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Original Article

# Post-COVID-19 Rhino-Orbito-Maxillary Mucormycosis Defect: Our Surgical Experience with Single Stage Delayed Reconstruction Using Free Flap

Akhilesh Humnekar[1] Prakash Chandra Kala[1] Pawan Kumar Dixit[1] Deepti Katrolia[1] Shilpi Karmakr[1] Priyanka Singla[1] Apoorva Pratap Singh[1]

[1] Department of Burns and Plastic Surgery, All India Institute of Medical Science, Jodhpur, Rajasthan, India

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**Address for correspondence** Akhilesh Humnekar, MS, MCh (Plastic Surgery), Department of Burns and Plastic Surgery, All India Institute of Medical Science, Jodhpur, Rajasthan, India (e-mail: ronith.humnekar@gmail.com).

## Abstract

**Introduction** The effect of the second wave of COVID-19 was immense in India, specifically in the form of vicious COVID-19-associated mucormycosis. A higher number of radical debridements are required for disease control in combination with antifungal drugs in cases of COVID-19-associated mucormycosis, which results in complex maxillofacial defects. We aimed to evaluate the clinical outcomes in patients with rhino-orbito-maxillary defects due to COVID-19-associated mucormycosis undergoing a single stage delayed free flap reconstruction.

**Methodology** This prospective, single-center, multisurgeon study was performed on eight patients with COVID-19-associated rhino-orbito-maxillary mucormycosis in the department of burns and plastic surgery. The postoperative clinical outcome was evaluated using the University of Washington Quality of Life Questionnaire for patient's quality of life (QOL), aesthetic numeric analog (ANA) scale for patient's satisfaction for aesthetics, and the functional intraoral Glasgow scale for speech and deglutition at 1 and 3 months.

**Results** The median age of the study patients was 40 years, with 75% of the patients being males. Diabetes mellitus (DM) was present in all the patients. Mucormycosis was diagnosed within the first 3 months of COVID-19 infection. Maxillary defect was present in 62.5% of patients, out of which 50% had bilateral maxillary defects. There was significant improvement in the QOL and the aesthetics of patients from 1 to 3 months ($p < 0.001$). Speech and deglutition were also improved at 3 months, but the difference was not statistically significant.

**Conclusion** Single stage delayed free flap reconstruction can be advocated in patients with COVID-19-associated rhino-orbito-maxillary mucormycosis defect as there is considerable improvement in patients' QOL, aesthetics, speech, and deglutition over a period of time.

**Keywords**
- COVID-19
- COVID-19-associated mucormycosis
- free flaps
- mucormycosis
- quality of life

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## Introduction

The effect of the second wave of COVID-19 was immense in India, specifically in the form of the vicious COVID-19-associated mucormycosis,[1] which was commonly referred to as the "black fungus."[2] Of the total number of mucormycosis cases reported till June 2021, 86% of the cases had a history of COVID-19 infection, and a history of diabetes mellitus (DM) was present in 62% of patients.[3] Generally, a higher number of radical debridement are required for disease control in combination with antifungal drugs in cases of COVID-19-associated mucormycosis. Most of these patients require adjuvant surgeries including orbital exenteration, sinus and thoracic cavity debridement, lung resection, and decortication, which leads to complex tissue defects involving the maxillofacial region. Thus, it is anticipated that most of the survivors of COVID-19-associated mucormycosis will approach for reconstruction surgeries over a period of time.[1] Numerous cases series have described the clinical presentation, radiological investigations, neurological aspect, and management of patients with COVID-19-associated mucormycosis,[4–9] and various local flaps like submental flap, facial artery musculomucosal flap, and various free flap including radial artery forearm free flap, deep circumflex iliac artery flap, anterolateral thigh (ALT) flap, and free fibula flap, but none of the studies have included details regarding the postoperative clinical outcomes of delayed reconstructive surgeries performed for rhino-orbito-maxillary (ROM) defects that occurred due to COVID-19-associated mucormycosis with DM. This study was conducted to evaluate the clinical outcomes in view of the quality of life, aesthetics, speech, and deglutition for short duration in patients with ROM defects due to COVID-19-associated mucormycosis with DM undergoing single stage delayed free flap reconstruction.

## Methodology

This prospective, single-center, multisurgeon study was performed on eight patients with COVID-19-associated ROM mucormycosis defect undergoing delayed single stage free flap reconstruction in the burns and plastic surgery department and fulfilling the inclusion and exclusion criteria. Patients with confirmed diagnosis of COVID-19-associated postmucormycosis ROM defect, who had complete resolution of the disease process, were eligible for free flap reconstruction, and were willing to give written informed consent were included in the study, while patients with an

**Fig. 1** Preoperative clinical picture of a patient with a orbitomaxillary defect: (**A**) frontal view, (**B**) right oblique view, and (**C**) orbital defect. Computed tomography (CT) scan three-dimensional (3D) reconstruction view: (**D**) anterior and (**E**) right oblique views.

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**Fig. 2** Preoperative clinical picture of a patient with a rhinomaxillary defect: (**A**) frontal view, (**B**) right lateral view, and (**C**) palatal defect. Computed tomography (CT) scan three-dimensional (3D) reconstruction view: (**D**) anterior view and (**E**) left lateral views.

active form of disease and defect due to causes other than COVID-19-associated mucormycosis were excluded from the study.

In all patients, proper history, examination (wound assessment), radiological workup, and preanesthetic check-up (with routine investigations) were done and recorded in a predesigned proforma (►**Figs. 1** and **2**). Written informed consent for the procedure was obtained from each patient prior to their enrollment in this study, so as to ensure patients' willingness to participate in the study. All the patients were briefed about the study and were given "patient information sheet." The surgical procedure was performed under general anesthesia after debridement (►**Figs. 3** and **4**). Regular follow-up of the patient was done. Patient's satisfaction with the appearance of the reconstructed area was evaluated using the aesthetic numeric analog scale (ANA), quality of life was evaluated using the University of Washington Quality of Life Questionnaire (UW-QOL),[10] and speech and deglutition were evaluated by using the functional intraoral Glasgow scale (FIGS). All these parameters were evaluated postoperatively at 1 and 3 months. The questionnaire was presented to the participants by a resident of the plastic surgery department who was not part of the study and the parameters were evaluated at 1 and 3 months by the same resident. The study was conducted in accordance with the ethical guidelines of Declaration of Helsinki, which are consistent with the good clinical practice (GCP) and applicable regulatory requirements. Data thus collected were entered in a Microsoft Excel Sheet and were subjected to statistical analysis. Statistical analysis was performed with help of Epi Info 7.2.2.2. Epi Info is a trademark of the Centers for Disease Control and Prevention (CDC). Descriptive statistical analysis was performed to calculate the means with corresponding standard deviations (s.d.). Test of proportion was used to find the standard normal deviate ($Z$) to compare the difference in proportions. The $t$-test was used to compare two means. A $p$ value less than 0.05 was considered statistically significant.

## Results

The mean age of the study patients was $42.38 \pm 12.42$ years, with a range of 25 to 63 years. In all, 62.5% of the patients were below 50 years of age. The majority of patients were males (75%), with a male-to-female ratio of 3:1. DM was present as a comorbidity in all the patients. Smoking habit was observed in 37.5% of patients. Six of eight patients was diagnosed with mucormycosis within the first 3 months of COVID-19 infection. A maxillary defect was present in 62.5% of patients, out of which 50% had bilateral maxillary defects ($p < 0.0001$). An orbital defect was present in 37.5% of

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**Fig. 3** Intraoperative picture of a patient with an orbitomaxillary defect: (**A**) flap marking; (**B**) orbitomaxillary defect; and (**C**) immediate postoperative picture. Postoperative follow-up pictures of the patient at 3 months: (**D**) frontal, (**E**) right oblique, and (**F**) right lateral views.

**Fig. 4** Intraoperative picture of a patient with rhinomaxillary defect: (**A**) flap marking; (**B**) flap harvesting; and (**C**) rhinomaxillary defect. Postoperative follow-up pictures at 3 months: (**D**) frontal, (**E**) right lateral, and (**F**) intraoral views.

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**Table 1** Demographic details of study patients

| Patient no. | Age (y) | Gender | Comorbidity | Habits | Mucor after COVID-19 infection (d) | Defect after operation | Delayed surgery (d) | No. of debridements before reconstruction |
|---|---|---|---|---|---|---|---|---|
| 1 | 33 | M | DM | Nil | 90 | Bilateral maxilla defect | 270 | 03 |
| 2 | 35 | M | DM | Tobacco chewing | 60 | Bilateral maxilla defect | 180 | 02 |
| 3 | 51 | M | DM | Smoking | 160 | Right orbital defect | 210 | 02 |
| 4 | 44 | M | DM | Smoking and opium addiction | 90 | Bilateral total maxilla defect | 90 | 02 |
| 5 | 25 | M | DM | None | 60 | Bilateral total maxilla defect | 120 | 03 |
| 6 | 36 | M | DM | Smoking | 90 | Right orbital defect | 270 | 03 |
| 7 | 52 | F | DM | None | 150 | Right maxilla defect | 330 | 04 |
| 8 | 63 | F | DM | Tobacco chewing | 90 | Left orbital defect | 720 | 04 |

patients. Delayed surgery was performed within 12 months in seven patients and after 24 months in one patient (►**Table 1**).

In 87.5% of patients, the size of the flap was more than 50 $cm^2$. Out of the three different types of free flaps performed in this study, free fibula flap (62.5%) was significantly higher than free ALT flaps (25%) and free vastus lateralis (VL) muscular flaps (12.5%), with $Z = 1.99$ and $p = 0.044$. In 75% of cases, the duration of surgery was $\leq$6 hours, which was significant ($Z = 7.07$; $p < 0.0001$). Facial artery was the recipient artery in seven of eight cases. In all eight patients, one artery and one vein anastomoses were performed. Donor area management was done by skin grafting (62.5%) and primary closure (37.5%). Complete flap loss was observed in two patients; extraoral medial wound dehiscence, hematoma, and intraoral wound dehiscence were observed in one patient each; and no complications were observed in three patients. Secondary procedures were performed in three patients and donor site complication was observed in only one out of eight patients. The duration of hospital stay was up to 3 weeks in 62.5% of patients (►**Table 2**).

At 1 month, only 16.7% of study patients reported very good QOL, while 66.7% patients reported very good QOL at 3 months, suggestive of significant improvement from 1 to 3 months (►**Table 3**). Similarly, the mean ANA score also improved significantly from 1 month ($7.33 \pm 0.82$) to 3 months ($8.67 \pm 1.21$). Speech and deglutition also showed improvement in all the patients from 1 to 3 months, but it was not statistically significant ($p > 0.001$; ►**Table 4**). Improvement in the speech of the patient with an orbito-maxillary defect and rhinomaxillary defect can be observed in ►**Videos 1** and **2**, respectively.

**Video 1**

Postoperative outcome using Free ALT flap at three months. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/ html/10.1055/s-0044-1785489.

**Video 2**

Postopertaive outcome using Free fibula flap at three months. Online content including video sequences viewable at: https://www.thieme-connect.com/products/ejournals/ html/10.1055/s-0044-1785489.

## Discussion

Epidemiological studies have indicated that rhino-orbito-cerebral mucormycosis (ROCM) is the most commonly encountered variant of COVID-19-associated mucormycosis.[11] India has experienced a relatively higher number of COVID-19-associated mucormycosis cases. Clinical presentation of COVID-19-associated mucormycosis was similar to the ROCM commonly seen in diabetic patients.[12] Recent reports support a strong association between COVID-19, corticosteroid therapy, and mucormycosis, although preexisting immunosuppressive conditions like DM should be considered as strong confounders.[13] Radical debridement is the most important surgical step that involves thorough debridement of all sites without leaving behind any residual disease. However, large-volume excision

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**Table 2** Surgical details of study patients

| Flap size | Free flap | Type of flap | Recipient artery | Artery and vein anastomosis | Duration of surgery (min) | Donor area management | Complications flap | secondary procedure | Donor site complication | Secondary procedure for donor site | Hospitalization days |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 60 $cm^2$ | Free fibula flap | Osteocutaneous flap | Facial artery | 1 artery and 1 vein | 300 | Skin grafting | Hematoma wound | Nasolabial | None | None | 21 |
| 48 $cm^2$ | Free fibula flap | Osteocutaneous flap | Facial artery | 1 artery and 1 vein | 330 | Skin grafting | None | None | None | None | 23 |
| 72 $cm^2$ | Free ALT | Fasciocutaneous flap | Superficial temporal artery | 1 artery and 1 vein | 300 | Primary closure | Complete loss | None | None | None | 20 |
| 66 $cm^2$ | Free fibula flap | Osteocutaneous flap | Facial artery | 1 artery and 1 vein | 330 | Skin grafting | None | None | None | None | 10 |
| 56 $cm^2$ | Free fibula flap | Osteocutaneous flap | Facial artery | 1 artery and 1 vein | 360 | Skin grafting | Complete loss | None | No | None | 7 |
| 78 $cm^2$ | Free ALT | Fasciocutaneous flap | Facial artery | 1 artery and 1 vein | 480 | Primary closure | Intraoral wound dehiscence | Radial artery forearm flap | None | None | 23 |
| 60 $cm^2$ | Free fibula flap | Osteocutaneous flap | Facial artery | 1 artery and 1 vein | 360 | Skin grafting | Extraoral medial wound dehiscence | Resetting of flap | Marginal loss STSG | Secondary healing | 40 |
| 84 $cm^2$ | Free VL muscular flap | Muscle flap | Facial artery | 1 artery and 1 vein | 480 | Primary closure | None | None | None | None | 25 |

Abbreviations: ALT, anterolateral thigh flap; STSG, split-thickness skin graft; VL, vastus lateralis.

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**Table 3** Quality of life (QOL) at 1 and 3 months

| QOL | At 1 mo | | At 3 mo | |
|---|---|---|---|---|
| | Number | % | Number | % |
| Very good | 1 | 16.7 | 4 | 66.7 |
| Good | 5 | 83.3 | 2 | 33.3 |
| Total | 6 | 100.0 | 6 | 100.0 |

results in huge anatomical defects, and reconstruction in such cases is often grueling. We conducted this study to investigate the short-term clinical outcomes of single stage delayed free flap reconstruction surgery in patients with ROM defects due to COVID-19-associated mucormycosis in terms of the quality of life, aesthetics, speech, and deglutition.

In our study, 5 of 8 patients were below 50 years of age. Agrawal et al[4] observed that most of the patients with COVID-19-associated ROM mucormycosis were in the age group of 40 to 50 years. However, in most of the cases of COVID-19-associated mucormycosis reported in the literature, patients were older 50 years.[5,8,14,15] This may be because our study included survivors of COVID-19-associated mucormycosis, who came for reconstructive surgeries after complete resolution of the disease. Mortality rate is higher in COVID-19-associated mucormycosis and chances of survival are higher in younger patients with better immunity and lesser comorbidities.

In our study, male dominance was observed in patients with COVID-19-associated ROM mucormycosis defects. Another study involving patients with COVID-19-associated ROM mucormycosis reported that 66.67% of patients were males.[4] In a recent review on cases with COVID-19-associated mucormycosis from 18 countries, Hoenigl et al[14] observed that 78% of the patients affected by this disease were males. This is in accordance with the previous studies that suggested male dominance among patients with COVID-19-associated mucormycosis.[6,8,9,14]

ROCM represents the commonest clinical form of mucormycosis in the Indian population and around 88% of these cases are associated with DM.[7,16] All the patients in our study were diabetic. Similarly, all the four patients with COVID-19-associated mucormycosis were diabetic in a recent case series by Roushdy and Hamid.[8] Balushi et al[6] also observed uncontrolled blood glucose levels in all 10 patients with COVID-19-associated mucormycosis in their case series. DM was also present in the majority of the patients with COVID-19-associated mucormycosis reported in the literature.[4,5,14,15]

In our study, 2 of 8 patients were diagnosed with COVID-19-associated mucormycosis within 2 months of COVID-19 infection, 4 patients were diagnosed in the third month, 1 patient after 5 months, and 1 patient after 160 days of COVID-19 infection. Various surgical procedures that were performed in each of these patient as a part of the management protocol included bilateral (B/L) maxillectomy along with an alveolar process and hard palate removal (patient 1); B/L infrastructure maxillectomy + B/L frontal sinusotomy (patient 2); right maxillectomy with orbital exenteration (patient 3); B/L maxillectomy involving anterior two-thirds hard palate with B/L frontal and ethmoidal sinusotomy (patient 4); B/L maxillectomy with B/L ethmoidal and maxillary sinusotomy (patient 5); right maxillectomy including alveolar process along with a bony defect wall of the maxillary and frontal sinus with right orbital exenteration (patient 6); right maxillectomy along with removal of the right zygoma, maxillary sinus, and right pterygoid plate (patient 7); and left suprastructure maxillectomy along with orbital exenteration (patient 8). This resulted in complex maxillofacial defects in patients postoperatively. Four patients presented with a B/L maxillary defect, three patients presented with an orbital defect, and one patient with a unilateral maxillary defect. Seven of eight patients presented within 12 months duration in whom surgery was performed within 1 year, while one patient presented after 24 months.

The mean flap size used in our study was $64.75 \pm 11.21\,cm^2$, with a range of 48 to $84\,cm^2$. In most of the patients, the flap size was between 51 and $75\,cm^2$. Out of eight patients, osteocutaneous free fibula (OFF) flap was performed in five patients, fasciocutaneous free ALT (FF-ALT) flap was done in two patients, and free VL muscular (FVLM) flap was performed in one patient. The recipient artery was the superficial temporal artery in one patient who underwent reconstruction using FF-ALT flaps, whereas in the rest of the patients, the facial artery was used accompanied with anastomosis between an artery and a vein. Duration of

**Table 4** Postoperative parameters at 1 and 3 months

| Parameters | | Mean | Median | Range |
|---|---|---|---|---|
| ANA | At 1 mo | $7.33 \pm 0.82$ | 7.5 | 6–8 |
| | At 3 mo | $8.67 \pm 1.21$ | 8.5 | 7–10 |
| Speech | At 1 mo | $3.33 \pm 0.52$ | 3 | 3–4 |
| | At 3 mo | $3.83 \pm 0.41$ | 4 | 3–4 |
| Deglutition | At 1 mo | $4.17 \pm 0.75$ | 4 | 3–5 |
| | At 3 mo | $4.67 \pm 0.52$ | 5 | 4–5 |

Abbreviation: ANA, aesthetic numerical analog.

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surgery ranged from 5 to 8 hours, with a median of 5 hours and 45 minutes. Primary closure at the donor site was done in patients who underwent FF-ALT flap ($n = 2$) and FVLM flap reconstruction ($n = 1$), while skin grafting was done in all patients who underwent OFF flap reconstruction ($n = 5$).

The majority of the cases of post- COVID-19-associated ROM defect reported in the literature have been rehabilitated prosthetically using intraoral obturators, partial dentures, palatal flaps, and other soft-tissue flaps.[5,17] A recent study by Gupta et al[18] used ALT flaps for covering COVID-19-associated mucormycosis defects in 14 patients. All flaps in their study survived, without any major or minor complications. However, in our study, complete flap loss was observed in two cases, wound dehiscence was observed in two cases, and hematoma was observed in one case. In our study, no complications were reported in three of eight patients, out of which two underwent a reconstruction using an OFF flap and one an FVLM flap reconstruction. Complete flap loss was observed in one patient who underwent an FF-ALT flap reconstruction and in a patient who underwent an OFF flap reconstruction. Hematoma was observed in one patient who received an OFF flap, intraoral wound dehiscence was observed in one patient who underwent an FF-ALT flap reconstruction and extraoral medial wound dehiscence was observed in one patient with an OFF flap reconstruction. In one patient, reconstructive surgery was performed using an ALT free flap to cover the complex orofacial defect after cessation of the disease process; unfortunately, the patient died in intensive care unit (ICU) postoperatively.[9]

Secondary procedures were performed in patients with complications in flaps except for those with complete loss of flap. Marginal loss of split-thickness skin graft (STSG) was observed at the donor site in a patient who suffered extraoral medial wound dehiscence, which healed by secondary healing. The length of hospital stay was 1 week for 1 patient, 2 weeks for 1 patient, 3 weeks for 2 patients, 4 weeks for 3 patients, and more than 4 weeks for 1 patient.

We evaluated the postoperative clinical outcomes using the UW-QOL[10] for the quality of life of patients, ANA scale for patient satisfaction for aesthetics, and FIGS for speech and deglutition at 3 and 6 months. There was significant improvement in the QOL and aesthetics of patients from 1 to 3 months ($p < 0.001$). Speech and deglutition were also improved at 3 months, but the difference was not statistically significant ($p > 0.001$). To the best of our knowledge, ours is the first study that has evaluated the postoperative outcome of single stage delayed free flap reconstructive surgery in patients with ROM defects due to COVID-19-associated mucormycosis in terms of QOL, ANA, speech, and deglutition.

## Conclusion

COVID-19-associated ROM mucormycosis is a serious life-threating complication of COVID-19, which has a very low survival rate. Survivors of this disease frequently present with complex maxillofacial defects after few months that need reconstructive surgeries for acceptable aesthetics. Single stage delayed free flap reconstructive surgery can be a reliable procedure in such patients as it improves patients' QOL, aesthetics, speech, and deglutition over time.

**Conflict of Interest**
None declared.

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