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Clinical paradigms in diagnosis of mucormycosis using nasal endoscopy in covid and post covid patients

Poonam Khairnar[1], Mahesh Thikekar[2], Rajesh Kar [3]

[1]Assistant Professor, Department of Otorhinolaryngology, MIMER Medical College Talegaon Dabhade, Pune, Maharashtra, India.
[2]Assistant Professor Department of Ophthalmology, PCMC'S PGI YCMH Pimpri, Pune, Maharashtra, India.
[3]Assistant Professor, Department of Otorhinolaryngology, MKCG Medical College, Berhampur, Odisha, India.

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Abstract

Background: Nasal endoscopy is a procedure to examine the nasal and paranasal sinus passages with 0 degree nasal endoscopes. Mucormycosis is an aggressive, life-threatening invasive fungal infection affecting paranasal sinuses, orbits and brain. Early diagnosis of mucormycosis is possible with diagnostic nasal endoscopy (DNE) in covid and post covid high risk patients. **Objective:** To substantiate the need of nasal endoscopy in high risk covid and post covid patients. **Materials and Methods:** Covid (48) and Post covid (64) patients (both male and female) underwent diagnostic nasal endoscopy at tertiary care hospital during period of Jan 2021 to Dec 2021. All study subjects were screened with nasal endoscopy in ENT OPD. On nasal endoscopy the target area showed eschar or blackish discolouration of turbinates and septal perforation. MRI (PNS+ORBITS+BRAIN) with contrast was carried out in suspected patients to know the extent of invasive fungal infection. All symptomatic patients were screened by opthalmologists to see extent of invasion. **Results:** Out of 112 patients, 70 patients were asymptomatic while only 42 patients were symptomatic for fungal invasion. Out of 70 asymptomatic patients, 52 patients were positive for fungal infection. Chronic diabetes mellitus and newly diagnosed diabetes mellitus (95 patients) was common co-morbidity associated with fungal positive HPR sampling.(71 patients). **Conclusion:** Follow up of the high risk post covid patients, for sequeale with diagnostic nasal endoscopy should be mandatory as majority of our patients are asymptomatic. Patient may present with atypical symptoms like earache, nasal polyposis so high degree of suspicion is essential. Besides mucormycosis, coinfection with aspergillus also observed in our study. So reporting of such cases is also important. A coordinated effort from a multidisciplinary team including otorhinolaryngology, ophthalmology, neurosurgery, critical care, microbiology, and pathology department is also important. A delay of initiating treatment of mucormycosis may lead to gross rise in morbidity and mortality rate

Keywords: Diagnostic nasal endoscopy, Mucormycosis, Post covid high risk patients.

Corresponding Author: Dr. Poonam Khairnar, Assistant Professor, Department of Otorhinolaryngology, MIMER Medical College Talegaon Dabhade, Pune, Maharashtra, INDIA.
Email: pk.41086@gmail.com

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Introduction

Mucormycosis is a rare but fatal, invasive fungal infection affecting paranasal sinuses, orbit, brain. The mucormycosis was first described in 1876 by Fürbinger in a cancer patient with right lung hemorrhagic infarct due to invasion of fungal hyphae and a few sporangia [1]. In 1885, Arnold Paltauf published the first case of disseminated mucormycosis, which he named "Mycosis mucorina" [2]. He showed the presence of sporangiophores and rhizoid-like structures, and this led to the conclusion that the infection was probably caused by Lichtheimia Corymbifera. Currently, Mucorales fungi are the next most common mold pathogens after Aspergillus, leading to invasive fungal disease in patients with malignancies or transplantation [3]. The incidence of mucormycosis significantly raised in patients with diabetes which is the one of the common underlying risk factor[4].Corzo-Leon et al. [5] proposed an algorithm for the diagnosis and treatment of rhino-orbito-cerebral mucormycosis in patients with diabetes mellitus. The "red flag signs" are cranial nerve palsy, diplopia, sinus pain, proptosis, periorbital swelling, orbital apex syndrome or a palatine ulcer.

In 1901, Hirschman, for the first time, used a modified cystoscope to examine the sinonasal cavity[6] Later on,Richart performed first endoscopic rudimentary maxillary sinus manipulation with a 7mm endoscope through oroantral fistula. In 1925, Maltz used nasal endoscope for diagnostic evaluation of the sinonasal cavity and coined the term. "Sinuscopy". The creation of Hopkin's rod system in 1960 was a milestone in the field of sinonasal endoscopy.

The role of Otorhinolaryngology is vital in diagnosis of Covid 19 through Nasopharyngeal swab and detection of Mucormycosis during covid and post covid period through diagnostic nasal endoscopy.

Need Of Study

Diagnostic nasal endoscopy is a rapid and convenient procedure with minimum morbidity and cost. While conventional fungal culture and sensitivity takes 3 - 4 weeks for identification of fungal species. In addition, it can provide guideline for taking biopsy and can definitely prove fungal invasion of the tissues. [7,8]

Methodology

Present study was a prospective study carried out among 112 Covid and Post Covid patients who were screened in the department of ENT in a Medical College and Rural Hospital. Study was conducted from Jan2021 to December 2021. Detailed history, clinical examination and consent for diagnostic procedure of the patient was documented. All study subjects were screened with nasal endoscopy and an endoscopic biopsy from middle meatus, middle turbinate region was taken and sent for the histopathological examination.

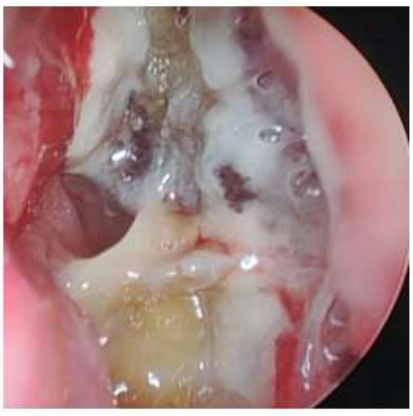

Figure 1.1

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Fig 1.1: The target area on nasal endoscopy typically showed black brown crusts, eschar with pus filled nasal cavity, fungal growth, erosion or blackish discoloration of turbinates and septal perforation.
Patients with any of above typical findings as seen in figure 1.1 were immediately subjected to MRI Paranasal sinuses, orbits with brain (plain + contrast) to know the extent of fungal invasion. Subsequently, those patients were posted for emergency surgical debridement and after confirmation with histopathology report, patients were started on antifungal therapy.

Inclusion Criteria

- Covid and post covid patients with history of facial pain, nasal discharge, retro-orbital pain, headache.
- Covid and post covid patients with history of treatment with steroids
- Post covid patients with history of diabetes mellitus or newly established cases of diabetes.
- Covid patients with Co- morbid conditions like Chronic renal disease or Chronic heart disease, Bronchial asthma.
- Covid patients with immuno-compromised conditions like HIV, patients on immunosuppressive therapy.
- Patients on oxygen therapy for covid treatment.

In our study, various parameters were assessed in detail which are as follows

1. Covid status during presentation of mucormycosis symptoms
2. Requirement of oxygen during covid treatment
3. Spectrum of nasal, orbital, palatal, ear symptoms.
4. Site of involvement of nasal mucosa
5. Associated co-morbidities like diabetes mellitus, bronchial asthma, hypertension, chronic renal disease, chronic heart disease.
6. Treatment received for covid -19 infection
7. Histopathological examination of nasal tissue biopsy sample.

Results

Out of 112 total screened patients, 48 patients had active covid infection while 64 patients were post covid (figure1.2)
As shown in figure 1.3, Out of 48 active covid patients,19 patients were on room air,29 patients were on oxygen requirement.

Figure 1.2

ACTIVE COVID PATIENTS	48
POST COVID PATIENTS	64
TOTAL NUMBER OF PATIENTS	112

Figure 1.3

Oxygen requirement	**Number of pts fungal positive**	**Fungal negative on HPR**	**Total**
RA	3	16	19
On oxygen	17	12	29
	20	28	48

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Fig 1.3 this table analysed using x2 test for test of significance,Chi- square X2 is computed is 8.66414,which is greater than 3.48 (confidence 95%) p=0.05, difference is statistically significant with 95% confidence

Fischer exact test is computed as 0. 00300, The exact value of p is 0. 00300 is less than 0.05 which means there is a statistically significant difference.

Figure 1.4

Status of the pt	Fungal positive on HPR	Fungal negative on HPR	TOTAL
symptomatic	38	4	42
asymptomatic	52	18	70
	90	22	112

Fig1.4 this table analysed using x2 test for test of significance,Chi- square X2 is computed is 4.35933,which is greater than 3.48 (confidence 95%) p=0.05, difference is statistically significant with 95% confidence.

Null hypothesis is rejected.

Mc Nemar Chi-squareX2 test (for paired nominal data) is computed as 41.14286 which greater than 3.48 (confidence 95%) which means that there is a statistically significant difference.

Among 95 diabetic patients, 71 patients had been detected with fungal invasion while out of 17 patients with other co morbidities like bronchial asthama, hypertension with CAD, 2 patients were positive for fungal invasion.

Figure

CO MORBITIES ASSOCIATED WITH FUNGAL INVASION	Fungal positive on HPR	Fungal negative on HPR	TOTAL
DM	71	24	95
Other comorbidities	2	15	17
	73	39	112

Other co morbidities includes hypertension with coronary artery disease./ bronchial asthma.

Chi- square X2 is computed as 25.19416 which is greater than 3.48 (confidence 95%) which means that there is a stastically significant difference.Null hypothesis is rejected.

Mc Nemar Chi-squareX2 test (for paired nominal data) is computed as 18.61538 which is greater than 3.48 (confidence 95%) which means that there is a difference.

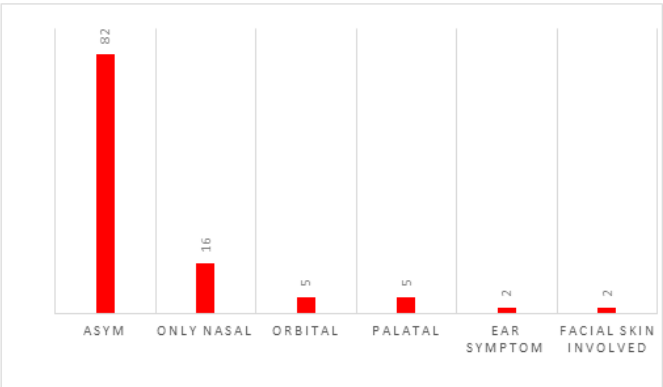

Figure 1.4: Distribution of patients with spectrum of symptoms

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Considering spectrum of clinical symptoms, maximum number of patients were asymptomatic (70) for mucormycosis who were screened through diagnostic nasal endocopy. While rest of 42 patients were symptomatic. 16 patients were presented with nasal symptoms like nasal blockade, nasal discharge, crust formation and nasal bleeding. 5 patients were presented with orbital symptoms like periorbital swelling, retroorbital pain, proptosis, sudden loss of vision, opthalmoplegia. All these patients underwent detailed opthalmological evaluation by opthalmologists. 5 patients presented with toothache, loosening of teeth, palatal ulceration with necrosis in surrounding tissues, palatal perforation. 2 patients were presented with vague symptom of ear pain without any nasal symptom. On screening with DNE of patient with earache, copious purulent nasal discharge in middle meatus and sphenoethemiodal recess region was present. And surprisingly biopsy sample of both patients turned to be mucormycosis on HPR. Rest 2 patients were presented with extensive involvement of facial skin over maxillary sinus and nose area.

Out of 42 symptomatic patients, 38 patients were positive for fungal invasion. Out of 70 asymptomatic patients 52 patients were positive for fungal invasion.

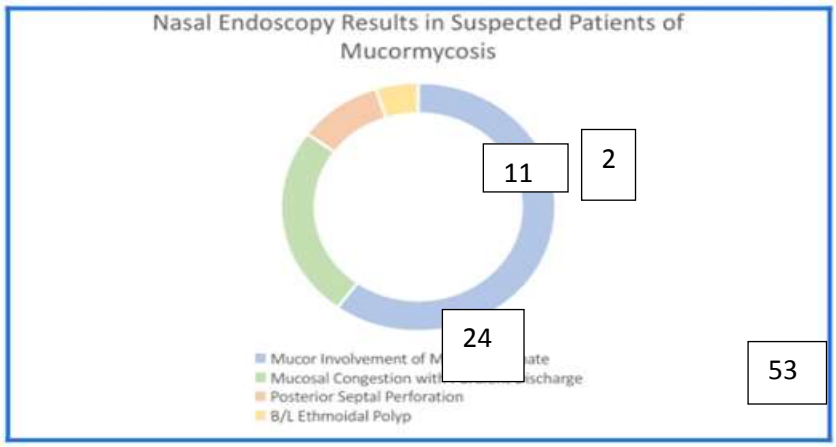

Figure 1.5: Comparative involvement of different nasal sites in suspected patients.

Endoscopic examination in suspected patients suggestive of most common site of involvement was middle turbinate (53 patients) in the form of blackish discoloration and dried blood clots with crust formation while in 24 patients mucosal congestion with purulent nasal discharge was present. In 11 patients, posterior part of septum was necrosed. 2 patient presented with bilateral ethmoidal polyps on biopsy of polyp unexpectedly turned out to be mucormycosis on histopathogical examination.

Histopathological Examination-

Of Nasal Biopsy Sample

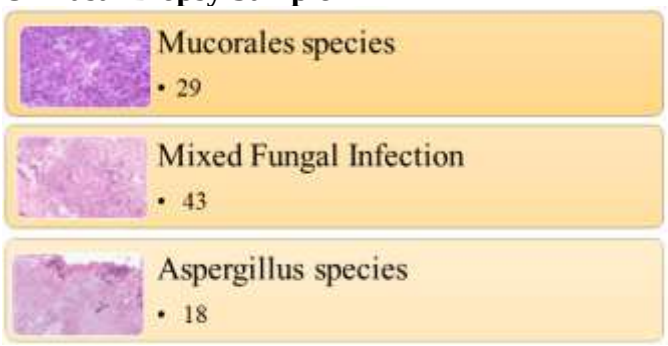

Figure 1.6

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In our study, on histopathological examination of nasal biopsy sample- Maximum number of patients had mixed fungal infection (43) while in 29 patients, mucorales species was detected. In 18 patients, aspergillus species was seen.

Treatment Given in Covid Patients

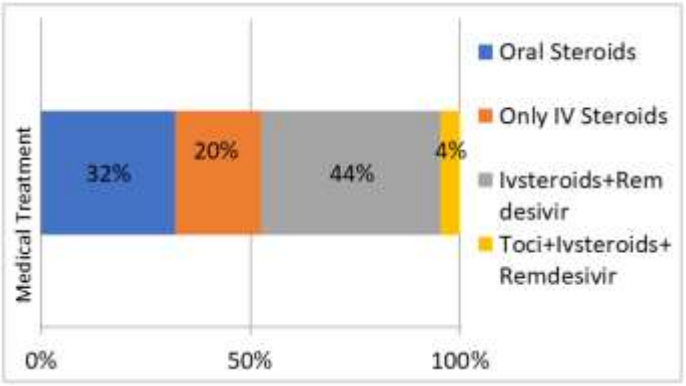

Figure 1.7

As shown in figure 1.7

32% of patients received oral steroid treatment for the treatment of covid infection, while 20% patients received intravenous steroids (injdexamethasone and prednisolone),44% of patients received injremdesivir in addition to iv steroids. And rest 4% of patients received tocilizumab with iv steroids with inj remdesivir.

Discussion

Mucormycosis of nose and paranasal sinuses is a fatal infection resulting in angioinvasion, thrombosis and ischaemic necrosis of nasal tissues [9] Mucor, Rhizopus, abidia, apophysomyces, and cunninghumella are the common organisms of the Mucorales. [10,11,12]

The factors predisposing to the development of the infection are uncontrolled diabetes mellitus, neutropenia, elevated free iron levels, desferoxamine therapy, hematological malignancies, stem cell transplants and organ transplant patients on immunosuppressants.[4,13,14,15] Inhalation of mucorspores through the nasal and oral cavity into the paranasal sinuses extend to orbit through thin lamina papyracea of ethmoidal bone, infratemporal fossa, inferior orbital fissure. Through perineural invasion and it may extend intracranially leading to complications like cavernous sinus thrombosis, sagittal sinus thrombosis, cerebral infarction and hemorrhage. The 1950 Smith and Krichner criteria [16] for the clinical diagnosis of mucormycosis are still considered to be gold standard and include: (i) Black, necrotic turbinate's easily mistaken for dried, crusted blood, (ii) Blood-tinged nasal discharge and facial pain, both on the same side, (iii) Soft peri-orbital or peri-nasal swelling with discoloration and induration, (iv) Ptosis of the eyelid, proptosis of the eyeball and complete ophthalmoplegia and, (v) Multiple cranial nerve palsies unrelated to documented lesion. In the present study, significant number of patients on oxygen (29) were seen to have varying involvement of nasal mucosa (17). This may be attruibuted to the contaminants in industrial oxygen as evident in a report by WHO, medical use of oxygen, health products and policy standards.

In india, industrial oxygen was used for medical use. According to the WHO, medical-use oxygen is different from industrial oxygen in purity and quality. Production, storage, and distribution processes involved with industrial oxygen could result in contamination.[17]

Reports and review by Kumar Nilesh and etal shows involvement of maxilla in conformity with the present study.[18] However, none of the studies recorded any otological complaints

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which is in contrast to the present study. The black turbinate sign on MR imaing was observed by S. Safder and etal, found middle turbinate as the commonest and first site of involvement which is in conformity with the recent study. [19]

As per observation by Dharmendra P Singh and et al aspergillosis co-infection was seen in immunocompromised patients with covid 19infection [20, 21]. In present study, most common comorbidity associated with covid-19 infection was diabetes mellitus, seen in 95 of patients which is similar to review of cases reported worldwide and in INDIA by Awadhesh Kumar Singh and etal. Covid-19 patients with associated co-morbidities such as diabetes mellitus, bronchial asthma, and use of immunosuppressive therapy like tocilizumab are more vulnerable to fungal infection.[22]. In diabetes mellitus, low pH due to acidosis is a fertile media for mucor spores to germinate. In addition, steroid use reduces the phagocytic activity of WBC, causes impairment of bronchoalveolar macrophages migration, ingestion, and phagolysosome fusion, making a diabetic patient susceptible to mucormycosis. COVID-19 often causes endothelialitis, endothelial damage, thrombosis, lymphopenia, and reduction in CD4þ and CD8þ T-cell level and thus predisposes to secondary or opportunistic fungal infection.[23]

Corticosteroids are mainstay of treatment modality for treating covid 19 infection by inhibition of cytokine storm. As per WHO guidelines, use of systemic corticosteroids (intravenous or oral) is recommended in severe and critical COVID-19 infection but not in mild cases.[24] A cumulative prednisone dose of greater than 600 mg or a total methyl prednisone dose of 2–7 g given during the month before, predisposes immunocompromised people to mucormycosis[25] Association between diabetes mellitus and post covid mucormycosis was supported by studies of awadesh k kirill, ali asghar *et al*. [26,27,28,29,30]. The recent guidelines in India recommend use of intravenous methylprednisolone 0.5–1 mg/kg/day or dexamethasone 0.1–0.2 mg/kg for 3 days in moderate cases while IV methylprednisolone 1–2 mg/kg/day or dexamethasone 0.2–0.4 mg/kg for 5–7 days is advised for severe cases. Worsening of clinical condition of the patient, worsening on radiological imaging, and raised inflammatory markers, can be treated with glucocorticoids for a short period of time (3–5 days).The NIH recommends the use of injection dexamethasone 6 mg/day for a maximum of 10 days for patients who are ventilated or require supplemental oxygen.[11,14] There are few case reports of mucormycosis resulting from even a short course (5–14 days) of steroid therapy, especially in people with DM.[22,26,29,32]

COVID-19 infection induces a production of IL-6 pro-inflammatory cytokine from bronchoepithelial cells. Tocilizumab is a recombinant humanized anti-IL-6 receptor monoclonal antibody approved by FDA, prescribed with steroids. Chronic use of this therapy weakens the immune response of patient leading to increasein the risk of mucormycosis in post-COVID-19 patients.[28]

Microbiological identification of the hyphae based on diameter, presence or absence of septa, branching angle (right or acute branching), and pigmentation, differentiates it from other fungal infections. Mucorales genera produce typically non-pigmented, wide (5–20 µm), thin-walled, ribbon-like hyphae with no or few septations (pauciseptate) and right-angle branching, while Aspergillus species shows typically 3–5 µm wide, septate and form acute-angle branching.[31]

Conclusion

Follow up of the high risk post covid patients, for sequale with diagnostic nasal endoscopy should be mandatory as majority of our patients are asymptomatic. patient may present with atypical symptoms like earache, nasal polyposis so high degree of suspicion is essential. Besides mucormycosis, coinfection with aspergillus also observed in our study. So reporting

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References

1. Fürbringer, P. Beobachtungenüber Lungenmycosebeim Menschen. Virchows Arch. 1876, 66, 330–365. [CrossRef]
2. Paltauf, A. Mycosis mucorina: Ein Beitragzur Kenntnis der menschilchen Fadenpiltzer-krankungen. Virchows Arch. Pathol. Anat. 1885, 102, 543–564. [CrossRef]
3. Slavin, M.; Van Hal, S.; Sorrell, T.; Lee, A.; et al. Invasive infections due to filamentous fungi other than Aspergillus: Epidemiology and determinants of mortality. Clin. Microbiol. Infect. 2015, 21, 490.e1–490.e10. [CrossRef] [PubMed]
4. Chakrabarti, A.; Das, A.; Mandal, J. The rising trend of invasive zygomycosis in patients with uncontrolled diabetes mellitus. Med. Mycol. 2006, 44, 335–342. [CrossRef] [PubMed]
5. Corzo-León, D.E.; Chora-Hernández, L.D Diabetes mellitus as the major risk factor for mucormycosis in Mexico: Epidemiology, diagnosis, and outcomes of reported cases. Med. Mycol. 2018, 56, 29–43. [CrossRef]
6. Ballenger, J. and Snow, J., 1996. Otorhinolaryngology. 15th ed. Baltimore: Williams & Wilkins, pp.173-180.
7. BlitzerA, LawsonW, MeyersBR, BillerHFPatient survival factors in paranasal sinus mucormycosis, Laryngoscope, 1980, vol. 90 (pg. 635-648)
8. LoftusBC General principles of management of fungal infections of the head and neck Otolaryngol Clin North America, 1993, vol.26 (pg. 1115-1121)
9. Werthman-Ehrenreich A. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. Am J Emerg Med. 2021 Apr;42:264.e5-264.e8. doi: 10.1016/j.ajem.2020.09.032. Epub 2020 Sep 16. PMID: 32972795; PMCID: PMC7493738.
10. Garg D, Muthu V, Sehgal IS, Ramachandran R, Kaur H. Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM): Case Report and Systematic Review of Literature. Mycopathologia. 2021 May;186(2):289-298. doi: 10.1007/s11046-021-00528-2. Epub 2021 Feb 5. PMID: 33544266; PMCID: PMC7862973.
11. Shah K, Dave V, Bradoo R, Shinde C, Prathibha M. Orbital exenteration in rhino-orbito-cerebral mucormycosis:A prospective analytical study with scoring system. Indian J Otolaryngol Head Neck Surg 2019;71:259-65.
12. LeeAS, Lee PW,AllworthA, Smith T, Sullivan TJ. Orbital mycoses in an adult subtropical population. Eye 2020;34:1640-7A
13. Revannavar SM, P S S, Samaga L, V K V. COVID-19 triggering mucormycosis in a susceptible patient: a new phenomenon in the developing world? BMJ Case Rep. 2021 Apr 27;14(4):e241663. doi: 10.1136/bcr-2021-241663. PMID: 33906877; PMCID: PMC8088249.
14. Mehta S, Pandey A. Rhino-Orbital Mucormycosis Associated With COVID-19. Cureus. 2020 Sep 30;12(9):e10726. doi: 10.7759/cureus.10726. PMID: 33145132; PMCID: PMC7599039.
15. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and Diagnosis of Mucormycosis: An Update. J Fungi (Basel). 2020 Nov 2;6(4):265. doi: 10.3390/jof6040265. PMID: 33147877; PMCID: PMC7711598.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

16. Smith H.W., Kirchner J.A. Cerebral mucor-mycosis: a report of 3 cases. Arch Otolaryngol. 1950;68:715–726.
17. WHO. Medical use of oxygen, health products and policy standards; 2021 [cited 2021 May 26].
18. Nilesh K, Vande AV. Mucormycosis of maxilla following tooth extraction in immunocompetent patients: Reports and review. J Clin Exp Dent. 2018 Mar 1;10(3):e300-e305. doi: 10.4317/jced.53655. PMID: 29721234; PMCID: PMC5923886.
19. Safder S, Carpenter JS, Roberts TD, Bailey N. The "Black Turbinate" sign: An early MR imaging finding of nasal mucormycosis. AJNR Am J Neuroradiol. 2010 Apr;31(4):771-4. doi: 10.3174/ajnr.A1808. Epub 2009 Nov 26. PMID: 19942703; PMCID: PMC7964235.
20. Rare case report of post-COVID Mucormycosis-Aspergillosis co-infection Dharmendra P Singh1, Rajesh K Verma -Article in Microbiologia Medica · December 2021 DOI: 10.4081/mm.2021.9918.
21. Stemler J, Hamed K, Salmanton-García J, Rezaei-Matehkolaei A, Gräfe SK, Sal E, Zarrouk M, Seidel D, Abdelaziz Khedr R, Ben-Ami R, Ben-Chetrit E, Roth Y, Cornely OA. Mucormycosis in the Middle East and North Africa: Analysis of the FungiScope® registry and cases from the literature. Mycoses. 2020 Oct;63(10):1060-1068. doi: 10.1111/myc.13123. Epub 2020 Aug 29. PMID: 32485012.
22. Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India. Diabetes Metab Syndr. 2021 Jul-Aug;15(4):102146. doi: 10.1016/j.dsx.2021.05.019. Epub 2021 May 21. PMID: 34192610; PMCID: PMC8137376.
23. Baldin C, Ibrahim AS. Molecular mechanisms of mucormycosis-The bitter and the sweet. PLoS Pathog. 2017 Aug 3;13(8):e1006408. doi: 10.1371/journal.ppat.1006408. PMID: 28771587; PMCID: PMC5542377.
24. World Health Organization. ((2020 Corticosteroids for .COVID-19: living guidance, 2 September 2020. World Health Organization. https://apps.who.int/iris/handle/10665/334125. License: CC BY-NC-SA 3.0 IGO.
25. Kontoyiannis, D.P.; Lewis, R.E. How I treat mucormycosis. Blood 2011, 118, 1216–1224. [CrossRef
26. Sen M, Lahane S, Lahane TP, Parekh R, Honavar SG. Mucor in a Viral Land: A Tale of Two Pathogens. Indian J Ophthalmol. 2021 Feb;69(2):244-252. doi: 10.4103/ijo.IJO_3774_20. PMID: 33463566; PMCID: PMC7933891.
27. Alekseyev K, Didenko L, Chaudhary B. Rhinocerebral Mucormycosis and COVID-19 Pneumonia. J Med Cases. 2021 Mar;12(3):85-89. doi: 10.14740/jmc3637. Epub 2021 Jan 19. PMID: 33984095; PMCID: PMC8040444.
28. Bhogireddy R, Krishnamurthy V, Jabaris S SL, Pullaiah CP, Manohar S. Is Mucormycosis an inevitable complication of Covid-19 in India? Braz J Infect Dis. 2021 May-Jun;25(3):101597. doi: 10.1016/j.bjid.2021.101597. Epub 2021 Jul 5. PMID: 34289382; PMCID: PMC8255098.
29. Ali Asghar S, Majid Z, Tahir F, Qadar LT, Mir S. Rhino-oculo cerebral mucormycosis resistant to amphotericin B in a young patient with diabetic ketoacidosis. Cureus. 2019;11(3):e4295. doi: 10.7759/cureus.4295. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
30. Monreal, E., Sainz de la Maza, S., Natera-Villalba, E. et al. High versus standard doses of corticosteroids in severe COVID-19: a retrospective cohort study. Eur J Clin Microbiol Infect Dis **40,** 761–769 (2021). https://doi.org/10.1007/s10096-020-04078-1

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 05, 2023

31. Ribes, J.A.; Vanover-Sams, C.L.; Baker, D.J. Zygomyc etes in human disease. Clin. Microbiol. Rev. 2000, 13, 236–301. [CrossRef]
32. Hoang, K.; Abdo, T.; Reinersman, J.M.; Lu, R.; Higuita, N.I.A. A case of invasive pulmonary mucormycosis resulting from short courses of corticosteroids in a well-controlled diabetic patient. Med. Mycol. Case Rep. 2020, 29, 22–24. [CrossRef]