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UNIVERSIDADE ESTADUAL PAULISTA
"JÚLIO DE MESQUITA FILHO"
Instituto de Ciência e Tecnologia
Campus de São José dos Campos

CASE REPORT

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# Maxillary osteomyelitis associated with COVID-19: mucormycosis or not? A series of cases

Osteomielite maxilar associada ao COVID-19: mucormicose ou não? Uma série de casos

**Mayank VERMANI[1], Megha CHOPRA[2], Neeti SWARUP[3], Ankita PAL[4]**

1 - Sarvodaya Hospital. Hisar, Haryana, India.
2 - MRIIRS: Manav Rachna International Institute of Research and Studies, Faculty of Dental Sciences, Department of Prosthodontics and Crown & Bridge. Faridabad, Haryana, India.
3 - University of California, School of Dentistry, Center for Oral and Head/Neck Oncology Research. Los Angeles, USA.
4 - Department of Prosthodontics and Crown & Bridge, Santosh Dental College and Hospital, Santosh Deemed to be University, Ghaziabad.

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## ABSTRACT

**Aim:** A series of cases have been presented involving the oral cavity focusing on the presentation, diagnosis and treatment of mucormycosis that can form a basis for successful therapy. **Background:** The management of severe coronavirus disease (COVID-19) in conjunction with comorbidities such as diabetes mellitus, hematological malignancies, organ transplants, and immunosuppression have led to a rise of mucormycosis which is an opportunistic infection. **Cases Description:** The various forms that have been enlisted till date are rhino-cerebral, rhino-orbital, gastrointestinal, cutaneous, and disseminated mucormycosis. From the dentistry and maxillofacial surgery perspective, the cases depicting extension of mucormycosis into the oral cavity have been less frequently recorded and thus, require a detailed study. The patients that reported to our private practice had non-tender swelling, draining sinuses and mobility of teeth. A similarity was observed in the clinical signs both in osteomyelitis and mucormycosis. Thus, a histopathological examination was used to establish the definitive diagnosis. **Conclusion:** Mucormycosis is a life threatening pathology that requires intervention by other branches to make an early diagnosis and commence the treatment. The characteristic ulceration or necrosis is often absent in the initial stage and thus, histopathological examination and radiographic assessment are required to formulate a definitive diagnosis. Early intervention is a necessity to avoid morbidity. The treatment involves surgical debridement of the necrotic infected tissue followed by systemic antifungal therapy. Mucormycosis has recently seen a spike in its prevalence, post the second-wave of coronavirus pandemic in India. It was seen commonly in patients with compromised immunity, diabetes mellitus, hematological malignancies, or on corticosteroid therapy. Mucormycosis invading the palate mostly via maxillary sinus has been less frequently described. In the post-COVID era the features associated with mucormycosis involving oral cavity, should warrant a possible differential diagnosis and managed appropriately.

## KEYWORDS

Eschar; Immunomodulation; Mucormycosis; Palatal ulceration; Rhino-Cerebral.

## RESUMO

**Objetivo:** Apresentar uma série de casos com enfâse na apresentação, diagnóstico e tratamento da mucormicose oral, assim como uma revisão sistemática que sirva como base para estabelecimento de terapias de sucesso. **Introdução:** A forma severa da infecção por coronavirus (COVID-19) associada a diabetes mellitus, doenças hematológicas malignas, transplante de órgãos e imunossupressão levaram a um aumento das infecções oportunistas de mucormicose. **Descrição dos Casos:** As diversas apresentações clínicas que foram descritas até o momento são a rinocerebral, rino-orbital, gastrointestinal, cutânea e mucormicose disseminada.

No que concerne a odontologia e a cirurgia maxillofacial, os casos que apresentam extensão de mucormicose para cavidade oral tem sido menos reportados e assim requerem mais estudos. Os pacientes que compareceram a nossa clínica apresentavam aumento de volume endurecido, drenagem de fluidos dos seios maxilares e mobilidade dentária. Clinicamente tanto a osteomielite quanto a mucormicose apresentaram-se de forma semelhante. Assim, análise histopatológica foi utilizada para estabelecimento do diagnóstico definitivo. **Conclusão:** A mucormicose é uma patologia grave que requer intervenção precoce para estabelecimento do tratamento. A ulceração e necrose características usualmente estão ausentes nos estágios iniciais da lesão, assim análise histopatológica e radiográfica são necessárias para o diagnóstico final. Intervenção precoce é necessária para diminuir a morbidade. O tratamento envolve o debridamento cirúrgico da área necrosada seguida de terapia antifúngica sistêmica. Recentemente, houve um aumento nos casos de mucormicose, após a Segunda onda da pandemia de COVID-19 na índia. Os casos acometiam principalmente pacientes imunocomprometidos, com diabetes mellitus, doenças hematológicas malignas e em uso de corticosteróides. A mucormicose invadindo o palato pelos seios maxilares foi raramente descrita. Na era pós-COVID a mucormicose envolvendo a cavidade oral deve entrar no painel de diagnósticos diferenciais para que o tratamento adequado possa ser instituído precocemente.

## PALAVRAS-CHAVE

Necrose; Imunomodulação; Mucormicose; Úlcera palatina; Rinocerebral.

## INTRODUCTION

The Coronavirus pandemic (COVID-19), despite having several prevention and treatment measures, continues to cause a significant problem worldwide [1]. According to Raut and Huy [2], the second wave of COVID-19 has affected India substantially, with the highest number of daily reported cases being slightly more than 0.4 million in the first week of May' 2021. Kumar et al. [3] and Mahalaxmi et al. [4] presented mucormycosis as an impending threat, as the treatment of the same was a major challenge for the clinician, and that was supposedly associated with the coronavirus-disease. The first case of COVID-19 associated mucormycosis (CAM) (Rao et al. [5]) was reported in Chile but most cases were reported in India and were linked to the Delta variant (B.1.617.2) [5].

'Mucormycosis' belongs to the order Mucorales of the class Zygomycetes, which are ubiquitous, especially in soil, decaying vegetation and organic matter such as leaves, compost piles, and animal dung [2,6]. The 'black fungus', is a rare but potentially fatal infection if there is a lack of treatment. It is also called mucormycosis and is transmitted by fungal spores of the Mucorales order [1].

In the second wave, the incidence of mucormycosis has risen more rapidly in comparison to the first wave with around 15,000 cases during the end of May '2021 [7]. These fungi are usually harmless, but can become pathogenic in certain circumstances like immunosuppression, diabetic acidosis, steroid therapy and, in transplant patients [8]. In susceptible patients, there is marked tissue necrosis of the adjacent structures, followed by rapid progression and angioinvasion from the nasal and sinus mucosa into the orbit and brain. This is known as the Rhino-orbital mucormycosis and Rhino-cerebral mucormycosis respectively [4]. Currently, the necrosis of hard and soft tissues of the oral cavity is also being noted, that often presents as a palatal perforation and is known as rhino-maxillary mucormycosis [9,10].

The clinical manifestation, diagnosis, treatment and prognosis of this COVID-19 associated mucormycosis has made the surgeon's skeptic as not much is available in literature at present. Mucormycosis invading the palate mostly via maxillary sinus has been less frequently described. In the post-COVID era the features associated with mucormycosis involving oral cavity, should warrant a possible differential diagnosis and managed appropriately. The present article reports a series of patients having rhino-maxillary mucormycosis with the aim to direct the attention towards the clinical presentation and pathogenesis of mucormycosis and an emphasis on the diagnosis and treatment part.

## CASE DESCRIPTION

A 44-year old afebrile female patient reported to the department of dentistry, with a painless and diffused gingival swelling and a pururlent discharge from the left buccal sinus with multiple mobile teeth (Grade II mobility) in the left upper quadrant. (21, 22, 23, 24 and 25) since last 10 days. (Dental and medical history related to COVID-19 tabulated in Table I).

**Table I -** Characteristics of seven cases reported

| Case ID | Present Complaint | Clinical Findings | Medical Condition | Haematological/ Serological Findings | CT/ Radiographic Findings | Differential Diagnosis | Histological Findings | Treatment |
|---|---|---|---|---|---|---|---|---|
| | | | | **Hb1AC/ D Dimer/CRP** | | | | |
| **Case 1: (44/F)** | Gingival swelling, draining buccal sinuses, multiple mobile teeth (21,22,23,24,25) | Access opening with respect to 25, draining sinuses present on the buccal aspect of 21-25 region, gingival swelling | Reported negative history for Covid-19 and Diabetes (DM incidental finding) | Hb1AC: 8.1 (raised)<br>D Dimer: 1.29(raised)<br>CRP: 59.9 (raised) | Ill-defined osteolytic area is seen in alveolar arch of maxilla (mainly towards left side), floor of left maxillary sinus & part of hard palate, adjacent soft tissue thickening was also seen. Mucosal thickening seen in left maxillary sinus-obliteration of left mucormycosis unit, mild mucosal thickening in left frontal and ethmoidal sinus. | Endo-perio lesion, necrotizing periodontitis, osteomyelitis and chronic granulomatous fungal infection | H/E section demonstrates necrotic material, haematoxylin stained non septate branching fungal hyphae | Mobile teeth were extracted, avascular alveolar bone debrided<br>Post-Operative Regimen: i.v. administration of Liposomal, lipid amphotericin (5mg/kg/day).<br>*Blood sugar levels were monitored. |
| **Case 2: (43/M)** | Mobile left upper teeth (21-28) | Mobility with respect to (21-28), i.e, all the teeth of upper left quadrant | Already a diagnosed case of mucormycosis-was treated by medial maxillectomy—after some days mobility observed and came to the dental department, he had a history of COVID 1 month back, was also hospitalized during this (Oxygen support and steroidal therapy but no diabetes) | | Mucosal thickening seen in bilateral frontal, ethmoid (left> right) and maxillary sinus, thinning of medial wall of left orbit with suspicious focal erosion. Extensive fat stranding in the left peri antral region and adjacent infratemporal fossa with mild relative thickening of the lateral pterygoid and temporalis muscles. | Periodontal infection, Periapical lesion, Osteomyelitis of maxilla | H/E section demonstrates caseous necrosis, hematoxylin stained non septate branching fungal hyphae with mixed eosinophilic and neutrophilic infiltrate | Surgical debridement, extraction of mobile teeth & Caldwell Luc operation was performed.<br>*Resected infected mass was a typical case of ***Black Fungus*** (as it was black in color) |
| **Case 3: (62/M)** | Non-healing palatal ulcer from past 15 days—inability to open the mouth | O/E a palatal ulcer was found on the right side in association with mobile 16, 17. The ulcer was (1*2 $cm^2$) with irregular borders: the ulcer was covered by necrotic slough and on the lateral aspect a part of underlying bone was also exposed. Two finger mouth opening. The ulcer was non tender but the patient complaint of bad taste. | Reported positive history for COVID-19 a month back—was hospitalized for the same (with oxygen support and steroidal therapy) Also, was a diabetic. | RBS: 250 mg/dl | Mucosal thickening is seen in right maxillary and sphenoid sinus on right side causing partial opacification of sinuses, Fat stranding is seen in right anterior and posterior periantral soft tissues. Soft tissue density is seen in right pterygopalatine fossa with fat stranding. Fat stranding is also seen in right masticator space and in the region of right inferior orbital fissure. | Periodontal infection, Periapical lesion, Osteomyelitis of maxilla, Osteomyelitis (Bacterial, fungal, parasitic) | Histopathological examination did not test positive for mucormycosis---though the clinical representation and medical history were same as that of the other mucormycosis patients. | Surgical resection and debridement.<br>Post-operative regimen was same as above. |

CT: Computed Tomographic Findings. * Post-operative regimen

**Table I -** Continued...

| Case ID | Present Complaint | Clinical Findings | Medical Condition | Haematological/ Serological Findings | CT/ Radiographic Findings | Differential Diagnosis | Histological Findings | Treatment |
|---|---|---|---|---|---|---|---|---|
| **Case 4: (57/M)** | C/C of mobile teeth in right upper back tooth region since 3 days | Mobile teeth (11, 12, 13, 14, 15, 16) and pus filled buccal sinus that had pus discharge on the right side--- In this case the mobile teeth were extracted—the underlying bone was necrotic which created suspicion of osteomyelitis. The sample was sent for histopathological examination along with the extracted teeth where the specimen tested positive for mucormycosis. Patient recalled—now the discharging (pus) was also seen on left side. | No history of COVID and Diabetes. | | There is evidence of mottled density involving alveolar process of maxilla on right side. Focal cortical thinning is seen involving lateral wall of right maxillary sinus. Note is made of mucosal thickening in bilateral maxillary sinuses (areas of polypoidal mucosal thickening in left maxillary sinus) with blockage of right osteo-meatal unit. Soft tissue thickening is seen in right buccal space with fat stranding in overlying subcutaneous plane | Periodontal infection, Periapical lesion, Osteomyelitis of maxilla | H/E section demonstrates necrotic material, hematoxylin stained non septate branching fungal hyphae, with occasional round to ovoid hematoxylin stained structure, indicative of conidia with mixed eosinophilic and neutrophilic infiltrate | Inferior maxillectomy was done.<br>Post-operative regimen same as above. |
| **Case 5: (70/M)** | Discoloration present on the palate since 15 days which was progressively increasing | Discolouration was present on the palate. It was non tender. (Pt had HRCT) | Reported positive history for COVID 20 days back—was hospitalized for the same for 7 days (with oxygen support and steroidal therapy), Also, was a diabetic (220mg/dl) | RBS: 220mg/dl | Mucosal thickening with partial opacification is seen in right maxillary sinus suggestive of sinusitis. There is obliteration of right osteo-meatal units. Mild mucosal thickening is seen in right ethmoid and left maxillary sinuses. The nasal septum is mildly deviated towards right side. Concha bullosa is seen on right side. Soft tissue thickening is seen on right submandibular and visualized upper cervical region. | Osteomyelitis of maxilla | H/E section demonstrates necrotic material, hematoxylin stained non septate branching fungal hyphae, with occasional round to ovoid hematoxylin stained structure, indicative of conidia with mixed eosinophilic and neutrophilic infiltrate | Treatment not done (financial reasons) |
| **Case 6: (56/F)** | Ulcer with red erythematous boundary with necrotic slough seen on the alveolus of right maxillary tooth region | Ulcer with red erythematous boundary and necrotic slough over the avascular bone and they were seen in association with mobile teeth (Grade2mobile: 13, 14 and 15; Grade3mobile: 16 and 17 | No COVID history, but was a diabetic since 3 years and was on medication | | | | Positive for mucormycosis (epithelial ulceration, inflammatory granulation tissue giant cell reaction and aseptate fungal hyphae) | Extraction of mobile teeth followed by right hemimaxillectomy.<br>Post-operative regimen same as above. |
| **Case 7: (46/M)** | Palatal discoloration (whitish coloration) that just started on the left lateral slope of palate that the patient noticed 3 days back | Whitish discoloration that had just started present on the lateral slope of palate at the junction of hard and soft palate | Reported positive history for COVID 25 days back-- was hospitalized for the same for 15 days (with oxygen support and steroidal therapy), Also, was a diabetic (221mg/dl) | FBS: 221 mg/dl | | Minor salivary gland, Epidermoid cyst, Pleomorphic adenoma | Histological examination was positive for mucormycosis | Systemic anti-fungal therapy:<br>(Tab. Isavuconazole-200mg TID on Day 1 and 2 and then 200 mg/day for 3-6 months). |

CT: Computed Tomographic Findings. * Post-operative regimen

After two days of the commencement of the root canal treatment (RCT), the mobility increased further and the patient was referred to us. On investigating the past medical history, the patient gave negative history for COVID-19 and Diabetes Mellitus. This demanded further laboratory investigations where, the patient was diagnosed with diabetes mellitus type II. The CRP (C - reactive protein) and D-Dimer were also raised. The patient presented with severe immunosuppression and a detectable viral load, that together lead to the formulation of a provisional diagnosis of necrotizing periodontitis and a differential diagnosis of endo-perio lesion, osteomyelitis and chronic granulomatous fungal infection. (Figure 1) (https://drive.google.com/file/d/1wA33wXR0BImPxEHiGbOvd2hkxnZt5a1Q/view?usp=drive_link):

For confirmation, excisional biopsy was done and the specimen was sent for histopathological examination. The biopsy confirmed the presence of necrotic material and hematoxylin-stained non septate branching fungal hyphae that were suggestive of mucormycosis. Also, adjacent soft tissue thickening was seen.

For the management of patient, aseptic conditions were maintained and under local anaesthesia the buccal mucoperiosteal flap was raised where a complete loss of buccal cortical plate was seen. The mobile teeth were extracted and the avascular alveolar bone was debrided with the use of a round bur until fresh bleeding was observed. Copious irrigation was done and site was sutured. The intravenous administration of Liposomal/ lipid Amphotericin (5 mg/kg/day for 5 weeks) was prescribed and the blood sugar levels were monitored during this time. The patient was recalled for suture removal after 7 days. (Clinical, radiological, histological, surgical treatment pictures presented in Figure 1).

In another case, the patient was diagnosed with COVID-19 and mucormycosis. Caldwell-Luc operation was performed for debridement and the resected infected mass was typical 'black' color (Figure 2) (https://drive.google.com/file/d/1yKH0nF9CqwcCMAAiuC9qk7J4281jA-rY/view?usp=drive_link).

On the contrary, a 62-year old patient did not test positive for mucormycosis though the clinical and medical history were similar to it which made us skeptic about the diagnosis and, a provisional diagnosis of Osteomyelitis was made that could be bacterial, fungal or parasitic. Also, the patient gave a positive history for COVID-19 and diabetes (Random Blood Sugar was 250 mg/dl) and he was hospitalized for the same with oxygen support and steroidal therapy (Figure 3).

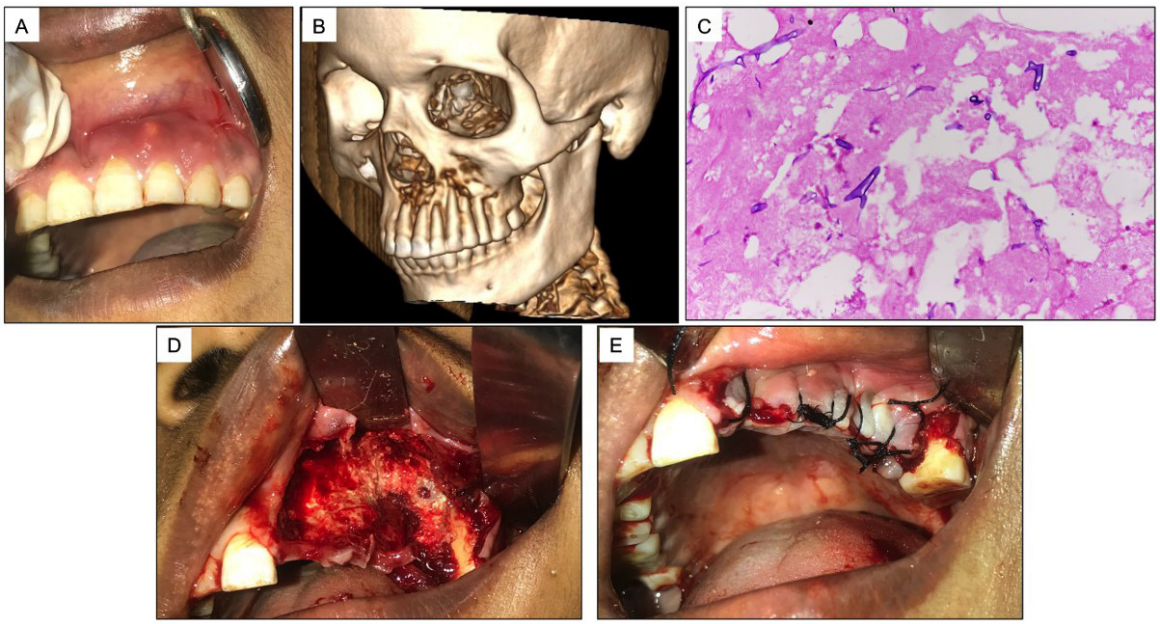


**Figure 1 -** Clinical presentation of Case 1: (44/F). **A.** Sinus opening can be demarcated well between the central and lateral incisor region in the left quadrant. **B.** 3D volume imaging shows Ill-defined osteolytic area seen in the anterolateral wall of left maxillary sinus, loss of buccal cortical bone can be appreciated. **C:** H &E stained sample (20X)revealed non-septate branching fungal hyphae along with necrotic material. **D:** Extraction of mobile teeth and debridement of avascular bone (demonstration of the surgical bed after debridement). **E:** Surgical site sutured.

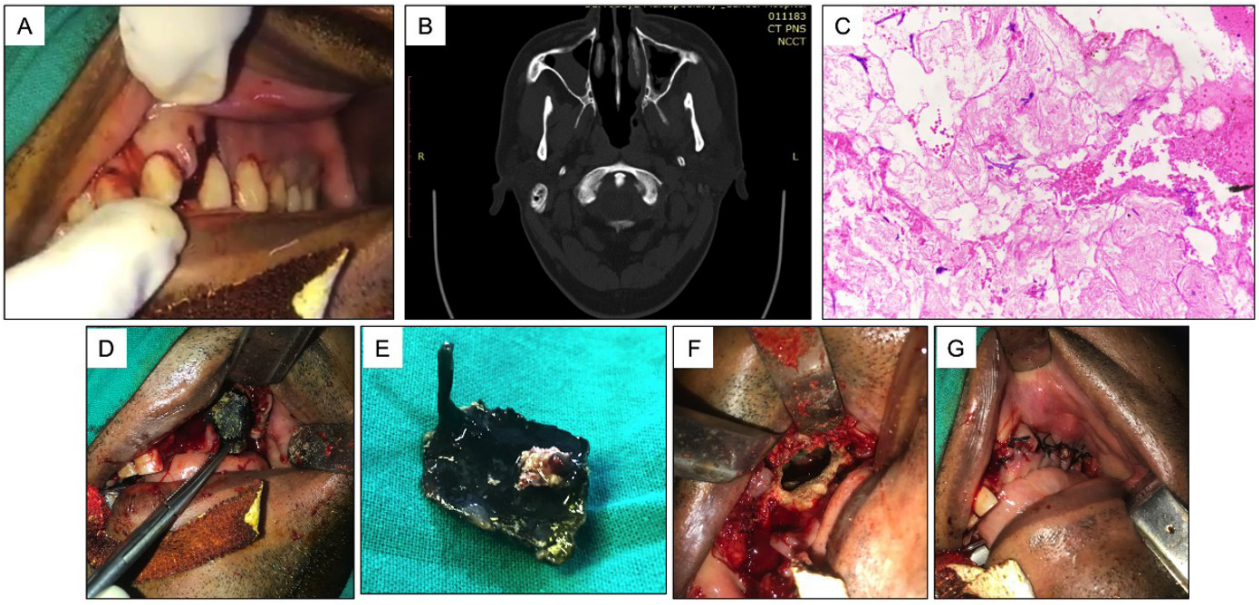


**Figure 2 -** Clinical presentation of Case 2: (43/ M). The patient was already a diagnosed case of mucormycosis (was treated by medial maxillectomy). **A.** Clinical presentation of the quadrant where the teeth were mobile. **B.** Axial section representing thickening of right maxillary sinus mucosal lining. **C.** H&E stained sample (10x) revealed caseous necrosis, hematoxylin stained non septate branching fungal hyphae with mixed eosinophilic and neutrophilic infiltrate. **D.** Presentation at the time of surgery. Characteristic 'black eschar' seen. **E.** Resected infected mass which has a typical 'black color' characteristic of mucormycosis. **F.** Surgical bed after resection of the infected mass. **G.** Sutured surgical site.

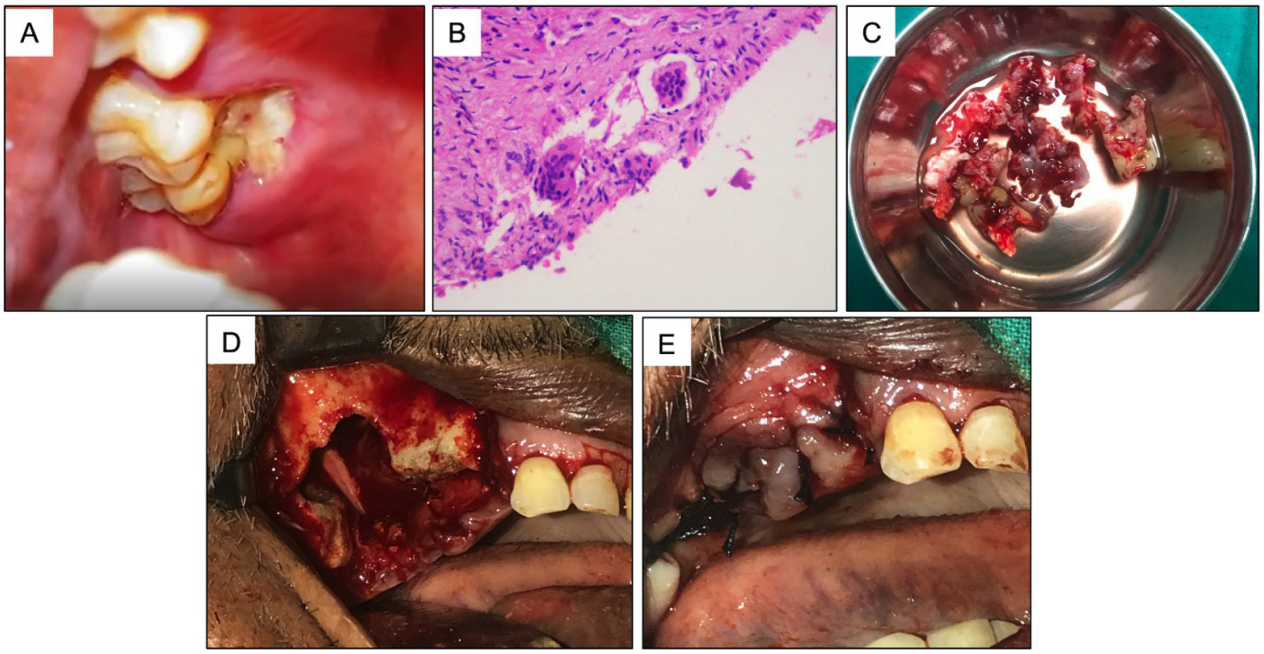


**Figure 3 -** Clinical presentation of Case 3: (62/ M). **A.** Intraoral photograph of the patient shows an ulcerative lesion (ulcer measuring 1 * 2 $cm^2$ with irregular borders, covered with necrotic slough present on the lateral aspect of the palate on the right side (underlying bone was also exposed). **B.** H&E stained sample (20x) demonstrated occurrence of mixed inflammatory infiltrate, with presence of giant cells. The sample did not test positive for mucormycosis, though the clinical representation and medical history were same as that of the other mucormycosis patients. **C.** Resected infected mass. **D.** Surgical bed post resection of infected mass. **E.** Post-operative picture.

Another patient 57 years old with no COVID-19 history was mucormycosis positive in histopathological staining.

The detailed findings and description of the cases reported is tabulated in Table I.

## DISCUSSION

COVID-19 has already claimed over a million lives worldwide. SARS-CoV-2 are a large group of viruses that cause illness in humans chiefly

through the airborne route and droplet release when the infected person coughs, sneezes and talks. COVID management ranges from palliative care at home for mild and moderate cases to respiratory support in the form of supplemental oxygen therapy at 5L/min and titration of flow rates to reach >90% SpO2 mark for the most severe cases [11,12].

Anti-inflammatory or immunomodulatory therapy comprised of Methylprednisolone (in doses of 1 to 2 mg/kg IV in 2 divided doses) or 0.2-0.4 mg/kg of Dexamethasone prescribed usually for a duration of 5 to 10 days. Also, glucocorticoids and particularly, Remdesivir has proven to decrease mortality in hypoxemic patients [13,14].

Extending the total equivalence dose of immunomodulatory therapy produced major adverse effects such as hyperglycaemia and multiple secondary infections. Particularly they lead to deterioration of the immune system and predisposes the patients to an increased risk of contracting fungal like Rhizopus, Mucor and Thamnostylum. This risk is attributed to the disrupted neutrophil function and depletion in native inflammatory response [15].

Mucormycosis can be classified into various clinical forms based on the anatomical site of involvement like rhino-orbito-cerebral, pulmonary and cutaneous [13]. Initiation of the rhino-orbito cerebral or the pulmonary type starts with inhalation of the fungus through nose into the paranasal sinus. It has a tendency to grow along the blood vessels via the elastic lamina leading to extensive endothelial damage resulting in the formation of thrombi and ischaemic necrosis that results in the characteristic 'black color'. This necrosed tissue creates an environment for the fungus to proliferate. In cases with rhino-orbital involvement, like involvement of nasal and sinus walls, a poor blood supply can lead to the invasion of the orbit via the venous channels and freely communicating foramen. The involvement of orbit and fungal invasion through orbital apex can involve the cranium and ultimately kills the host [14].

A predisposing factor that has been subjected as the cause for mucormycosis is the presence of iron in the host that predisposes patients with diabetic ketoacidosis to mucormycosis. Other conditions that make a patient vulnerable are comorbidities like uncontrolled diabetes mellitus, diabetic ketoacidosis and neutropenia and those who had prolonged stay in hospitals as in India [16,17]. It can be postulated that as the numbers were on a high during this second peak, there must have been a sterilization failure considering the oxygen ventilation masks as the resources were limited (Figure 4) [18].

The generalized presentation comprises of one-sided facial pain, numbness or swelling; toothache, loosening of teeth (as in the case series in this article: the major chief complaint was sudden mobility of teeth); blurred or double vision with pain, fever, skin lesion, thrombosis and necrosis, in some cases, chest pain, pleural effusion, hemoptysis and worsening of respiratory symptoms [19]. Similar oral findings were described by Mohanty et al. [20], rhino-maxillary mucormycosis frequently presents as osteomyelitis of the maxillae which is associated with facial swelling, black discoloration, mobility of teeth and palatal perforations. The rhinomaxillary form is considered to be a less fatal form of the rhinocerebral type of mucormycosis. The case series presented in this article aims at the diagnosis and treatment of this rhino-maxillary form of mucormycosis having palatal involvement.

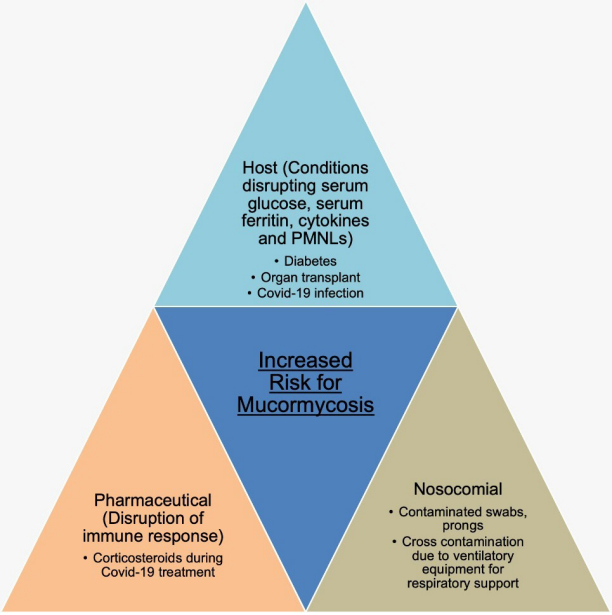


**Figure 4 -** Risk factors predilection for mucormycosis in India Post-Covid-19.

The management of mucormycosis mainly involves monitoring and controlling diabetic ketoacidosis, reduction of steroids, discontinuation of immunomodulatory drugs, extensive surgical debridement to remove all the necrotic debris material, and maintenance of adequate systemic hydration, and antifungal therapy for at least 4-6 weeks [21].

Of the seven cases reported so far, two of them belonged to the rural background and the rest were from urban setup in India. The mean age was 54 years and 5 were men. Five patients had a positive history for COVID-19 and one patient did not report any history for COVID-19 but on investigation D-Dimer and CRP, both were raised; that are generally raised post-COVID-19 (the patient did not go for examination of post-COVID-19 antibody titre). The five patients that gave a positive COVID-19 history had acute respiratory distress syndrome (ARDS) and they were hospitalized for oxygen support, where the ventilation mechanisms also may have acted as a risk factor for mucormycosis.. Six cases out of seven reported, presented with symptoms such as mobility of teeth, purulent sinuses, palatal ulcers with irregular borders covered with a necrotic slough (the ulcers were generally non-tender) and palatal discolorations that were suggestive of mucormycosis. The clinical presentation in one of the cases was a non-tender palatal ulcer with irregular borders and exposed avascular bone presentation exactly like that of a typical mucormycosis patient but the histology reports did not reveal fungus presence.

Differential diagnosis of the lesion should include squamous cell carcinoma, osteomyelitis (bacterial/ fungal/ parasitic), periodontal infection, periapical lesion, palatal minor salivary gland, epidermoid cyst, pleomorphic adenoma and chronic granulomatous infection like tuberculosis [22,23]. The lesion appears as a persistent chronic ulcer with raised margins suggestive of Squamous Cell Carcinoma, however, when this lesion is present with a history of diabetes and immunosuppression, then a diagnosis of fungal infection is favoured, which is later confirmed by histopathological investigation.

Six out of the seven reported cases were treated with surgical debridement of the necrotic avascular alveolar bone along with the extraction of teeth with mobility. Copious irrigation was done throughout this procedure. Amphotericin-B was prescribed and daily monitoring of blood sugar and other vitals was done. Hyperbaric oxygen therapy, granulocyte colony-stimulating factor (G-CSF) and topical application of Amphotericin-B could have been used as adjuncts in the treatment but were not used in any of the cases [24]. Though mucormycosis has a high mortality rate, the six patients who underwent treatment have survived and are responding well.

## CONCLUSION

An increase in number of mucormycosis cases has been noted post-second wave of COVID in India. It is a life-threatening and an aggressive pathology that involves inter professional cooperation to make an early diagnosis and prompt treatment. The trio of diabetes, excessive use of corticosteroids in the COVID-19 scenario appears to be the main causal of mucormycosis. The characteristic feature of ulceration or necrosis is often absent in the initial stages of infection. The definitive diagnosis is formulated in assistance with advanced radiological techniques such as CT, and histopathological investigation. The treatment ranges from surgical debridement of the dead, infected and necrotic tissue to systemic antifungal therapy in the form of amphotericin-B or the more effective liposomal amphotericin-B. Dentists and surgeons at their end, have a chance to mark a diagnosis and treat this fatal rhino-maxillary form of mucormycosis to reduce the morbidity and mortality rate.

## Author's Contributions

The author's contributions are as follows:

MV: Conceptualization, Manuscript Design, Manuscript Writing, Review. MC: Conceptualization, Literature Search, Manuscript Writing and Review. NS: Conceptualization, Investigation, Manuscript Preparation. AP: Manuscript Review.

## Conflict of Interest

No conflicts of interest declared concerning the publication of this article.

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## Regulatory Statement

This study was conducted in accordance with all the provisions of the local human subjects oversight committee guidelines and policies of: Institutional Ethics Committee of Sarvodaya Multispeciality & Cancer Hospital.

The approval code for this study is: ECR/999/Inst/HR/2021. ANS: The policies and approval code have been updated in the above comments.

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**Megha Chopra**
**(Corresponding address)**
MRIIRS: Manav Rachna International Institute of Research & Studies, Faculty of Dental Sciences, Department of Prosthodontics and Crown & Bridge, Faridabad, Haryana, India.
Email: drmeghachopra@gmail.com

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## Appendix 1. Supplementary files.

Case 1: https://ojs.ict.unesp.br/index.php/cob/article/view/3811/4694

Case 2: https://ojs.ict.unesp.br/index.php/cob/article/view/3811/4695

Case 4: https://ojs.ict.unesp.br/index.php/cob/article/view/3811/4696

Case 6: https://ojs.ict.unesp.br/index.php/cob/article/view/3811/4697