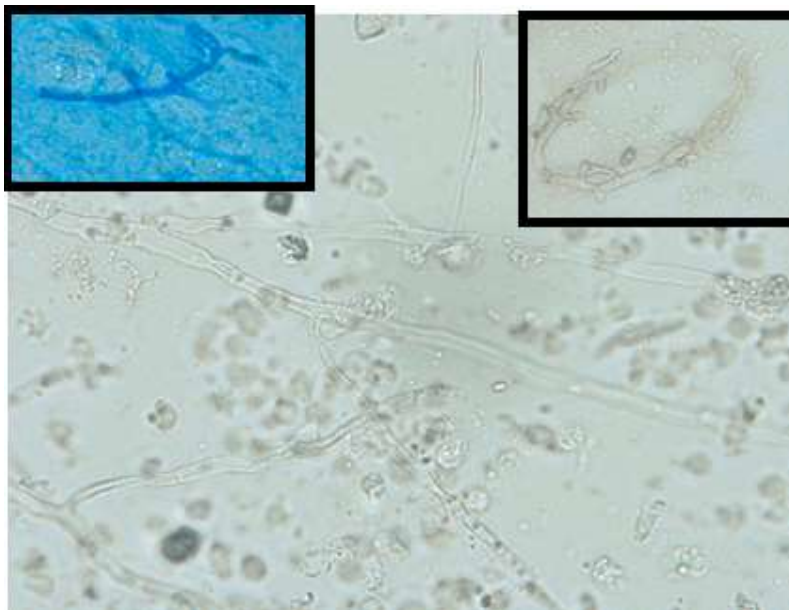
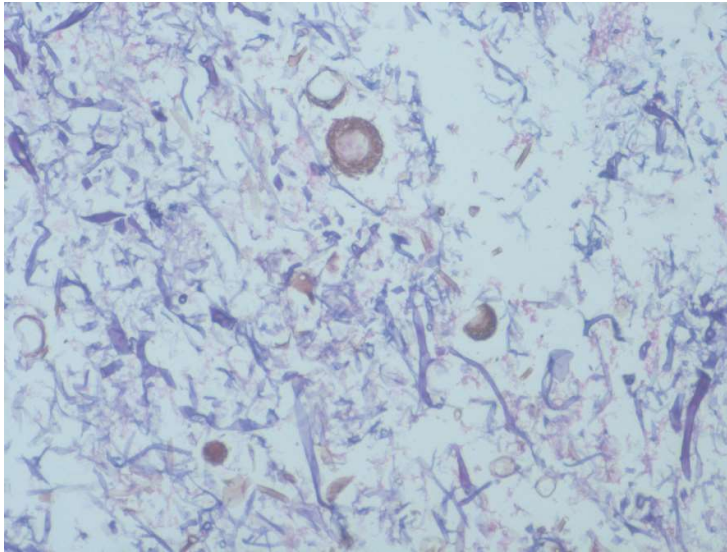


Figure 2: Mucor- Hyphae & Spores (H & E Stain - High Power)

Discussion

COVID-19 is the disease caused by a new coronavirus called SARS-CoV-2. It is characterized by Fever, Dry cough and Fatigue. It may be associated with loss of taste or smell, nasal congestion, conjunctivitis, sore throat, headache, muscle or joint pain, skin rash, nausea or vomiting, diarrhoea, etc.

If COVID-19 infection is mild the patient can be treated at home. If the person is older or having other comorbid illness like diabetes or hypertension, the chances of severe Covid infection is higher. Steroids reduce inflammation in the lungs for Covid-19 and also reduces damage to the immune system and hence used into severe COVID-19 infection.

Mucormycosis, a rare fungal infection has higher rate mortality, triggered by the use of steroids, a life-saving treatment for severe and critically ill Covid-19 patients. The risk of Mucormycosis or black fungus is even higher Covid, diabetes, kidney disease, liver or cardiac disorders, age-related issues, or those on medication for auto-immune diseases like rheumatoid arthritis.

As a tertiary care teaching hospital, we identified exponential rise in mucormycosis cases during last two months due to second wave of COVID-19 pandemic. As a result of COVID-19 pandemic the resurgence of mucormycosis. The incidence was increases in January 2021 after the first wave of COVID-19 infection. The second wave of COVID-19 infection, lead to resurgence of fungal infection in April and May. Many of them were recovered from COVID-19 infection and were later on suffered with fungal infection. The infection is higher in male compare to female with M: F ratio of 2.29:1.

The incidence is higher in in 6th decade of life with 34.52 % due to high incidence of diabetes, hypertension and use of steroid.

The most common complain is Headache (36.82 %) followed by Eye swelling/ Eye pain (17.15%) & most common site is nasal cavity (77.44 %), this is due to occurrence of rhino-

orbital-cerebral mucormycosis, our twelve male and eleven female patients had surgically removed their eye due to fungal infection.

Dr Nair, who works in three hospitals in Mumbai, reported 40 patients suffering from the fungal infection in April, due to second wave of COVID-19 infection.⁵ Dr Raghuraj Hegde, from southern city of Bengaluru, reported 19 cases of mucormycosis in the past two weeks.⁵

The incidence of mucormycosis has risen more rapidly during the second wave compared with the first wave of COVID-19 in India, with at least 14 872 cases till May 2021.⁶ The state of Gujarat alone contributed to the highest number of cases, with at least 3726 cases of mucormycosis in patients with active and recovered COVID-19, followed by the state of Maharashtra⁶

The fungal infection- mucormycosis was treated with antifungal medicine, usually amphotericin B, posaconazole, or isavuconazole intravenously or oral posaconazole and isavuconazole.

Conclusion

COVID-19 is associated with a significant incidence of secondary infections, particularly fungal infection probably due to immune dysregulation. Additionally, the widespread use of steroids/ broad spectrum antibiotics may lead to increase incidence of mucormycosis, which is still higher in diabetics or other immunocompromised patients. The use of therapeutic agents should be monitored to achieve a therapeutic effect at the lowest dose and shortest durations. The use of broad-spectrum antibiotics, especially in the absence of infection, should be re-evaluated.

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