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Mucormycosis: A Potentially Lethal Infection In Post Covid Patients – A Study From Tertiary Care Center, Gujarat

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ABSTRACT

Background: Mucormycosis is a life-threatening, angio-invasive fungal infection, mainly seen in immunocompromised persons. An increase in number of mucormycosis cases has been observed during COVID-19 pandemic. We aimed to study the prevalence and distribution of mucormycosis cases amongst the post covid patients visiting a tertiary care center in Gujarat.

Materials and methods: Present retrospective observational study included 30 patients presenting with warning symptoms and signs at a tertiary care centre in Gujarat. All age – groups and both gender cases with a history of COVID were included. All the data regarding demography, co – morbid condition, clinical examination, routine blood investigations, KOH and lactophenol cotton blue(LPCB) preparations, computed tomography(CT) scan- paranasal sinuses(PNS) and histopathological examinations(HPE) were collected and analyzed.

Results: Out of total of 30 patients highest number (15) of the patients was from age group 51-60 years (50%), 18 (60%) were males and 12 (40%) were females with male to female ratio of 1.5:1. 27(90%) patients had diabetes mellitus and 03(10%) were non – diabetic. KOH and LPCB preparations from 25(83.3%) cases showed presence of fungal hyphae and 5(16.7%) cases were negative. On CT Scan – PNS, 26(86.6%) cases presented with rhino – orbital, 02(6.7%) cases with rhino – orbito – cerebral and 02(6.7%) cases with nasal type mucormycosis. Histopathological examination confirmed the diagnosis of mucormycosis.

Conclusion: Mucormycosis is a disease with high mortality rate. Already immunocompromised patients with superadded COVID-19 infection, have shown increased surge of mucormycosis. Surgical debridement should be performed as soon as possible once the diagnosis is confirmed along with medical management.

KEY WORDS: Mucormycosis, Post covid, Fungal infection.

INTRODUCTION

Throughout the world, millions of people have been affected by SARS COV-19 virus. It is predominantly a disease of respiratory system and presentation ranges from a common cold to more severe pneumonia and death. The transmission is via inhaled droplet infections or entering the body by touching infected surfaces. SARS COV-19 was first identified in December 2019 in Wuhan, China.^[1] It has created the global health crisis claiming many lives.^[2]

Mucormycosis is a rare angio - invasive, life-threatening fungal infection that occurs in immunocompromised patients e.g. those with uncontrolled diabetes mellitus, acquired immunodeficiency syndrome, iatrogenic immunosuppression and haematological malignancies, and those who have undergone organ transplantation.^[3]

There has been increasing number of mucormycosis cases during COVID pandemic and also as post COVID sequelae.^[2] It can be categorized into rhino-orbitocerebral, cutaneous, disseminated, gastrointestinal, and pulmonary subtypes.^[2-4]

Gujarat has reported the highest number of mucormycosis cases in India. With more than 2000 cases and more than 250 deaths due to mucormycosis. The Gujarat government declared the Mucormycosis an epidemic under the Epidemic disease Act 1857.^[5]

The treating physicians must be aware of the warning symptoms and signs of mucormycosis. If a patient exhibits any of the symptoms and signs listed in Table 1, mucormycosis should be suspected.^[6]

Table 1: Warning symptoms and signs of rhino-orbito-cerebral mucormycosis⁶

Nasal stuffiness	Regional pain – orbit, paranasal sinus or dental pain
Foul smell	Proptosis
Epistaxis	Sudden loss of vision
Nasal discharge - mucoid, purulent, blood-tinged or black	Facial paresthesia, anesthesia
Nasal mucosal erythema, inflammation, purple or blue discoloration, white ulcer, ischemia, or eschar	Sudden ptosis
Eyelid, periocular or facial edema, facial discoloration	Ocular motility restriction, diplopia
Facial pain	Facial palsy
Worsening headache	Fever, altered sensorium, paralysis, focal seizures

Our aim was to study the prevalence and distribution of mucormycosis cases amongst the post covid patients visiting a tertiary care center in Gujarat.

MATERIALS AND METHODS

We have done a retrospective observational study. The present study included 30 patients presenting with warning symptoms and signs of fungal infection at a tertiary care centre in Gujarat. Majority of patients were immunocompromised. We included the cases from all age – groups and both gender. All patients had a history of COVID positive test. All the demographic and co – morbid condition data were obtained and recorded. The data regarding diagnostic details e.g. clinical examination, routine blood investigations, KOH

and lactophenol cotton blue(LPCB) preparations, computed tomography(CT) scan- paranasal sinuses(PNS) and histopathological examinations(HPE) were collected and analyzed. These data were entered into Microsoft excel and presented in the form of frequency, percentage, pie chart and bar diagrams.

RESULTS

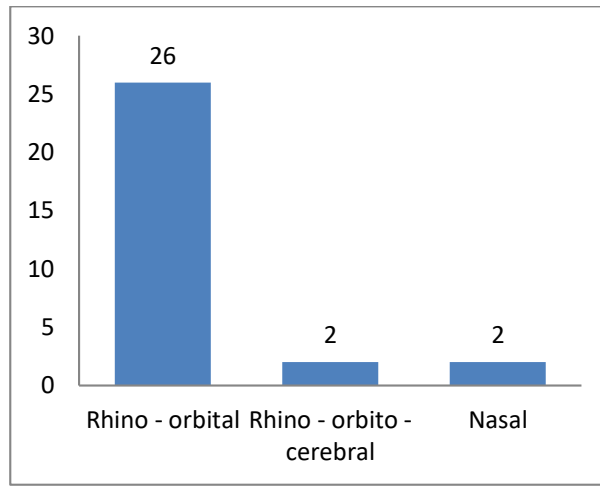
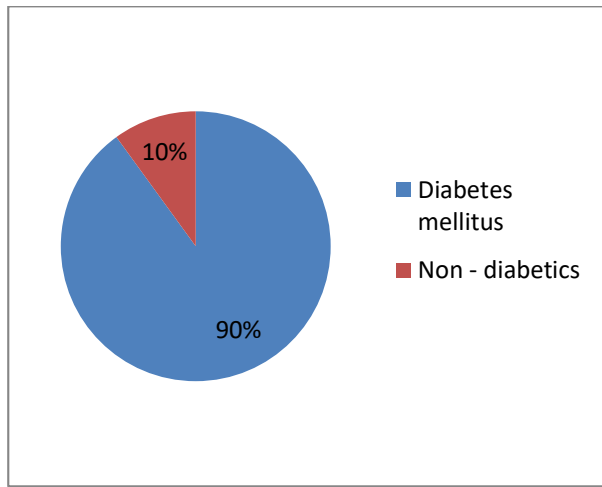
The present retrospective observational study was carried out at a tertiary care centre in Gujarat. Total of 30 patients with all age groups and both gender were included in the study.

Highest number (15) of the patients was from age group 51-60 years (50%). Out of total 30 patients, 18 (60%) were males and 12 (40%) were females with male to female ratio of 1.5:1.(Table – 2)

Table – 2. Age and Gender distribution

Age group (years)	Male	Female	Total
Less than 20	0	0	0
20-30	0	0	0
31-40	0	0	0
41-50	2	0	2
51-60	9	6	15
61-70	4	5	9
71-80	3	1	4
Greater than 80	0	0	0
Total	18	12	30

Out of 30 patients, 27(90%) patients had history of diabetes mellitus and 03(10%) were non – diabetic. (Figure-1) KOH and LPCB preparations from 25(83.3%) cases showed presence of broad, non – septate fungal hyphae and 5(16.7%) cases were negative which later on turned positive for mucormycosis on biopsy examination. On CT Scan – PNS, 26(86.6%) cases presented with rhino – orbital, 02(6.7%) cases with rhino – orbito – cerebral and 02(6.7%) cases with nasal type of mucormycosis.(Figure – 2)



Fig– 1. Cases with diabetes and non–diabetics

Fig – 2. Type of mucormycosis

Histopathological examination from the biopsies of all cases revealed presence of mucosal lining epithelium, underlying stromal mixed inflammatory infiltrate, oedema and necrosis. There was presence of scattered large, broad non - septate branching hyphae at 45 – 90 degree angles with thin wall infiltrating surrounding tissue.(Figure-3-a,b) Diagnosis of mucormycosis was confirmed.

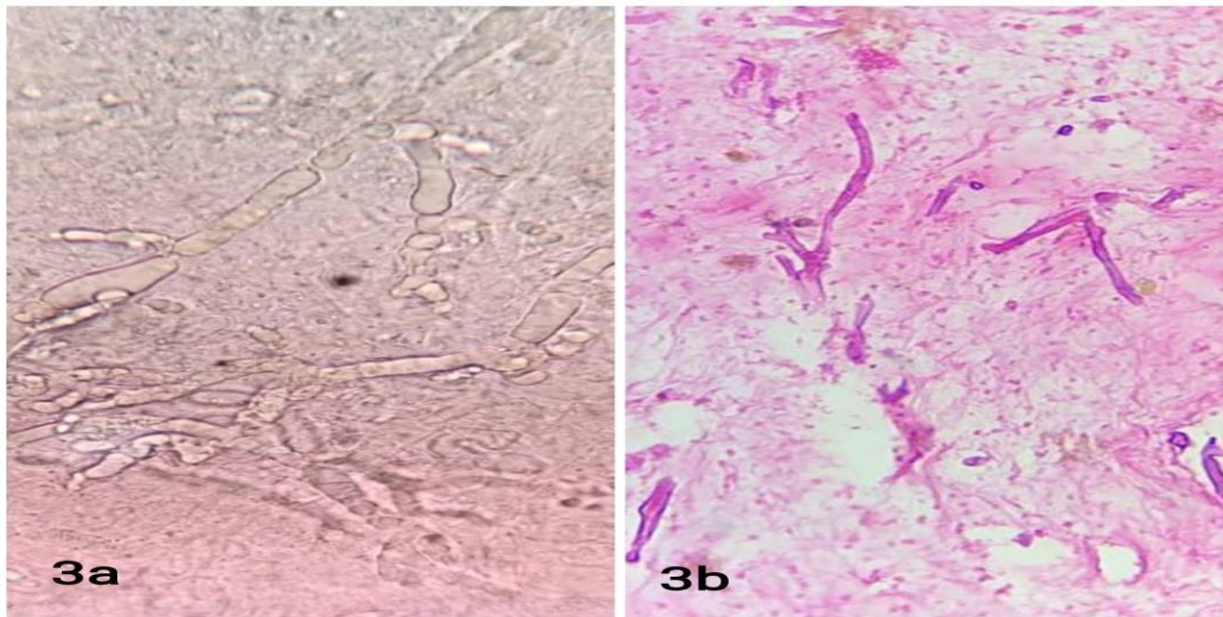


Fig – 3-a.KOH Mount preparation, 3-b. Broad, non-septate fungal hyphae(H & E stain, High power(40x).

DISCUSSION

Mucormycosis first described in 1885 by Paltauf, is an aggressive fungal infection that usually affects immunocompromised patients. It is a lethal fungal disease, with rhino - orbito - cerebral presentation being its most common form.^[7]

Although it has a low incidence rate, varying from 0.005 to 1.7 per million populations, many cases have been seen recently, amounting to a significant increase in its incidence in the wake of the ongoing corona virus pandemic.^[8] In Indian population the prevalence of mucormycosis is 0.14 per 1000, which is about 80 times higher than developed countries.^[1]

Patients with COVID-19 has increased risk for invasive fungal infections particularly in individuals having chronic respiratory diseases, corticosteroid therapy, intubation/mechanical ventilation, cytokine storm, HIV, transplants, diabetes, cancer etc.^[1]

Mucormycosis is one of the most rapidly progressing and lethal form of fungal infection in humans which usually begins in the nose and paranasal sinuses, subsequent inhalation of spores, and probable extension to the brain and successively, sinuses, nose and eyes are affected. Its clinical manifestation starts with palatal and sinuses necrosis, further enters to the orbit prior to getting intra-cranial structures. Appearance of reddish - black nasal turbinate and septum along with a nasal discharge is also seen. Progression of disease into cranial vault leads to blindness, lethargy and seizures followed by death.^[1,4]

Emerging data suggests that COVID-19 is common in patients with Diabetes, Hypertension, and Cardiovascular disease (CVD). Patients with diabetes are predisposed to infections in general, there are several specific factors responsible for increased risk and severity of infection with SARS CoV2 in diabetes. e.g. Increased ACE-2 Expression, Increased Furin, Impaired T-Cell function and Increased Interleukin-6 (IL-6).^[9] In patients with diabetes, blood sugar is high and the tissues become relatively acidic – a good environment for mucorales fungi to grow.^[1]

Mucormycosis was more prevalent in diabetics as compared to non – diabetics in present study. These findings were similar to previous study done by Sharma M et al.^[3]

Phagocytes are the major host defense mechanism against mucormycosis. Hyperglycemia and acidosis are known to impair the ability of phagocytes to move toward and kill the organisms by both oxidative and nonoxidative mechanisms, hence predisposing such patients to mucormycosis. Neutropenic patients like COVID positive are at increased risk of developing mucormycosis, furthermore these covid positive patients were on corticosteroids which worsened the hyperglycemia.^[2] Furthermore, Covid-19 affected patients show an overexpression of inflammatory cytokines, and impaired cell-mediated immunity with decreased cluster of differentiation 4 and 8 positive T-helper (CD4+ T and CD8+ T) cell counts, indicating susceptibility to fungal co-infections.^[10] Critically ill patients, especially those admitted to intensive care units and those who required mechanical ventilation, or who had a longer duration of hospital stays were more likely to develop fungal co-infections.^[11] Extensive use of steroids in Covid-19 management can also suppress immunity, allowing opportunistic fungal infections to colonise.^[3]

Our study showed high preponderance of disease in males as compared to the females with male to female ratio of 1.5:1, which was comparable to the study carried out by Sharma M et al and Satish et al.^[2-3]

Y.P. Talmi et al noted rhinocerebral mucormycosis is an infection in the sinuses that can spread to the brain. This form of mucormycosis is most common in people with uncontrolled diabetes and in people who have had a kidney transplant.^[12] In a study carried out by Satish D et al. showed most common type of mucormycosis was rhino – orbital type(48%) followed by rhino – orbito – cerebral (24%) and nasal (28%).^[2] Our study also showed the similar findings.

Song et al. studied the association between Covid-19 and invasive fungal sinusitis in April 2020, and concluded that a large number of patients affected by or recovered from Covid-19 are at increased risk of developing invasive fungal diseases.^[10] In a recent review, 8 per cent of coronavirus-positive or recovered patients had secondary bacterial or fungal infections during hospital admission, with widespread use of broad-spectrum antibiotics and steroids.^[13]

Diagnosis is made by clinical examination, CT scan, KOH Mount, LPCB preparations, fungal cultures and HPE. Biopsy is the gold standard method to confirm the diagnosis.^[4]

CT scan from majority of cases revealed non-enhancing hypodense mucosal thickening with multiple air foci without air-fluid levels in sinuses. In some cases bony destruction and erosion of the walls of sinuses were present with loss of right periantral fat planes. Intra-orbital spread and bilateral proptosis was noted in few cases which suggested possibility of invasive fungal sinusitis. KOH and LPCB preparation showed presence of broad, non-septate fungal hyphae. Hematoxylin and Eosin stained sections from biopsy showed the presence of scattered large, broad non-septate branching hyphae at 45–90 degree angles with thin wall infiltrating surrounding tissue which confirmed the diagnosis of mucormycosis.

Treatment strategies include surgical debridement and antifungal agents. Amphotericin B has been the standard of treatment for invasive mucormycosis. The treatment recommendations can be supported by the global guideline for the diagnosis and management of mucormycosis in 2019 by European Confederation of Medical Mycology (ECMM) and Mycoses Study Group Education and Research Consortium which generally supports an early complete surgical treatment for mucormycosis whenever possible, in addition to systemic antifungal treatment. Antifungal therapy includes IV Amphotericin B (50 mg/day) with cumulative dose of 1.5-2 gms, lipid complex, liposomal Amphotericin B (5-10mg/kg) and posaconazole (400mg bid).^[2] The prognosis generally depends on the extent of manifestation of the disease and effective treatment initiated in response to the diseases.^[4]

CONCLUSION

Mucormycosis is a disease with high mortality rate. Already immunocompromised patients with superadded COVID-19 infection, have shown increased surge of mucormycosis. Explanation of warning symptoms and signs to patients and the family on discharge following treatment of COVID-19 may prompt them to seek early medical attention. Awareness of, and due attention to warning symptoms and signs, a high index of clinical suspicion and early diagnosis are the key to alleviate the disease. Surgical debridement of the infected area should be performed as soon as possible once the diagnosis is confirmed along with medical management.

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