



MUCORMYCOSIS SPIKE IN COVID-19 SECOND WAVE: THE PERFECT TSUNAMI IN INDIA

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ABSTRACT **Background**-The unprecedented increase of COVID-19 associated Mucormycosis (CAM) during the 2nd pandemic wave was a perfect Tsunami in India! A review article published in 2021 surprisingly reported that 81 % of the total cases of CAM worldwide were from India. Hence there was a need to understand the biological behaviour of this unholy combination to identify risk factors and establish standard protocols to reduce morbidity and mortality in India. **AIM**- To study the epidemiological profile of CAM patients. **MATERIAL AND METHODS**-This retrospective observational study included 57 cases of CAM reported to Department of Otorhinolaryngology from May 2021 to July 2022. **RESULTS**- Out of 57 CAM cases 75.4% were males. Youngest patient was of 12 years and oldest 75 years. Diabetes mellitus was present in almost 79%. Corticosteroid intake was seen in 52.63%, Oxygen therapy was given in 45.61% and 7% needed ventilator support during COVID-19 infection. Sinonasal involvement was seen in all patients with palatal involvement in 19.3%. Rhinorbital mucormycosis was seen in 12.2% and rhinocerebral type was seen in 3.51%. All patients underwent endoscopic debridement. FESS with maxillary sinus debridement was done via total maxillectomy in 8.77%, partial maxillectomy in 10.53%, modified Denker's approach in 0.57% and Caldwell Luc approach in 0.57%. All patients received emulsion Amphotericin-B in the range of 1gm to 5.7gm. On discharge all were put on gastro-resistant Posaconazole tablet for 21 days. Mortality was seen in only 1 patient (0.57%). **CONCLUSION**-Diabetes Mellitus, steroid therapy and oxygen support during COVID-19 treatment were the risk factors for sudden spike in cases of Mucormycosis during the 2nd wave. Prompt diagnosis, repeated debridement, optimal systemic and oral antifungal therapy markedly reduced the mortality to much lower rate than expected in our study.

KEYWORDS : COVID-19 associated Mucormycosis, Diabetes Mellitus, Steroid, Oxygen therapy, Amphotericin-B.

INTRODUCTION

A rare and life-threatening fungal infection "Mucormycosis" had a drastic rise during the second wave of COVID pandemic worldwide. India, with a vast burden of SARS-CoV-2 affected population i.e. 32,036,511 cases as reported on August 11th 2021, also had the highest number of Covid-19 associated Mucormycosis CAM cases¹. Hyperglycemia, the single most important risk factor may either be due to pre-existing or new-onset Diabetes Mellitus or deranged glucose metabolism as reported in a recent review article¹. Mucormycosis is an angioinvasive opportunistic infection caused by order Mucorales with a worldwide distribution⁴.

The genera responsible for human infection are Rhizopus, Mucor and Rhizomucor, Cunninghamella, Lichtheimia and Apophysomyces⁵. However, even with the best management, high mortality has been reported in past. Clinically, CAM can be categorised into Rhino-Orbital, Paranasal Sinus, Rhino-Cerebral, Rhino-Orbital-Cerebral, Oral, Pulmonary, Gastrointestinal, Cutaneous, and Disseminated type⁶. The most common presentation being palatal ulceration or necrosis and later palatal perforation due to the spread of infection from the nasal cavity or paranasal sinuses via palatal vessels¹. With this background, our study was specifically designed to present the epidemiological profile of the CAM cases admitted and managed in our tertiary care centre during the second wave of COVID-19 pandemic.

MATERIAL AND METHODS

This retrospective observational study included 57 cases of CAM reported to Department of Otorhinolaryngology at our tertiary care hospital from May 2021 to July 2022. Clinical diagnosis of Mucormycosis was made followed by contrast magnetic resonance imaging, then functional endoscopic sinus surgery and finally histopathology confirmation of Mucormycosis.

Data about demographics, clinical manifestations, associated comorbidities, haematological investigations, medical management, surgical management and prognosis was collected after obtaining informed written consent from all patients and approval from the institutional Ethical committee.

STATISTICAL ANALYSIS

Data and master chart was prepared in MS EXCEL 2007. Percentages of different groups were compared by using chi-square test. P<0.05 was considered statistically significant and P<0.0001 was considered statistically highly significant. To test the association of organ involvement and Inj. Amphotericin-B dose chi-square test was used.

RESULTS

During the study period 57 cases of mucormycosis were admitted at our tertiary care hospital. Out of 57 patients we had 1 paediatric patient of Type I Diabetes in the age of 12 years and 1 adolescent in age of 18 years.

All the 57 patients reported to our tertiary care centre presented with (Fig.1) swelling numbness over one/both sides face, nasal obstruction, loosening of tooth, diplopia, headache and generalized weakness. Mucormycosis involving nose and sinuses was seen in all patients hence all patients underwent endoscopic debridement surgery (Fig.1.c). Modified denkers procedure was done in one patient and Caldwell luc approach was done in one patient. 10.5%(n=6) underwent partial maxillectomy surgery (Fig.1.d) and 8.77%(n=5) underwent total maxillectomy surgery (Fig.2.e). None of patients required orbital exenteration. One presented with meningitis and the other with frontal lobe abscess who underwent craniotomy abscess drainage followed by FESS.

Inj Amphotericin-B emulsion (LFAB) was given to all 57 patients after renal function assessment. Inj. Amphotericin -B was administered in 500ml of 5% dextrose with pre and post flushing with 100ml normal saline. Whole assembly was wrapped up in black polythene wrap as amphotericin-B is photosensitive. Test dose of 2mg was given to every patient prior starting full dose. Renal function test was done every 72 hours to look for any nephrotoxicity. Inj. Amphotericin was given till debrided tissue histopathology report was negative for Mucormycosis. Dosage received has been shown in Table.1. Mortality was seen in only one female patient who died due to cardiac arrest. To improve the quality of life in patients who underwent maxillectomy, oral rehabilitation was done with Interim and Definitive Obturators. Interim obturators were given after 7-10 days of surgery and Definitive obturators was given 3 months post-operatively to 11 patients.



Fig.1.(a) Facial swelling due to left maxillary involvement (b) Left palatal necrosis respecting the midline (c) Endoscopic picture of eschar in left nostril (d) Intraoperative partial maxillectomy (e) Intraoperative total maxillectomy (f) Post operative specimen of total maxillectomy.

Table.1 Showing demographic profile, Inj. Amphotericin dosage and organ involvement of CAM patients

Risk Factors		No. of patients affected	Percentage	Chi-square test	P value
Age in years	0-20	2	3.5%	48.00	<0.0001
	20-40	7	12.28		
	40-60	36	63.15		
	>60	12	21.05		
Sex	Males	43	75.43	14.75	<0.0001
	Females	14	24.56		
Diabetes Mellitus		45	78.94		
Covid-19		57	100		
Steroids	<5 days	9	15.79	4.8	0.0255
	>5 days	21	36.83		
Inj. Remdisivir		37	64.9		
O2 Therapy		26	45.61		
Ventilator support		4	7.01		
Vaccination		15	26.31		
Organs involved	Sinonasal	57		4.4	0.88
	Palate	11			
	Eye	7			

	Brain	2		
Inj. Amphotericin-B Dosage	< 2 grams	11		
	2-4 grams	25		
	> 4 grams	21		
Total No. of patients		57	100	

DISCUSSION

The second wave of COVID-19 pandemic had a great impact especially on uncontrolled diabetic patients with severe complications and high fatality rate. Its association with mucormycosis was a perfect Tsunami in India. India being one of the most affected countries by Covid-19, witnessed a rapid surge of Mucormycosis during the 2nd wave. Distinctive feature of Mucormycosis is angioinvasion followed by thrombosis and tissue necrosis. Various contributing factors during the treatment of Covid-19 have been suggested for CAM. Hence to study the demographic profile, staging of the disease and outcome of management of CAM patients, we conducted this study. Comparison of our findings with various studies is shown in Table.2

Table.2 Comparison of our findings with various studies.

Sr no	Author Name	Age >40 years	Sex Male predominance	DM	Cortic o- Steroid intake	Oxygen Therap y	Inj Re mdisiv ir	Sinonasal involvem ent	Orbital involve ment
	Our Study	63.15 %	75%	79%	52.63 %	45.61%	64%	100%	12.2%
1.	W.Jeong et al ¹²	63%	63%	74%	33%	-	-	55%	2%
2.	SS Chavan et al ¹⁵	68%	76%	61%	-	-	-	96%	35.5%
3.	Manjunath vijapur et al ¹⁷	63%	75%	-	-	-	-	-	-
4.	Ravani SA et al ¹⁶	57%	56.3%	96%	61%	-	-	-	-
5.	Sen et al ¹³	-	61%	-	-	47%	7%	-	-
6.	Anson jose et al ⁷	-	-	93%	-	-	-	50%	50%
7.	Kamleshun et al	-	66%	-	-	-	-	-	-
8.	Singh et al ¹¹	-	-	91%	-	-	-	-	-
9.	Prakash et al	-	-	57%	-	-	-	-	-
10.	Vaughan et al ¹³	-	-	64%	51%	-	-	-	-
11.	Yohai et al ¹⁴	-	-	78%	-	-	-	-	-
12.	Akhil Pratap singh et al ¹¹	-	-	79%	54%	-	-	-	-
13.	Mona G alshash way et al ¹⁹	-	-	-	76.3%	-	-	-	-

CONCLUSION

Diabetes mellitus, steroid therapy and oxygen support during COVID-19 treatment were the risk factors for sudden spike in cases of mucormycosis during the 2nd wave. Prompt diagnosis, repeated debridement and optimal systemic/oral antifungal therapy reduced the mortality to much lower rate in our study.

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