

## Clinical characteristics of 62 cases of post covid-19 mucormycosis: Experience with MJPJAY from tertiary care center in North Maharashtra

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### Abstract

**Introduction:** Covid-19 pandemic, the dark chapter in human history started in Wuhan, Hubei Province, China on 31st of December 2019 when the 2019-nCoV associated pneumonia cases were reported to the World Health Organization (WHO) by the Chinese government. Very soon its black shadow covered almost every land of the globe. This black shadow of covid-19 uncertainty further darkened with the rise of black fungus, mucormycosis. Over 45,000 Cases Of Black Fungus Reported In India till 15 July 2021 as Parliament informed by a report from press trust of India. **Aims and objectives:** To study the clinical characteristics of post covid-19 mucormycosis cases and financial support management by Mahatma Jyotiba Phule Jan Arogya Yojana at our Government medical college Dhule in times of ongoing covid-19 pandemic. **Material and Methods :** This is a prospective observational study from 1<sup>st</sup> April 2021 to 15 July 2021. All patients having mucormycosis of the paranasal sinuses with or without having a history of coronavirus disease infection were included in the study. Detailed history and Clinical characteristics were recorded. Management included multidisciplinary approach. All clinical departments shared clinical management along with imaging and laboratory investigations. Intravenous liposomal amphotericin B and appropriate surgical procedures were the main stay of management. **Results :** All the patients were symptomatic with mucormycosis (n=62) and had recovered from covid-19 recently (n=61). Total 62 patients studied including 42 males (67.74%) and 20 females (32.25%). Mean age was 50.58 years. 61 patients (98.38%) had history of covid-19 infection confirmed by RTPCR test. Diabetes mellitus was present in 54 patients. Mean diabetes duration was 4.6 years and it was not controlled in 28 cases. Covid-19 positivity (98.38%), Diabetes mellitus (87.09%) and steroid use (75.80%) were prime risk factors noted. Hypertension (25.80%) and ischemic heart disease (06.54%) were next common comorbidities. The ethmoids (77.41%) were the most common sinuses affected followed by maxillary (58.06%). Majority of patients (67.74%) had multiple sinuses involvement. The combination of ethmoid, maxillary and sphenoid sinuses involvement was most frequent. Intra-orbital extension was seen in 41.93% of cases, while intracranial extension was only seen in 17.74%. The most common presentation was local pain, headache and swelling of face followed by nasal obstruction, nasal discharge and eyelid swelling. Serious eye signs were ptosis (19.35%), chemosis (17.74%) and impaired vision (17.74%). Intravenous liposomal amphotericin B was given to all patients for an average 17 days. Exenteration was required in 10 patients (16.12%). No mortality noted. Under MJPJAY scheme enrollment of 53 (85.48%) cases were succeeded. Procedure packages for rhinocerebral mucormycosis (n=53), Endoscopic sinus surgery (n=17), orbital exenteration (n=10) were obtained. Till 1<sup>st</sup> August 2021, claim approved were 20, claims submitted or in process were 30 and claims pending were 3. From the approved 20 claims revenue generated costs Rs 8,00,000. Total expected revenue generation is Rs 26,25,000. Economically exhausted 53 families got financial support under MJPJAY. **Conclusion:** Post covid-19 immuno-compromised host in combination of uncontrolled diabetes is an ideal destination for mucorals to invade. Covid-19 and mucormycosis of the paranasal sinuses is a deadly combination. Already stretched families during coronavirus infection now got totally exhausted by this sudden financial crash. MJPJAY is a ray of light in the life of these exhausted families!

**Keywords:** COVID-19; diabetes mellitus, Mahatma Jyotiba Phule Jan Arogya Yojana, Mucormycosis, Preauthorization

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### Introduction

A total of 45,432 cases of Mucormycosis or Black Fungus have been reported by states and Union Territories till July 15 of which 21,085 affected people are receiving treatment and 4,252 have died, the Rajya Sabha was informed on Tuesday[1].

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Among these a large majority of Mucormycosis patients (84.4%) had reported a history of COVID-19. Most common presentations of mucormycosis include rhino-cerebral (77.6%), cutaneous (4.3%) and pulmonary (3.0%). Till June 24, Maharashtra has reported a total of 8,367 cases of mucormycosis with the highest numbers in Pune, 1,234, and Nagpur, 1,339. Aurangabad has the third highest number of cases, at 945, according to a state analysis of cases[2].

Covid-19 is a life-threatening, infectious disease; affected patients show an over expression of inflammatory cytokines, and impaired cell-mediated immunity with decreased cluster of differentiation 4 and 8 positive T-helper (CD4<sup>+</sup> T and CD8<sup>+</sup> T) cell counts, indicating susceptibility to fungal co-infections[3]. A complex interplay of factors that include diabetes mellitus, any previous respiratory pathology, immunosuppressive therapy, nosocomial infection sources and systemic immune alterations of Covid-19 infection itself may lead to secondary infections, which are increasingly being recognized in view of

their impact on morbidity and mortality[4]. Mucormycosis is an angio-invasive disease caused by opportunistic fungi of the order Mucorales in immunocompromised patients[5]. Mucormycosis infection of the sinuses is a form of life-threatening invasive fungal sinusitis that typically affects immunocompromised individuals with an impaired neutrophilic response[6]. The pathogen is ubiquitous, occurring naturally in the environment, the body surface, and orifices. The spores inoculate the paranasal sinuses and the nasopharynx with subsequent spread to the orbit and intracranial cavity in persons with decreased cellular and humoral defenses. The pathogen invades the vascular lamina propounding the inflammation with infarction and necrosis[7]. Mucormycosis is characterised by the presence of hyphal invasion of sinus tissue and a time course of less than four weeks[8,9]. Histological features include mycotic infiltration of blood vessels, vasculitis with thrombosis, tissue infarction, haemorrhage and acute neutrophilic infiltrate[10]. Clinically, rhino-cerebral mucormycosis can present with atypical signs and symptoms similar to complicated sinusitis, such as nasal blockage, crusting, proptosis, facial pain and oedema, ptosis, chemosis, and even ophthalmoplegia, with headache and fever and various neurological signs and symptoms if intracranial extension is present[11,12]. A black eschar is often seen in the nasal cavity or over the hard palate region, but is not characteristic[13,14]. Even with prompt diagnosis, treatment of underlying diseases, and aggressive medical and surgical intervention, the management is often not effective, leading to an extension of the infection and ultimately death[15]. During weaning of second covid-19 wave there was a sudden rise in cases of invasive fungal sinusitis, mucormycosis. Since the rise of corona-virus, majority of population faced economic crisis due to several lock downs, job cuttings, less income resources and fear burden of this devil disease. So many families exhausted their savings to pay the hospital. Poor public infrastructure, unaffordable private medical care and limited access to the state health insurance scheme were pushing Covid patients and their families into long-term debt[16]. During this economic hardship MJPJAY is a ray of light in the life of these exhausted families! This is clinico-epidemiological study of patients of post covid-19 mucormycosis at teaching hospital of north Maharashtra.

#### Material and methods

This was a prospective observational clinico-epidemiological study at Government Medical college, Dhule, Maharashtra. From 1<sup>st</sup> April 2021 to 15<sup>th</sup> July 2021 over a period of three and half months, all patients with invasive mucormycosis of the paranasal sinuses who got admitted were included in the study. At the time of admission they were either coronavirus-positive or had recovered from coronavirus infection.

This positivity was confirmed by reverse transcription-polymerase chain reaction (RT-PCR) of nasopharyngeal or throat swab. All the patients biodata, clinical findings, imaging features, blood investigations, histopathology reports, co-morbidities, management, operative details, and follow-up information were recorded on a proforma sheet and analysed. The patients were treated by a multidisciplinary approach involving clinical and investigative departments. A mucormycosis team of senior doctors were formed for overall administration and treatment management of these patients. CT scan and/or MRI of orbits, paranasal air sinuses and brain was done with or without contrast. Special care given for comorbidities such as diabetes, hypertension and ischemic heart disease. Neurosurgeon consultation was sought whenever suspicion of intracranial extension was in doubt. All patients underwent operative procedures (sinus debridement), keeping complete surgical debridement as the aim with intravenous Amphotericin. Intravenous liposomal Amphotericin B in a dose of 3 to 5 mg/kg body weight/day was used. Most of the patients were enrolled in MJPJAY scheme and all the beneficiaries claims were settled. It was a timely help for these economically burdened families.

#### Results

A total of 62 patients presented and admitted; 40 males (67.74%) and 22 females (32.25%). Male to female ratio was 1.8:1. Almost all (n=60) were in fourth, fifth and sixth decade of life. Only one male patient had age 29 and another female had 72 years of age. The mean age was 50.58 years. [Table no 1]

**Table 1: Epidemiology : Age and gender distribution**

Age group (in years)	n=62	%
<20	00	00
21-30	01	1.61
31-40	25	40.32
41-50	21	33.87
51-60	14	22.58
61-70	01	1.61
>70	00	00
Gender	n=62	%
Male	42	67.75
Female	20	32.25

The major risk factors were Covid-19 positivity and diabetes mellitus with concurrent steroid use. [Table 2]. Most of the patients (n= 61) were Covid -19 infected in recent past. The duration from treatment with Covid-19 positivity to presentation of mucormycosis was on an average of 2 months. Five patients were having active Covid -19 and RTPCR report positive at admission for mucormycosis. One female patient of age 45 years had no history of covid-19 like infection in past but presented with typical signs and symptoms of mucormycosis. She was a known case of diabetes and hypertension from 8 years.

**Table 2: Risk factors predisposing to mucormycosis**

Risk factors	n = 62	%
COVID-19	61	98.38
Diabetes mellitus	54	87.09
Controlled	18	
Uncontrolled	28	
Newly detected	08	
Intravenous Methylprednisolone	47	75.80
Hypertension	16	25.80
Controlled	12	
uncontrolled	04	
Ischemic Heart Disease	04	06.54

Risk factors	n = 62	%
HIV	01	0.61

All patients (n=61,98.38%) having history of covid-19 infection also had history of recent hospital admission and treatment with Oxygen and /or treatment with intravenous methylprednisolone (n=47,75.80%). Along with covid-19, most common comorbidity was diabetes mellitus (n = 54,87.09%) which includes uncontrolled (n=28) and newly detected diabetes mellitus (n=8) patients. Use of methyl prednisolone in previous treatment during hospital admission (n=47) was the next most common comorbidity followed by hypertension (n=16) and ischemic heart disease (n=04). One 52 year male patient was having Human Immuno deficiency (HIV) infection as comorbidity. [Table No 2] The median duration of symptoms was 15 days (range : 6–50 days). After covid-19 infection and treatment, the onset of mucormycosis was noted on an average of 2 months. Active COVID-19 infection with rhino-orbital mucormycosis was seen 5 cases (8.06%). The most common presenting complaint was pain at local site (n=52,83.87%), headache (n=46,74.19%), swelling of cheek /face (n=41,66.12%), nasal obstruction (n=36,58.06%), nasal discharge (n=32,51.61%) then watering of eyes (n=24,38.70%) and eyelid swelling (n=18,29.03%). Eye pathology caused impaired vision in 11 patients (17.74%). [Table no 3]

**Table 3: Chief complaints and clinical presentation of mucormycosis patients**

Chief complaints and Clinical presentation	Number	%
Local pain at PNS site	52	83.87
Headache	46	74.19
Swelling of cheek/face	41	66.12
Nasal obstruction	36	58.06
Nasal discharge	32	51.61
Watering of eye	24	38.70
Eyelid swelling	18	29.03
Ptosis	12	19.35
Impaired vision	11	17.74
Chemosis	11	17.74
Loosening of teeth	04	06.45
Nasal bleeding	03	04.83

In our study, the most common paranasal sinus involved was ethmoid sinus (n=48,77.41%). It was followed by maxillary (n=36,58.06%) and sphenoid sinus (n=20,32.25%). Majority of patients (42,67.74%) had multiple sinuses involvement. The combination of ethmoid, maxillary and sphenoid sinuses involvement was most frequent. Majority had unilateral sinus involvement (n=44,70.96%) than bilateral sinus involvement (n=18,29.03%). [Table no 4]

**Table 4: sinuses involved in mucormycosis**

Sinuses involved	Number	%
Ethmoid	48	77.41
Maxillary	36	58.06
Sphenoid	20	32.25
Frontal	03	04.83
Maxillary +ethmoid	17	27.41
Maxillary+ethmoid+sphenoid	42	67.74
Pan-sinusitis	6	09.67

CT (n=62) and MRI (n=56) imaging were main stay in planning of operative procedures. Main finding on CT was minimally enhancing hypo-dense soft tissue thickening in involved sinuses, while MRI had T2 iso-intense to mildly hypo-intense soft tissue thickening and heterogeneous post contrast enhancement as the main finding. These imaging showed ethmoid (n=48, 77.41%) and maxillary (n=36,58.06%) sinuses involvement predominantly. Beyond the sinuses extension to the orbit (n=26,41.93%), face (n=19,30.64%), deep skull base (n=7,11.29%) and brain (n=11,17.74%) was noted. Bone erosion was seen (n=34,54.83%) and extension across grossly intact appearing bones also noted (n=26, 41.93%). On CT, three types of contrast enhancement were seen, with mild enhancement being the most common form (n=39,62.90%). A spectrum like findings on CT and MRI were noted in this study of rhino-cerebral mucormycosis. Imaging played a major role in assessing the extent of involvement and complications and was a key deciding factor in management. [Table no 5]

**Table 5 : CT Scan and MRI commonest Imaging findings**

CT scan Finding	N	%
Mucosal thickening	62	100
Bony erosions	34	54.83
Enhancement pattern		
● Non- enhancing	18	29.03
● Mild enhancement	39	62.90
● Heterogenous	05	8.06
MRI Finding	N	%
T1 W signal hyperintense	56	100
2W signal		

CT scan Finding	N	%
Isointense/Hypointense	23	37.09
● Heterogenous	17	27.41
● Hyperintense	16	29.03

All patients (n=62,100%) were managed with Liposomal Amphotericin B with or without surgical debridement. The average duration of intravenous amphotericin B was 17 days. Adverse reactions noted were nephrotoxicity (n = 6), hypokalaemia (n = 7), hypomagnesemia (n = 3) and bone marrow suppression (n = 2). Oral Posaconazole tablets (at a dosage of 300 mg OD) were used in such cases. The mean duration of hospitalization was 32 days. Surgical procedures included unilateral or bilateral functional endoscopic sinus surgery [FESS](39,62.90%), orbital exenteration(10,16.12%) and maxillectomy(2,3.22%) There were no mortality in this study. [Table no 6] Comorbid conditions (61,98.38%) were noted in almost all the study patients. During mucormycosis management proper care of these conditions like

controlled and uncontrolled diabetes, hypertension, ischemic heart disease was taken.

The diagnosis is confirmed by microbiology and pathology study. In microbiology by demonstrating the fungal hyphae in KOH mount and fluorescent staining with calcofluor. These shows the characteristic feature of mucormycete and the fungus could be cultivated and identified as *Rhizopus arrhizus* or *Rhizopus* spp. On histopathology twelve cases showed coagulative necrosis or angioinvasion or perineural invasion features which suggests acute disease process. While sixteen cases had granulomatous inflammation with giant cells which suggest chronic mucormycosis.

**Table 6: Management Details : Medical and Operative procedures.**

Treatment mode	number	%
Intra venous liposomal Inj. Amphotericin B	62	100
Sinus Surgery	41	66.12
Functional endoscopic sinus surgery	39	
Maxillectomy	02	
Exenteration of eyeball	10	16.12
Management for comorbidity	61	98.38

Under Mahatma Jyotiba Phule Jan Aarogya Yojna (MJPJAY) total expected revenue collection is 26,25,000. Expected contribution from Rhinocerebral mucormycosis [code:M13U1.5], sinus surgery (FESS) [code:S2B3.1] and Orbital exenteration [code : S11J2.1] are Rs 21,20,000, Rs 2,55,000 and Rs 2,50,000 respectively. Till 1<sup>st</sup> August 2021, total revenue generated was Rs 8,00,000. Total 20 claims were approved ,30 claims in were process or claims submitted and 3 claims were pending.

**Table 7: Mjpjay details: As on 1<sup>st</sup> August 2021**

MJPJAY Beneficiary	Numbers	MJPJAY Package code	MJPJAY Package amount	Estimated Revenue
Total patients admitted	62			--
Patients enrolled in MJPJAY Rhinocerebral mucormycosis	53	code :M13U1.5	40,000	21,20,000
Sinus debridement under MJPJAY	17	Code:S2B3.1	15,000	2,55,000
Orbital exenteration under MJPJAY	10	Code : S11J2.1	25,000	2,50,000
<b>Total revenue Expected</b>				<b>26,25,000</b>
Revenue generated till 1 <sup>st</sup> August 2021	20*			8,00,000
<b>MJPJAY cases in process</b>				
● Preauthorization approved	53			21,20,000
● Total claims approved	20*			8,00,000
Claims in process/ claims submitted	30			17,05,000
● Claims pending	03			1,20,000

\* The process of insurance completed. Beneficiary got benefit and amount is deposited in hospital personal ledger accounts [PLA] fund.

### Discussion

Covid-19 is a disease caused by a new strain of coronavirus. 'CO' stands for corona, 'VI' for virus, and 'D' for disease. Formerly, this disease was referred to as '2019 novel coronavirus' or '2019-nCoV[17]. The word "novel" indicates a "new pathogen of a previously known type" (i.e. known family) of virus[18]. Corona viruses are common in non-human animals, but SARS-CoV-2 has never been previously seen in humans (hence "novel"). The word novel is based on Latin novellus "new, young, fresh." If something is novel, it is new but also original, fresh and unique. Our study also conducted and completed during this ongoing novel coronavirus pandemic itself making it novel !

**Mucormycosis : A saprophytic opportunistic demon**

Mucor is a saprophytic fungus; its spores exist widely in nature, and are spread in soil, air, food and decaying organic material[15]. Because of the low virulence potential, it may be present in the nasal mucosa of healthy people as a commensal[19]. Mucormycosis or zygomycosis, also called phycormycosis, initially described in 1885 by Paltauf, is an uncommon and aggressive fungal infection that usually affects patients with alteration of their immunological system[20]. Covid-19, a immunity wrenching disease with use of steroids and oxygen during its treatment with associated comorbidity makes the covid victim a fertile soil for mucor to grow. It is a lethal fungal disease, with rhinocerebral presentation being its most common form[21]. Rhinocerebral mucormycosis is a life-threatening infection caused by

saprophytic fungi belonging to the genera *Mucor*, *Rhizopus* and *Absidia* [22, 23] All of these belong to the order Mucorales and class Zygomycetes[24].

#### Incidence

India has the highest burden of mucormycosis and before the pandemic, the exact estimate of Mucormycosis in India was 0.14 per 1000, nearly 70 times higher than the worldwide data[25]. Although it has a low incidence rate, varying from 0.005 to 1.7 per million population, many cases have been seen recently, amounting to a significant increase in its incidence in the wake of the ongoing coronavirus pandemic[26]. Diabetes controlled or uncontrolled plays a crucial role in pathogenesis of mucormycosis. And India has the second-largest number of adults aged 20–79 years with diabetes[27]. In the study on epidemiology of mucormycosis in India, Prakash H *et al*[28]. reported an increase in incidence rates from 24.7 to 89 cases per year. While another study with diabetes reported the incidence of mucormycosis 0.15 % [29]. Till date only a few cases of covid-19-mucormycosis co-infection have been reported in literature[30].

#### Age and gender profile

In our study profile the mean age noted was 50.58 years. Male gender outnumbered female in 1.8:1 ratio. In six cases of rhino-orbital mucormycosis, Sen *et al*[31]. also reported mean age of 60.5 years. In the study from regional Institute of Ophthalmology, Ravani SA *et al* also reported similar findings of the mean age of presentation of 56.3 years with a skew deviation toward the male gender (64.5%) vis-à-vis females (35.5%) and also noted demographic profile of the patients was similar to those reported in the world literature[7].

#### Clinical presentation

All study patients were diagnosed cases of rhino-orbital-cerebral mucormycosis. Rhino-orbital mucormycosis was the commonest presentation. Even though mucormycosis can involve different body organs the most common type is the rhino-cerebral form [22]. Patel *et al* [32] in a prospective multi center study conducted at 12 tertiary-care centers across India also reported rhino-orbital mucormycosis as the most common presentation(315/465, 67.7%) of mucormycosis. The clinical presentation in the early stages is typically with fever, headache, facial pain, nasal discharge, nasal obstruction and crusting[22]. Most of our study patients also presented with chief complaints of local pain (83.87%) and headache (74.19%) followed by swelling over face(66.12%). Nasal complaints were nasal obstruction (58.06%) and nasal discharge(51.61%) Classically, the clinical presentation has been described as an orbital cellulitis with proptosis, visual loss, and apical neuropathies[33]. We also noted similar ophthalmic complaints as watering of eye (38.70%) eyelid swelling (29.03%) ptosis (19.35%) and impaired vision (17.74%).

#### Post-covid mucormycosis

Mucormycosis incidence is raising all over the world after covid-19 outbreak. In our study post covid mucormycosis was the presentation(n=61,98.38%). Only one patient was not having history of documented covid-19 illness but she was suffering from uncontrolled diabetes since eight years which was uncontrolled at presentation. Similarly Sharma S *et al*[34] also found that all his 23 mucormycosis patients were coronavirus positive at the time of diagnosis or had been infected previously. Song *et al*[3] also 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. Ravani SA *et al*[7] reported 61.2% patients had a positive documented history of covid-19 infection in the recent past. This association was also reported by Mehta and Pandey,[35] Mekonnen *et al.*, [36] and Werthman-Ehrenreich[27] in their single case study on covid-19 infection with invasive rhino-orbital mucormycosis.

#### Immunity and risk factors

Diabetes mellitus is the single most common risk factor for mucormycosis in India[28]. It is a “classic” risk factor for mucormycosis with increased morbidity and mortality in covid-19[37]. The increased incidence of mucormycosis in the covid-19 may have many causes. The pandemic has caused widespread sociological and economic disturbances, severely restricting adequate access to healthcare. This has caused decompensation of previously well-controlled comorbidities in patients with chronic illnesses, like diabetes and chronic kidney disease[30] If the patient becomes immunosuppressed, this fungus may germinate within the paranasal sinuses, and spread intracranially or to other nearby structures such as the orbit[34]. Pre-existing conditions such as uncontrolled diabetes mellitus, solid organ transplants, haematological malignancy, neutropenia, or use of immunosuppressants predispose to the development of mucormycosis[30]. Several studies observed uncontrolled diabetes, covid-19 positivity and concurrent steroid use further decreasing immunity were the most common systemic risk factors for opportunistic mycoses, including mucormycosis[ 3,7,31,38]. Present study also noted similar associated risk factors as follows, covid-19 infection (n=61,98.38%), Diabetes mellitus (n=54,87.09%) and concurrent steroid use (n=47,75.80%). One male patient was Human Immunodeficiency Virus (HIV) positive with covid-19 infection in recent past.

#### T cells, endothelial injury and iron

Covid-19 patients always have immunosuppression with a decrease in CD4<sup>+</sup> T and CD8<sup>+</sup> T cells[39]. Emphasizing the role of T cells, according to one study, a protective role of Mucorales specific CD4<sup>+</sup> T and CD8<sup>+</sup> T cells have been hypothesized during active mucormycosis[40]. In addition to hyperglycemia, an alteration of iron metabolism occurs in severe covid-19[41]. Iron overload and excess free iron seen in acidemic states are one of the key and unique risk factors for mucormycosis. Endothelial adhesion and penetration are critical early steps in mucormycosis[42]. Postmortem series in covid-19 deaths noted widespread endothelial injury in patients who died of multi-organ failure[43]. Interestingly, acidemic states and hyperglycemia induce the endothelial receptor glucose-regulated protein (GRP 78) and the Mucorales adhesin spore coat protein homologs (CotH), creating a “perfect storm” for increased adhesion and penetration of Mucorales to the endothelium. Of interest, GRP 78 has been postulated as one of the receptors responsible for SARS-CoV-2 entry[44].

#### CT and MRI imaging: key role in decision making

Non-contrast computed tomography of the paranasal sinuses is usually the first investigation of choice, with gadolinium-enhanced magnetic resonance imaging being resorted to if intra-orbital or intracranial extension is suspected. Focal bony erosion and extrasinus spread are strongly suggestive of the diagnosis[15]. In present study CT and MRI were done in 100% and 90.32 % cases respectively. Mucosal thickening (n=62,100%) bony erosion (n=34,54.83%) and mild enhancement pattern (n=39,62.90%) were commonest findings on CT scan. MRI of the sinuses and orbits showed three patterns : Iso to hypo intense (n=23,37.09%), heterogenous (n=17,27.41%) and hyperintense (n=17,29.035) appearance on T2. The T2 hypo intense appearance may be due to presence of iron and manganese in the fungal elements [45] Notably, T2W signal or enhancement patterns are variable and not reliable markers for invasive fungal infection[46]. MRI is very useful in detection of complications like orbital cellulitis, cavernous sinus thrombosis and internal carotid artery thrombosis[47,48].

#### Medical management

Multidisciplinary care was given to all patients. A team comprising of senior faculties from Medicine, Otorhinolaryngology, Ophthalmology, Surgery, Pathology, Radiodiagnosis and Microbiology departments were taking care. A special mucormycosis committee headed by respected Dean madam was governing each and every aspect of the treatment and overall administration. The liposomal preparation of Amphotericin-B was the anti-fungal drug of choice. It has decrease nephrotoxicity[34]. In cases refractory or intolerant to amphotericin therapy, posaconazole is considered a suitable alternative option[49,50]. In present study, liposomal Amphotericin B was the primary drug used (100%), and posaconazole was second drug used in combination when required (08.00%) Brunet and Rammaert[51] also used and recommended liposomal amphotericin B as drug of choice with or without surgical treatment.

#### Surgical management

Surgery alone has been reported not to be curative, but an aggressive surgical approach has been shown to improve survival[19,50]. Surgery was done in 62.2% and 100% of cases in study of Ravani S *et al*[7] and Sharma S *et al*[34] respectively. Nithyanandam *et al*[9] also reported that debridement of sinuses was necessary in all cases of rhino-orbital cerebral mucormycosis in their study. In present study sinus debridement was done in 66.12% (n=41) cases. Caldwell Luc surgery (CWS) unilateral or bilateral was done in 27.41% (n=17) cases. orbital exenteration was required in 16.12 % (n=10) cases. These patients presented late with severe loss of vision and extensive orbital cellulitis with threat of cerebral extension.

#### Outcome and mortality

Reported mortality rates of 33.3–80 per cent and going up to 100 per cent was noted in disseminated infections[49,52]. But in this present study no mortality recorded. All patients had good recovery and discharged. Similar finding of no mortality was also noted by Sharma *et al*[34].

#### Mahatma Jyotiba Phule Jan Aarogya Yojna (MJPJAY)

Mahatma Jyotiba Phule Jan Aarogya Yojna (MJPJAY) is functional at our institute from its inception. We enrolled 53 patients (n=62) under this scheme. Rest 9 patients we could not enroll due to technical difficulties. All enrolled study patients were benefited under it. Low socioeconomic families having annual income under 1.5 lakh can avail its benefits. Only original ration card and aadhar card is mandatory. Total 901 diseases are included under this insurance scheme. Total 53 families were financially supported. This scheme proved as a boon for financially burdened and already weaker section of society in covid-19 pandemic era. Till 1<sup>st</sup> August 2021, total revenue generated was Rs 8,00,000. Total 20 claims were approved, 30 claims in were process or claims submitted and 3 claims were pending.

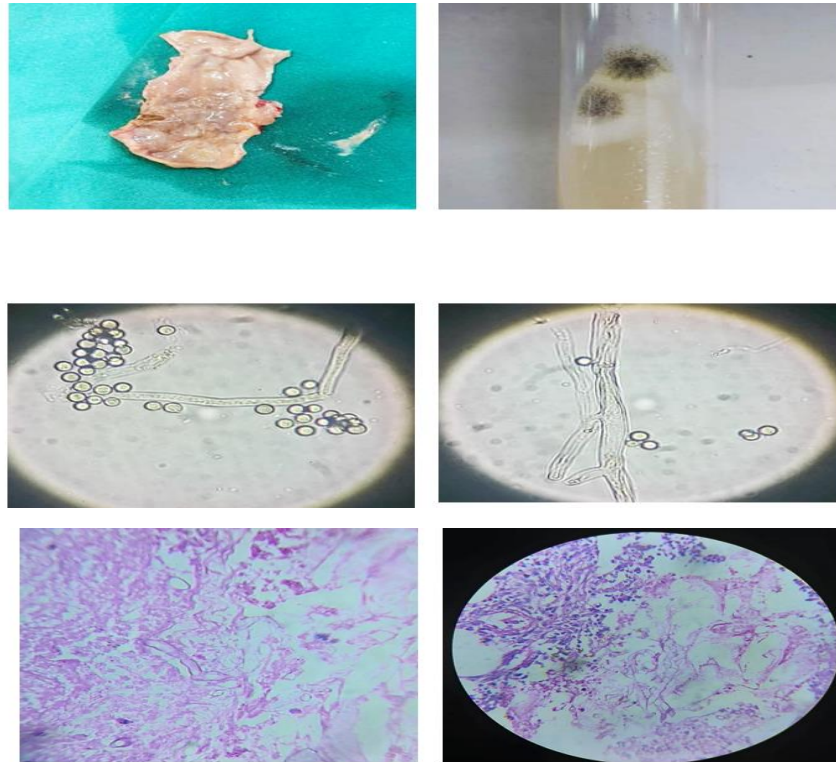
#### Conclusion

Since the start of covid-19 pandemic, medical fraternity all over the world is facing daily newer challenges to handle the unprecedented demon, “novel” coronavirus. Long term manifestations and complications of this immunity wrenching disease are unknown and yet to bring to light. Many aspects of coronavirus are revealed and many remain concealed, only time will give the answer. There is sudden rise in the cases of mucormycosis. The causes for this

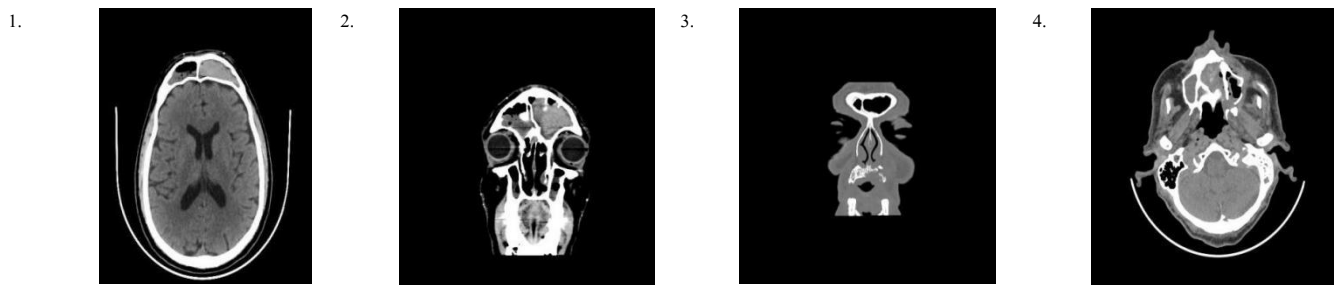
are multi-factorial like decompensation of underlying comorbidity, hospital acquired Mucormycosis, and over-zealous use of steroids. Rhino-orbital cerebral mucormycosis and diabetes must be treated aggressively. Cost of lyophilised Amphotericin B and overall treatment expenditure of mucormycosis is beyond reach of common man. Cases are on record that these patients committed suicides under this decompensated financial stretch. MJPJAY scheme stands really helpful in the management of mucormycosis and overall management of covid-19 pandemic. To conclude, high index of suspicion, early diagnosis, high quality CT and MRI imaging, immediate sinus debridement with liposomal Amphotericin B therapy were the key factors in present study. Mahatma Jyotiba Phule Jan Aarogya Yojna (MJPJAY) proved as a ray of light in the darkness of potential economical debt of individual families.

**Recommendations**

- Health education and awareness of early detection and prompt regular monitoring of comorbidities specially diabetes mellitus is recommended.
- Mucormycosis and yet unknown long term complications of this immunity wrenching covid-19 disease should be notifiable .
- Uncertainty and cost treatment of covid-19 and its complications are out of economic amplitude of poor families. MJPJAY and government insurance schemes playing a key role in this financial management. All the “covid-19 disease complex” should be under such schemes and should be on top priority in health administration at state and national level.



**Fig 1: Excised gross specimen, microbiological and histopathological demonstration of hyphae of mucormycosis**



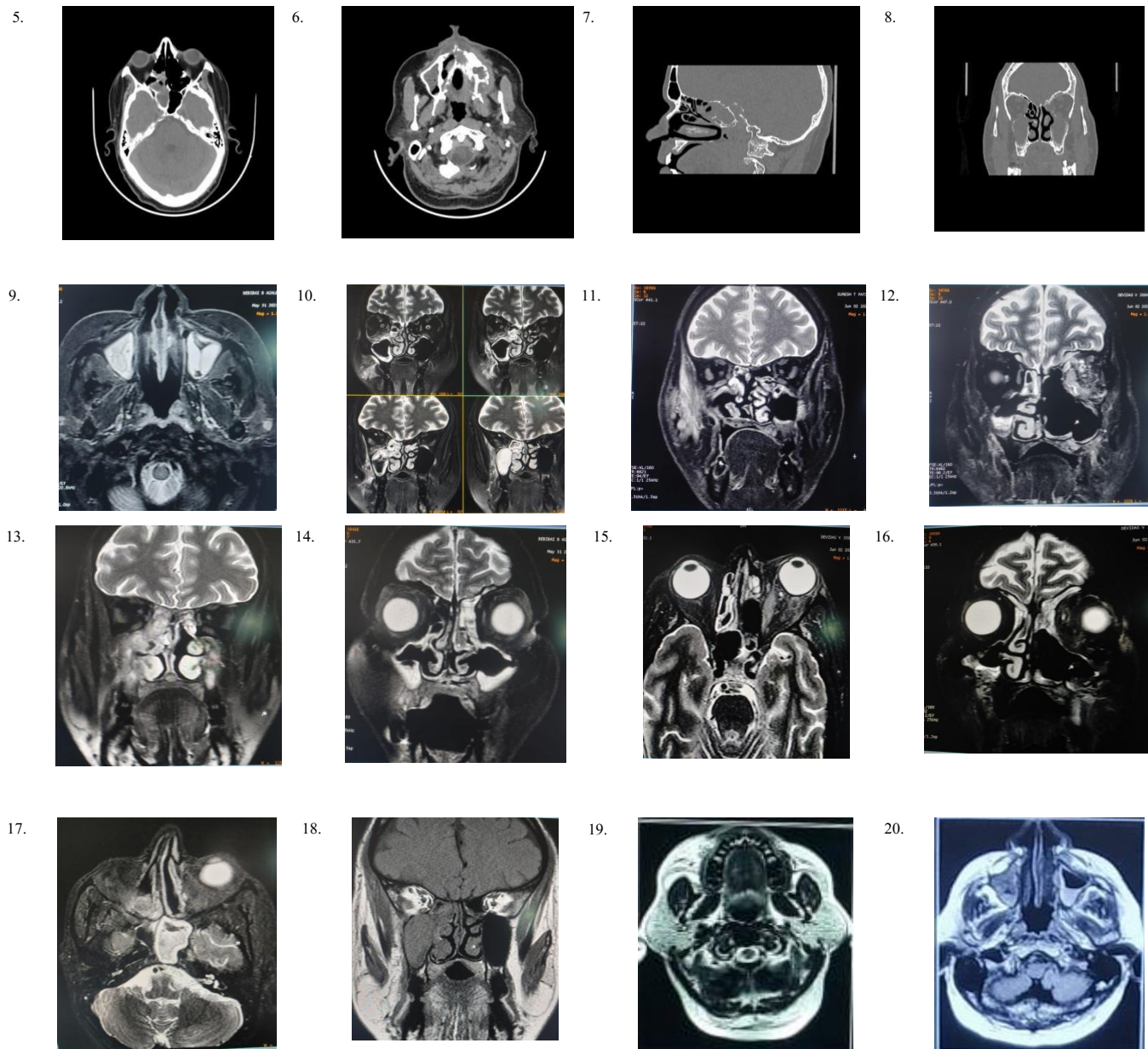


Fig 2 : CT and MRI Imaging

[CT and MRI Imaging as follows

1. Axial CT image showing opacified left frontal sinus with hyper-dense contents.
2. Coronal CT image showing hyper dense contents in left frontal sinus
3. Coronal CT image showing erosion and lytic destruction of left maxillary alveolus and hard palate with surrounding irregular soft tissue.
4. Axial CT image showing mucosal thickening and fluid collection in maxillary sinus with irregular lytic destruction of hard palate and surrounding inflammatory soft tissue.
5. Axial CT image showing mucosal thickening and collection in right sphenoid sinus with erosion of orbital wall.
6. Axial CT image showing mucosal thickening in bilateral maxillary sinus with irregular lytic destruction of maxillary alveolus.
7. Sagittal CT image with bone window showing sphenoid sinusitis with erosion of anterior wall.
8. Coronal CT image with bone window showing bilateral maxillary sinusitis erosion of sphenoid and lateral walls.
9. Axial T2W image showing bilateral maxillary sinusitis with hypo-intense area suggestive of fungal etiology.
10. Coronal T2W image showing right maxillary sinusitis with spread of inflammatory changes beyond sinus wall laterally and in right orbit.
11. T2W coronal image showing right maxillary sinusitis with spread of infective process into soft tissue on right side of face, zygoma,temporal and infratemporal fossa.
12. T2W coronal image showing right maxillary sinusitis with post-operative changes on right side Left orbital cellulitis and proptosis noted.
13. T2W coronal image showing right maxillary, ethmoid,bilateral frontal sinusitis with hypo-intense areas suggestive of fungal etiology.
14. T2W coronal MRI image showing bilateral maxillary ethmoid and left frontal sinusitis with involvement of alveolar process on right, hard palate and bilateral nasal cavities.
15. T2W axial image showing right ethmoid sinusitis with post-operative changes on left.Extensive left orbital cellulitis, edematous rectus muscle and proptosis noted.

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16. T2W coronal MRI image showing postoperative changes on left with bilateral frontal and ethmoid sinusitis with extensive left orbital sinusitis,
  17. T2W axial image showing sphenoid sinusitis with abnormal anterior soft tissue. Hypo-intense areas are suggestive of fungal etiology.
  18. T2W coronal image showing right maxillary and ethmoid sinusitis with abnormal soft tissue.
  19. Moderate mucosal thickening of right maxillary sinus, marrow edema in the wall of right maxillary sinus. Mucosal thickening obstructs right maxillary sinus.
  20. Moderate mucosal thickening in bilateral maxillary, ethmoid and sphenoid sinus.]





Fig 3: Clinical and operative presentation

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