



# Post COVID-19 Rhino-orbito-cerebral mucormycosis: A case series

Dr. Enosh Steward

B.D.S., M.D.S. (Oral and Maxillofacial Surgery), F.F.P.S. (Fellowship in Facial Plastic Surgery)

Consultant Oral & Maxillofacial Surgeon, Basal Implantologist and Facial Plastic Surgeon

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## ABSTRACT:

**Introduction:** Mucormycosis is a rare life threatening fungal infection; its incidence has increased during this COVID -19 pandemic era especially in the second wave in India. The state of Gujarat leads in the number of rhino-orbito-cerebral mucormycosis cases as post COVID-19 infection. This observational study explores correlation between mucormycosis, diabetes mellitus and corticosteroid therapy, with the aim to understand disease pattern, predisposing factors, presenting features and outcomes with times surgical and antifungal therapy.<sup>1,2</sup>

**Methods:** This retrospective clinical analysis includes data collection of 20 patients from an ENT hospital located in Kheda district of the state of Gujarat, India for a period of two months from 1<sup>st</sup> April 2021 to 31<sup>st</sup> May 2021. All these patients were post COVID 19 and had presented after varying number of days post the infection and had undergone indoor treatment in various hospitals.

**Result:** Data was collected from ENT Hospital indoor and outdoor case records. Of the 20 patients, three were from proper Nadiad, rest were from peripheral areas, aged between 32-72 years, 19 are males with one female. All the patients were having diabetes mellitus pre-covid and majority underwent corticosteroid medications and supplemental oxygen therapy during COVID treatment. Mucormycosis infection was observed with palatal involvement in seven patients and six patients with eye involvement. Two patients were deceased by other causes and one is in critical condition at present.

**Conclusion:** Close correlation was observed between invasive rhino-orbito-cerebral mucormycosis, diabetes mellitus and corticosteroids administration in COVID-19 positive patients. Possible follow up and larger sample size will justify.

**Keywords:** Covid-19 sequelae, mucormycosis, diabetes mellitus, corticosteroids, predisposing factors, oxygen

## I. INTRODUCTION

Corona virus disease (COVID-19) might developed by Severe Acute Respiratory Syndrome (SARS-COV-2).<sup>3</sup> Dominant pandemic SARS-COV-2 associated Pneumonia, stroke, kidney dysfunctions, and vascular thrombosis etc. had afflicted and succumbed more than millions of people worldwide within last 2yrs. Recent viral storm in India, has noticed severe devastating co-infection mucormycosis, a "Black fungus" caused by Mucorales species in patients who are recovering from COVID-19.<sup>4</sup> Duration of time for infection to occur is couple of days to weeks from covid recovery. Involvement of Maxillofacial area has led to worse outcome during a deep COVID crisis in immunocompromised patients with uncontrolled diabetes and subsequent corticosteroid therapy.<sup>1,4,5</sup> Tissue necrosis is the signet of mucormycosis.<sup>6</sup> Severe pain, necrotic ulcer in palate, eye swelling, visual problems as blurring and/or loss of vision,<sup>4,7</sup> cough and shortness of breath are all associated clinical signs and symptoms. Lethality % is increased with rhinocerebral (brain and sinus)<sup>8</sup> involvement.

Alarming rise in mucormycosis cases in post covid patients has stressed to think some triggering causative factors beyond the steroid use and immunocompromised status by diabetes mellitus or other diseases.<sup>9</sup> Diagnosis by Magnetic Resonance Imaging (MRI), superintendence of contributory factors, Functional Endoscopic Sinus Surgery (FESS),<sup>6</sup> conservative management by antifungal drugs and surgical debridement are the best treatment protocol.<sup>4</sup>

## II. METHODS

Recent study includes clinical analytical survey of 19 male patients and 1 female with 32-70 age range, cases of post covid infections of maxillofacial region presenting in ENT Hospital of Nadiad, Kheda District in the west zone of Gujarat, India. We have seen 20 patients till date in last 40



days of that 18 in last 15 days. None have been treated for COVID in our hospital. All are treated surgically with either surgical debridement of necrotic areas, maxillectomy and infratemporal fossa curettage. Analytical data of all patients includes correlation between mucormycosis, diabetes mellitus, and corticosteroid usage and

contributor factors to urge this disease as an epidemic one in India.

### III. RESULT

We have tried to show the data of all patients in the form of tables. Demographic and clinical profile of all the patients is presented in table 1

Table 1

No.	Age	Sex	Diagnosis	Covid status at hospitalization	Duration post covid	Diabetes history		Steroid Therapy
						past	present	
1	55	M	Mucormycosis	Negative	6-7days	10yrs		Y; short term
2	67	M	Mucormycosis	Negative	6-8 days	4-5 months		
3	33	M	"	"	2-3 weeks	N positive		Y
4	70	M	"	"	3 weeks	Nil		Y
5	70	M	"	"	7 days	15yrs		Y short term
6	35	M	"	"	1 week	Y		Y
7	59	M	"	"	2weeks	Y 10-15yrs		Y
8	40	M	"	"	4-5days	positive at test		Y
9	58	M	"	No	No	3yrs		Y
10	55	M	"	Negative	5 days	Y		Y
11	53	M	N	N'	1 week	5yrs uncontrolled		Y
12	48	M	Y	N'	1 week	Y		Y
13	61	M	Y	N'	5-10days	Y		Y
14	50	M	Y	N'	1 month			Y
15	52	M	No data					
16	64	F	Y	N'	7-10days	Controlled		Y
17	33	M	Gram bac. aspergillosis	N'	2-3days	At present yes		Y short term
18	57	M	Mucor	N'	7 days	Y		Y
19	32	M	"	N'	5-7 days	N		Y
20	48	M	"	N'	1 month	Y		Y

All symptoms of an individual are summarized in table 2.

Table 2

No.	Symptoms	Loss of Vision	Sinusitis
1	Eye swelling- pain in all area- nose, sinus, palate involvement	N	Y
2	Facial paralysis, numbness- nose, sinus, palate involvement	N	Y
3	Headache , pain in ear & nose, sinus teeth mobility, mouth ulcer in palate	N	Y
4	Giddiness, swelling, black dots in Nose, Fluctuating pain in nose, sinus, eye	N	N
5	cheek swelling ,black dots in nostrils Pain in nose ,sinus ,eye	N	N
6	Nose ,sinus ,eye and CNS involvement	Y	Y
7	Nose and ear pain, headache, sinus involved	N	Y



8	Cheek, Eye swelling from 1 month	swelling only	Y
	Nose , sinus, eye, palate, CNS involvement		
9	Mouth stickiness 5-6days, teeth pain	N	Y
	Nose, sinus, palate involvement		
10	Nose ,sinus involvement	N	Y
11	Left eye vision loss- Nose, Eye ,sinus involvement	Y left eye	N
12	Nose , sinus, eye, palate	Y	Y
14	Sticky mouth, nose etching, gum pain, palatal pain, brain involved	N	N
15	NO DATA		
16	Eye swelling, headache	Yes	Y
	sinus, nose, maxillary teeth pain		
17	Pain below eye, nose, numbness	N	Y
	nasal and palatal pain, sinus		
18	Nose, sinus involvement	N	Y
19	Nose ,sinus involvement	N	Y
20	Orbit, palate, sinus, involvement	Y	Y

Table 3 represents sequelae, treatment and outcome of all patients.

Table 3 Sequelae, treatment and outcome

No.	Maxillary Necrosis	Intracranial Extension	Treatment	Co morbidity	Survival Status
1	Y	Y	Hemimaxillectomy with infratemporal fossa debridement	High blood pressure	survive
2	facial paralysis, swelling	Orbital	"	No	Survive
3	Y	Y	"	N	"
4	N	N	Surgery planned	No	"
5	N	N	Hemi maxillectomy	Past-Bypass surgery	"
6	N	Y	Referred to civil hospital	N	Survived
7	N	Y	Hemi maxillectomy infratemporal clearance	N	Succumbed not by mucor or surgery
8	N	N	"	No	survived
9	N	Y	Debridement	Throat cancer Treated	Critical
10	N	N	infratemporal clearance	Liver dysfunction, Anand shift	
11	N	N	N	Recent Brain stroke	"
12	Y	N	Hemimaxillectomy with infratemporal clearance	No	Survive
13	Y	N	Surgery planned	No	
14	N	N	curettage in nose	No	Survived
15	<b>Not collected</b>	-	-	-	-
16	N	N	Avoid by patient	No	Survived



17	N	N	recent admission	No	
18	N	N	Medication, surgery planned		
19	N	N	“	-	-
20	Y	Y	“	-	-

A case is represented by Fig. 1, Fig. 2 and Fig 3 depicting the palatal involvement of mucormycosis with its scan and the excised hard tissue.



Fig 1 Depicting palatal involvement of mucormycosis

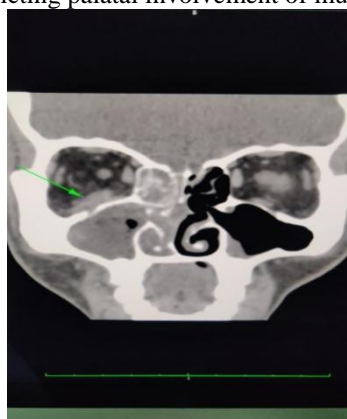


Fig 2: Radiographic scan to evaluate the sinus and palate condition



Fig 3: Excision of the palate along with teeth

#### IV. DISCUSSION

Mucormycosis is a rare, aggressive, angioinvasive<sup>5</sup> opportunistic co-infection of rhino-

orbito-cerebral<sup>7</sup> in an immune-compromised patients<sup>6</sup>, diagnosed by uncontrolled diabetes<sup>10</sup> who underwent corticosteroids therapy during COVID treatment. Amongst SARS-COVID associated



bacterial and fungal infections like aspergillosis, candidiasis,<sup>10,11,12,13</sup> a rhino-orbito-cerebral mucormycosis<sup>14,15,16;</sup> is an emerging concerned co infection<sup>17</sup> in india today. This study includes series of 20 cases are diagnosed within a month of april-may 2021 in our ENT hospital, Nadiad, Gujarat, India with clinical signs and symptoms of maxillofacial mucormycosis as a post covid sequelae.

### Few causative factors

\*Ferritin, a key mediator contributor of cytokine storm and predictor of COVID severity.<sup>18,19,20,21</sup> Very high level of serum ferritin was found in almost all the patients as ferritin feeds and thrives the fungus, mucormycosis. Non Toxic iron chelating agent desferrioxmine and reduction in dietary iron is useful to regulate serum ferritin level.<sup>18</sup>

\*Glycaemic control (hyperglycaemia and insulin resistant), is an important measure to reduce secondary infection and to improve COVID outcome.<sup>22</sup> Poor glycaemic control<sup>22,23</sup> along with nutritional support leads to apoptosis and tissue fibrosis. Patients with comorbidities like diabetes mellitus and immune suppression condition are at high risk of infection. Timely glucose management reduces morbidity and mortality rate.<sup>23</sup>

Heated and humidified high-flow nasal oxygen (HFNO)<sup>24</sup> is feasible and successfully utilized respiratory supporter to avoid mechanical ventilation in majority of patients with severe hypoxaemia. Extracorporeal Membrane Oxygenation (ECMO) is recommended in patients with severe forms of acute respiratory distress syndrome (ARDS)<sup>25,26</sup> Higher oxygen saturations, lower respiratory and heart rates, and arterial oxygen partial pressure to fraction inspired oxygen ratio (PaO<sub>2</sub>/FiO<sub>2</sub>)<sup>27</sup> have weaning effect within 6 hours of commencement of HFNO, result in successful outcome in patients. FiO<sub>2</sub> < 0.3 for higher flow 1-6 L/Min causes nasal crusting and irritation leads to Mucormycosis.<sup>28</sup> Standard oxygen mask, correct positioning of surgical mask on patient's face reduces the bio aerosol nosocomial<sup>28</sup> droplet infection of medical staff and HFNO failure.<sup>24</sup> Prolonged use of ECMO cause membrane rupture, plasma leakage and SARS-Cov-2 dissemination via its exhalation pathway leads to haemorrhage and cardiac arrest along with bacterial infection and septic shock.<sup>29</sup> Strict monitoring with trained staff is must to avoid these sequelae.<sup>25</sup>

Multisystem thromboembolism is a non-respiratory complication due to abnormal

coagulation cascades by prothrombotic nature of COVID 19 leads to micro thrombosis.<sup>30,31</sup> Corneal conjunctivitis with congestion, eyelid hyperaemia, sudden onset of blindness due to central retinal artery occlusion and acute macular neuro retinopathy are presenting ocular features of COVID-19.<sup>4</sup> Active clinical and radiographic surveillance by CT angiography and MRI Brain along with balanced management between anticoagulants<sup>31</sup> use and bleeding risk are useful to assess the thromboembolism.<sup>26,30</sup>

Immunomodulator drugs like tocilizumab effectively used in seriously ill COVID 19 patients to quell the cytokine storm<sup>32,33</sup> Single or more dose of tocilizumab may weaken the innate immunity, Predispose patients to secondary infections,<sup>34</sup> bacteremia,<sup>35</sup> Fungal infection,<sup>36</sup> after 30 days of drug administration.

Several observations emerged from this analysis, that majority of the patients are diagnosed as mucormycosis and one with aspergillosis. As India has the second largest number of patients suffering from diabetes mellitus aged between 30-70 years serves as a risk factor for<sup>17</sup> mucormycosis infection. Data shows all patients between this age group. Out of 20 patients 19 are males. This study records almost all the patients are diabetic (pre-covid/post-covid). Duration of infection is noticed either by patients or diagnosed by medical checkup range from couple of days to weeks after recovery. Corticosteroids has enhanced the prevalence of mucormycosis, risk of invasion and necrosis during covid or after recovery from it in immune-compromised individuals.<sup>14,15,16</sup> Symptoms of mucormycosis as a complaint of headache, facial swelling, fluctuating pain in nose, palate and eye with visual impairment.<sup>4</sup> In many of them along with itching in the involved areas during O<sub>2</sub> administration at the time of hospitalization or after recovery from the COVID. Few patients have noticed black dots in nostrils (a necrotic eschar)<sup>6</sup>, facial numbness and teeth mobility. Rapid progress was noticed, of 2-3 days from the onset of visual symptoms. Patients were prescribed by antifungal Medicines prior surgery.

Clinical findings along with MRI, lab tests, nasal endoscopy (FESS) has assessed the disease extension and an invasion pattern in an individual. Surgical debridement<sup>4</sup> is dependent on extension of an infection to get successful outcome from maxillary necrosis, orbital involvement, nasal crusting and intracranial involvement with facial paralysis.<sup>6</sup> Partial maxillectomy, debridement of necrotic tissue and infra-temporal curettage were performed as a surgical procedure under prescribed necessary medications with time. Two patients





were succumbed, two had refused of surgical procedure and rests are survive till today with better results.

## V. CONCLUSION

This clinical observational survey includes few points to be considered such as possible avoidance of glucocorticoids in mild COVID-19 cases (without hypoxemia) or maintained doses of glucocorticoids in critical cases of COVID. Antifungal medications, super surveillance of immune-compromised status of diabetes mellitus in all patients, screening of COVID 19, early diagnosis of fungal co-infection, focus on triggering contributor factors and timely required treatment are a valuable means to control disease and its severe outcome.

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