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A PROSPECTIVE STUDY ON MUCORMYCOSIS IN COVID-19 AFFECTED PATIENTS IN A TERTIARY CARE HOSPITAL

Microbiology

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ABSTRACT

Background and aim: Mucormycosis is an invasive fungal infection and carries a significant mortality and morbidity. A number of cases have been reported in association with COVID-19. It affects severely immunocompromised patients with certain risk factors like diabetes, steroid therapy, etc. We studied the association of risk factors in COVID-19 affected patients during active infection and in the recovery phase of infection. Material and Methods: We studied 500 clinically suspected cases attending ENT OP from May 2021 to August 2021. Samples were processed and identified by direct microscopy and culture. **Results:** Out of 500 samples tested, 110 were identified as Mucormycosis. Among them 81% were Rhizopus spp, 16% were Mucor spp and 3% were Rhizomucor spp. Of all 110 cases, 18% were identified by microscopy alone, 39% were identified by culture alone and 47% were identified by both microscopy and culture. Among them 59% were hyperglycaemic and 76% were on steroid therapy. Majority of the cases were presented in the recovery phase of COVID-19 (81%) than during the active phase of infection (19%). **Conclusion:** Mucormycosis is an opportunistic fungal infection commonly affecting severe immunocompromised patients. Judicious use of steroids and stringent glycaemic control are vital to prevent mucormycosis. Early diagnosis and intervention can prevent the severity of disease.

KEYWORDS

COVID-19, Diabetes, Mucormycosis, Recovery phase, Steroid therapy

INTRODUCTION

Mucormycosis is an infection caused by a group of filamentous molds belonging to the order Mucorales. These saprophytic fungi are found ubiquitously in the soil, environment, food items and also frequently encountered as laboratory contaminant. Infection can occur by inhalation, percutaneous inoculation or ingestion. In the developed countries, Mucormycosis occurs primarily in severe immunocompromised hosts. In contrast, in developing countries like India, most of the cases of Mucormycosis occur in patients with poorly controlled diabetes mellitus and also immunocompetent subjects following trauma.

Opportunistic fungal infections including Mucormycosis, Aspergillosis, Penicilliosis and invasive Candidiasis have been reported in patients with severe COVID-19 or those recovering from the disease. Of all these, Mucormycosis is the most severe co-infection associated with COVID-19. India has reported a recent surge in Mucormycosis cases during this COVID-19 pandemic. Mucormycosis in severe cases of COVID-19 might be due to factors like increased glycaemic status, use of corticosteroids, granulocytopenia, increased serum ferritin and immunosuppressive conditions.

Mucormycosis has a predilection for vascular invasion causing thrombosis and infarction, thereby leading to necrosis of affected tissue. In such type of clinical setting, infection with Mucormycosis carries very poor prognosis. High fatality rate for severe infection was found despite active treatment.

Therefore, early intervention and prompt treatment can help to prevent high morbidity and mortality in Mucormycosis infection. As there was a rapid increase in Mucormycosis cases during this pandemic I have taken up this study for early diagnosis and treatment.

MATERIAL AND METHODS

A prospective study was conducted on a total number of 500 clinically suspected cases attending ENT outpatient department from May 2021 to August 2021. Samples were taken either by tissue biopsy, deep nasal swab, scrapings from nasal mucosa, swab from nasal sinuses or sometimes sputum.

Mucormycosis was identified by direct microscopy and culture. The samples were processed by direct microscopy using 10% potassium hydroxide in which Mucormycetes showed characteristic broad, non-septate or sparsely septate, ribbon like hyphae with wide angle branching at irregular intervals. Direct microscopy is followed by inoculation of specimen on two SDA slopes (Sabouraud's dextrose agar) with antibiotics and without cycloheximide and incubated at 25oC and 370C respectively. Growth was seen within 2-4 days as floccose, dense cotton candy or fluffy growth filling the entire tube. Adhesive tape technique with lactophenol cotton blue (LCB) mount was done from the culture growth for observing the microscopic morphology of the fungal growth. Slide culture was also done on cornmeal agar to know the undisturbed morphology of fungal isolate.

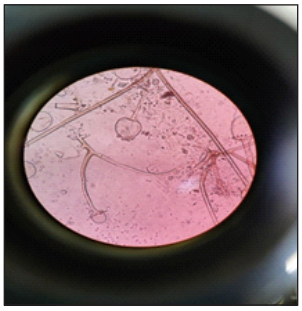

Fig.1. KOH mount showing broad, non-septate hyphae with wide angle branching

Fig.2. SDA slope showing fluffy dense cottony colony

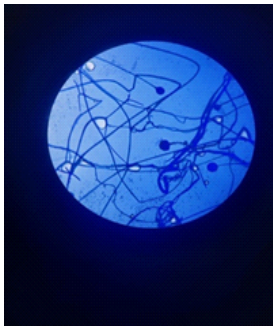

Fig.3. LCB mount by adhesive tape technique

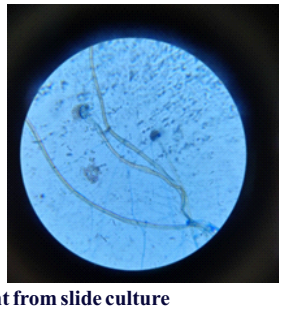

Fig.4. LCB mount from slide culture

RESULTS

A total number of 500 clinically suspected cases of Mucormycosis, attending ENT OP were screened for Mucormycosis by fungal culture and microscopy.

Table 1. Distribution of fungal positivity

Total tested	No. identified		No fungi grown/identified
	Mucormycetes	Other fungi	
500	110	186	204

Out of 500 tested, 110 cases were found to be positive for Mucormycetes by microscopy and/or culture. Other fungi were isolated in 186 cases and no growth was observed in 204 cases.

Table 2. Sex wise distribution of Mucormycosis cases (n=110)

Sex	No. of positives	Percentage
Male	86	78%
Female	24	22%

Out of 110 Mucormycosis cases, 78% were found to be males and 22% were found to be females, showing male preponderance.

Table 3. Species wise distribution of Mucormycosis isolates (n=110)

Isolate	No. of positives	Percentage
Rhizopus spp.	89	81%
Mucor spp.	18	16%
Rhizomucor spp.	03	03%

Out of 110 identified, predominant isolate was found to be Rhizopus spp (81%), followed by Mucor spp (16%) and around 3% were Rhizomucor spp.

Table 4.Comparision of direct microscopy and culture (n=110)

Method	No. of positives	Percentage
Microscopy positive Culture negative	20	18%
Culture positive Microscopy negative	43	39%
Both Culture and Microscopy positive	47	43%

Out of 110 cases, 20 cases were identified by only microscopy (18%) and 43 by only culture (39%), whereas both microscopy and culture were positive in 47 cases (43%).

Table 5. Association of Mucormycosis with blood glucose levels (n=110)

Diabetic status	No. of cases	Percentage
Known Diabetic	35	32%
Non-diabetic	Increased blood glucose	30	27%
	Normal blood glucose	45	41%

Among 110 cases, known diabetics were 35 and non-diabetics with increased blood glucose levels under treatment of COVID-19 were 30 and non-diabetic with normal blood glucose levels were 45. Majority of cases were found to be associated with increased blood glucose levels.

Table 6. Association of Mucormycosis with steroid therapy (n=84)

No. of cases on steroid therapy	No. of cases on steroid therapy in known Diabetes	No. of cases on steroid therapy who are non-diabetic and developed drug induced hyperglcaemia	No. of cases on steroid therapy who are non-diabetics and with normal blood glucose level
84	30	22	32

Among 110 Mucormycosis cases, 84 were on steroid therapy during COVID-19 treatment. Of these, 30 were found to be known Diabetics and 22 were non-diabetics but developed high blood glucose levels during treatment. Remaining 32 were non-diabetics with normal blood glucose level even with steroid therapy.

Table 7. Association of Mucormycosis with oxygen therapy

Total positives	No. of cases on oxygen	No. of cases not on oxygen
110	44	66

Among 110 cases, 44 cases were found to be on oxygen therapy during COVID-19 treatment and 66 were found to be without oxygen therapy.

Table 8. Association of Mucormycosis cases with active covid and post covid period (n=110)

Stage of infection	No. of positives	Percentage
Active covid	21	19%
Post covid	89	81%

Among 110 cases, 21 were in active phase of covid infection and 89 were found to be in the recovery phase of covid-19. Majority of the cases were presented in the recovery phase of the COVID-19 than during active phase.

DISCUSSION

Mucormycosis is a sporadic disease that occurs almost exclusively in immunocompromised patients[6]. The order Mucorales includes the genera Mucor, Rhizopus, Rhizomucor, Lichtheimia, Syncephalastrum, Apophysomyces, Cokeromyces, Cunninghamella and Saksenaea species. In our study, we identified Mucor spp, Rhizopus spp and Rhizomucor spp, of which Rhizopus was found to be the predominant isolate.

The sudden surge in the incidence of Mucormycosis during COVID-19 pandemic raises the possibility that COVID-19 infection may itself predispose to Mucormycosis. This may occur directly through its impact on immune system and other systems or indirectly due to the interventions in COVID-19 management[7].

We found that COVID-19 patients who were treated with steroids and patients with increased blood glucose levels were more affected with Mucormycosis.

The high case fatality rate in COVID-19 disease is due to significant cytokine storm, which is the host's excessive immunological response, responsible for the host tissue damage (pulmonary alveolar destruction and systemic inflammation), resulting in respiratory and multi-organ failure[1]. Corticosteroids have been proven to reduce cytokine release but it also leads to drug induced hyperglycaemia in non-diabetics and aggravation of blood glucose levels in known diabetics.

Pathological changes in the pancreas were observed in patients with severe COVID-19 indicating that SARS-COV-2 virus can cause pancreatic injury[2]; and this could be one of the reasons why COVID-19 patients without previous history of diabetes have high blood glucose levels[3]. Diabetes related hyperglycaemia is thought to cause immune response dysfunction, resulting in an inability to control the spread of invading pathogens[4]. Hence co-existence of diabetes, steroid therapy and covid -19 might have lead to severe fungal

colonisation such as Mucormycosis.

In our study, majority of patients who were identified with Mucormycosis were found to be having increased blood glucose levels.

Furthermore use of high-flow oxygen also considered as a factor to cause fungal colonisation. Contamination with the use of industrial oxygen, low quality oxygen piping systems, low quality oxygen cylinders and ordinary tap water in ventilators are also considered as causative factors[5]. But in our study, we didn't find any association of Mucormycosis with oxygen therapy.

Use of other unproven treatment regimes for COVID-19 like zinc and iron supplements, aid the fungus to grow by providing the right environment.

Other factors like prolonged use of ventilators and humidifiers and unhygienic use of masks are also associated with the rise of mucormycosis cases.

In our study majority of mucormycosis cases were seen 2-3 weeks after the onset of COVID-19 symptoms as steroid therapy was started during 2nd week of infection which favours fungal colonisation.

CONCLUSION

Mucormycosis is an opportunistic fungal infection associated with high mortality and morbidity. It can be easily diagnosed by direct microscopy and culture. As early diagnosis and intervention can prevent the severity of the disease and helps to reduce mortality, it is advisable to collect the sample for diagnosis at the first sign of suspicion.

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