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IP Annals of Prosthodontics and Restorative Dentistry

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Short Communication

Prosthodontic rehabilitation of patients with Rhinocerebral mucormycosis: An update of evidence

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ARTICLE INFO

Article history:
Received 26-05-2023
Accepted 02-06-2023
Available online 15-06-2023

Keywords:
Mucormycosis
Rhizopus Spp
Obturator

ABSTRACT

Mucormycosis is a devastating disease with serious manifestations in the affected individuals. It spreads through angioinvasion, and the spores have high affinity for olfactory epithelium, and pterygomandibular raphe of immunocompromised patients. Surgical debridement of invaded structures leads to extensive defects, which need prosthodontic rehabilitation to improve the quality of life of the patients. This article is compilation of data presented in literature to showcase the patients who were treated with maxillary obturators to manage post mucormycosis intraoral defects. Lacunae in presentation of clinical cases with future recommendations have also been discussed in brief.

1. Introduction

Mucormycosis is a fatal disease with serious manifestations as it leads to extensive tissue necrosis and spreads rapidly through vascular route.[1] Incidental findings while examining a patient for common dental pain or facial swelling may benefit in the early diagnosis of the disease. Depending upon the type and stage of disease, a course of treatment may lead to aggressive resection of various structures such as the maxilla, alveolus, and extraction of otherwise healthy teeth. Rhino orbito cerebral mucormycosis (RCOM), which is reported to be the most common type in developing countries, may also lead to additional loss of orbital and associated facial structures.[2] Consequences include a physically debilitated patient with enormous psychological trauma. Prosthodontists play a pivotal role in improving the functional and overall quality of life of such patients by fabricating maxillary obturators and facial prostheses.

Santos et al, in a recent article on Mucormycosis, presented a review of literature based on PubMed search, wherein the authors included data from 19 papers including their own case.[3] The authors highlighted that there were only 3 documented cases with history of Mucormycosis and rehabilitation with palatal obturator between 2007-2019. With no intention to negate the efforts of the authors and based on my experience with rehabilitation of patients with maxillofacial defects, a literature search was performed to update the evidence on patients who suffered with Mucormycosis who underwent prosthodontic rehabilitation with obturators.

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https://doi.org/10.18231/j.aprd.2023.024

Table 1: Presentation of clinical data (Search engine: PubMed)

	Author/ Year Country	Age/ Gender	Genus/ Species	Risk Factors	Location	Imaging tests	Treatment	Rehabilitation	Follow-up
				Articles between 2007-2019					
1.	Pruthi G et al., 2010[4], India	55/ Male	Unspecified	Diabetes, Rhino cerebral mucormycosis	Aramany Class IV	Unspecified	Right maxillary resection	Definitive maxillary obturator and silicone eye prosthesis	Unspecified
2.	I. Abu El-Naaj et al./ 2013[5], Israel, case 1	15/ Female	Zygomycete compatible with mucormycosis	Acute Lymphoid Leukemia, Rhinocerebral Mucormycosis	Aramany Class IV	Computed tomography, MRI, Fiberoptic Endoscopic Sinus Surgery (FESS) for tissue culture and debridement	Liposomal Amphotericin B Posaconazole Left total hemimaxillectomy, left ethmoidectomy and partial left sphenoidectomy	Definitive maxillary obturator	18-month follow-up
	I. Abu El-Naaj et al./ 2013[5], Israel, case 2	56/ Female	Unspecified	B-cell lymphoma Rhinocerebral Mucormycosis	Unspecified	Computed tomography	Subtotal maxillectomy. Isovuconazole, Amphotericin B, Voriconazole Posaconazole	Could not be done	Death
	I. Abu El-Naaj et al./ 2013[5], Israel, case 3	25/ Female	Unspecified	Acute Myeloid Leukemia Rhinocerebral Mucormycosis	Unspecified	Computed tomography	Total maxillectomy. Amphotericin-B Posaconazole,	Could not be done	Death
	I. Abu El-Naaj et al./ 2013[5], Israel, case 4	22/ Male	Unspecified	Chronic Myeloid Leukemia Rhinocerebral Mucormycosis	Unspecified	Computed tomography	Subtotal maxillectomy. Amphotericin-B, Voriconazole	Could not be done	Death
	I. Abu El-Naaj et al./ 2013[5], Israel, case 5	75/ Male	Unspecified	Acute Myeloid leukemia Rhinocerebral Mucormycosis	Unspecified	Computed tomography	Subtotal maxillectomy. Amphotericin-B, Voriconazole	Could not be done	Death

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Table 1 continued

	I. Abu El-Naaj et al./ 2013[5], Israel, case 6	64 / Female	Unspecified	Aplastic anemia Rhinocerebral Mucormycosis	Unspecified	Computed tomography	Total maxillectomy. Amphotericin-B, Voriconazole	Could not be done	Death
3.	Hatami et al./ 2013[6], Iran	65/ Male	Unspecified	Diabetes, Diabetic keto acidosis, Rhinocerebral mucormycosis	Open communication between the oral, nasal, and orbital cavities***	Not specified	Resected portions included anterior part of hard palate, nasal septum and conchae, left maxillary sinus, and orbital contents	Magnet retainer intraoral definitve obturator and facial prosthesis	2 years
4.	Gowda et al./ 2013[7], India	52/Male	Unspecified	Type II Diabetes Mellitus	Aramany Class 1	Panoromic radiograph	Left hemimaxillectomy	Interim hollow bulb obturator, Definitve implant and magnet retained obturator	6 months
5.	Vidyasankari et al./ 2014[8], India	62/ Male	Unspecified	Rhino cerebral mucormycosis	Maxilla***	Not specified	Left eye exenteration and left maxillectomy	Orbital prosthesis and a definitive intra-oral obturator	Not specified
6.	Faheemuddin M et al./ 2014[9], Pakistan	49/ Female	Unspecified	Diabetes, Hypertension,	Maxillae***	Not specified	Bilateral total maxillectomy	Definitive Maxillary obturator	2 months
7.	Shah R et al./ 2014[10], India, Case 1	48/ Female	Unspecified	Mucormycosis	Maxilla, completely edentulous***	Orthopanto-mography, Computed tomography	Maxillectomy	Definitive maxillary obturator	5 years
8.	Shah R et al./ 2014[10], India, (Case 2)	42/ Female	Unspecified	Mucormycosis	Maxilla***	Not specified	Bilateral oronasal openings	Definitive maxillary obturator	>1 year
9.	Kalaskar et al./ 2016[11], India	18 months/ male	Unspecified	Rhinocerebral mucormycosis	Aramany class IV	Occlusal radiograph	Amphotericin B	Palatal obturator	3 months
10.	Inbarajan et al./ 2018[12], India	60/ Female	Unspecified	Uncontrolled Type 2 Diabetes Mellitus, Mucormycosis	Maxillary defect with completely edentulous arch***	Not mentioned	Surgical debridement, oronasal fistula	Definitive maxillary obturator	3 months

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Table 1 continued

11.	Manjunath et al./ 2018[13], India	Elderly female	Unspecified	Uncontrolled Type 2 Diabetes Mellitus, Mucormycosis	Maxilla***	Computed tomography	Surgical debridement Amphotericin B	Interim maxillary obturator	3 weeks
12.	Salinas TJ et al./ 2019[14], Rochester, Minnesota	32/ Female	Unspecified	Lymphoblastic Lymphoma, Chemotherapy, Invasive mucormycosis	Aramany Class VI	Unspecified	Serial debridement of the maxilla, anterior maxillectomy, right intranasal, and alar resection followed by microvascular free flap	Interim acrylic obturator followed by metal-ceramic fixed prosthesis supported by 8 osseointegrated dental implants.	Unspecified
13.	Mani UM et al./ 2019[15], India	64/Male	Zygomyces	Uncontrolled diabetes	Aramany class IV	Unspecified	Total maxillectomy on left side and right subtotal maxillectomy	Split thickness graft was done in lateral wall of the defect, maxillary definitive 2-piece hollow obturator	
14.	Punjabi et al./ 2019[16], India	50/ Male	Unspecified	Uncontrolled diabetes, Mucormycosis	Aramany class VI	Not specified	Resection of hard palate and maxilla	Definitive obturator with silicone relined titanium bulb	Not specified
				Case reports after 2019					
15.	Pandilwar PK et al./ 2020[17], India	60/ Male	Unspecified	Uncontrolled diabetes Rhinomaxillary Mucormycosis	Completely edentulous maxilla***	Orthopantomogram and Cone-beam computed tomography	Total maxillectomy	Interim palatal obturator	Not specified
16.	Pandilwar PK et al./ 2020[17], India	67/ Male	Unspecified	Uncontrolled diabetes, Mucormycosis	Maxilla***	Cone-beam computed tomography	Surgical debridement of maxilla Amphotericin B	Palatal obturator	2 months
17.	Mohamed et al./ 2020[18], India	48/ Male	Unspecified	Invasive mucormycosis	Left maxilla***	Unspecified	Hemi maxillectomy	Delayed surgical obturator	Not specified
18.	Mohamed et al./ 2020[18], India	55/ Male	Unspecified	Mucormycosis	Maxilla***	Unspecified	Bilateral complete maxillectomy	Delayed surgical obturator	Not specified

Continued on next page

Table 1 continued

19.	Eswaran et al./ 2021[19], India**	31/ Male	Mucorales	Covid 19, Mucormycosis	Aramany class IV	MRI, Computed tomography	Liposomal Amphotericin B, Polymixin B injection, Bilateral oral Posaconazole maxillectomy and right frontal craniectomy with Debridement and repair with Titanium mesh.	Interim obturator	One month
20.	Ravi MB et al./ 2022[20], India (case 1) *	34/ Female	Rhizopus	Uncontrolled Diabetes / COVID 19/ Mucormycosis	Aramany class I	Unspecified	Surgical debridement and resection of right maxilla, Piperacillin, Tazobactam Posaconazole Insulin	Hollow sectional magnet retained prosthesis	Unspecified
21.	Ravi MB et al./ 2022[20], India (case 2) *	60/ Male	Broad aseptate hyphae of Mucorales.	Diabetes / COVID 19/ Right Rhinosinomaxillary Mucormycosis with Left Mucormycosis	Aramany Class IV	Gadolinium enhanced MRI, a plain Computed tomography of para nasal sinuses	Right Total Maxillectomy and left Hemi maxillectomy Posaconazole Amphotericin	Hollow bulb obturator	24, 48, and 72 hours of denture insertion.
22.	Kondaka S et al./2022[21], India*	40/ Male	Not mentioned	Diabetes/ Post Covid Mucorm-ycosis	Bilateral maxille-ctomy***	Post surgical debridement CBCT	Left total Maxillectomy, right subtotal maxillectomy and left orbital decompression along with the resection of the left zygomatic arch and rim.	Obturator supports by patient specific implants	Till 90 days.
23.	Rathee M et al./2022[22], India (Case 1)*	50/Male	Not mentioned	Diabetes/ Post Covid Rhinocerebral Mucormycosis	Aramany Class II	CT scan	Surgical debridement	Immediate Surgical obturator	Not specified

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Table 1 continued

24.	Rathee M et al./2022[22], India (Case 2)*	24/Male	Not mentioned	Early onset Diabetes, Post COVID Mucormycosis	Aramany Class III	Not specified	Surgical debridement	Immediate Surgical obturator	Not specified
25.	Rathee M et al./2022[22], India (Case 3)*	40/Male	Not mentioned	Diabetes, Post COVID Mucormycosis	Aramany Class III	Not specified	Surgical debridement	Immediate Surgical obturator	Not specified
26.	Rathee M et al./2022[22], India (Case 4)	46/Female	Not mentioned	Diabetes, PCM	Aramany Class III	Functional endoscopic sinus surgery	Surgical debridement	Interim obturator	3 months or more
27.	Rathee M et al./2022[22], India (Case 5)	56/Male	Not mentioned	Post Covid Rhinocerebral mucormycosis	Completely edentulous***	Not mentioned	Partial maxillectomy	Interim obturator/ Magnet retained definitive 2 part prosthesis	Not mentioned
28.	Rathee M et al./2022[22], India (Case 6)	48/Male	Not mentioned	Post Covid Rhinocerebral mucormycosis	Completely edentulous***	Not mentioned	Total maxillectomy	Interim obturator/ Definitive magnet retained obturator	Not mentioned
29.	Rathee M et al./2022[22], India (Case 7)	65/Male	Not mentioned	Diabetes, Post Covid Rhinocerebral mucormycosis	Class IV	Not mentioned	Partial maxillectomy	Interim obturator	Not mentioned
30.	Rathee M et al./2022[22], India (Case 8)	46/ Male	Not mentioned	Rhinocerebral mucormycosis	Not specified	Not mentioned	Partial maxillectomy	Interim obturator	Not mentioned
31.	Rathee M et al./2022[22], India (Case 9)	38/Female	Not mentioned	Diabetic, PCM	Aramany Class I? / Closed flap***	Not mentioned	Hemi maxillectomy	Definitive cast partial denture	
32.	Artopoulou I et al./ 2022[23], Greece	53/Male	Rhizopus	Diabetes, PCM	Closed with palatal flap***	CT scan	Bilateral subtotal maxillectomy with aggressive debride ment	Definitive obturator with bilateral acrylic projections	6 months

*Post Covid Mucormycosis

**On Google scholar, ***Difficult to decipher or classify according to Aramany's classification (1978)

Table 2: Presentation of clinical data (Search engine: Google scholar, Google)

	Author/ Year Country	Age/ Gender	Genus/ Species	Risk Factors	Location	Imaging tests	Treatment	Rehabilitation	Follow-up	
1.	Dhiman R et al./ 2007, India,	17/ Male	Unspecified	Uncontrolled diabetes and Mucormycosis	Aramany class IV	Not mentioned	Subtotal right maxillectomy and enucleation of right eye	Magnet-retained, silicone eye prosthesis and a polymethyl-methacrylate hollow bulb obturator.	Unspecified	Rehabilitation of a rhinocerebral mucormycosis patient. The Journal of Indian Prosthodontic Society. 2007;7(2):88-91.
2.	Rathee et al./ 2013, India	68/ Male	Unspecified	Uncontrolled diabetes, Rhinocerebral Mucormycosis	Anterior maxilla***	None	Surgical debridement of maxilla	Interim palatal obturator	Not mentioned	Management of Palatal Perforation in an Immunocompromised Diabetic Patient with Mucormycosis Using Surgical and Interim Obturator. Int J Clin Cases Investig 2013;5:63:67.
3.	Naveen et al./ 2015, India	48/ Male	Unspecified	Uncontrolled diabetes, Rhinocerebral Mucormycosis	Maxilla, Aramany Class IV	Computed tomography, panoromic radiograph	Partial maxillectomy, Amphotericin B	Hollow bulb definitive obturator	Not specified	Mucormycosis of the Palate and its Post-Surgical Management: A Case Report. J Int Oral Heal 2015;7:134.
4.	Ilusika et al./ 2018, India	47/ Male	Mucorales	Diabetes, Mucormycosis	Aramany Class VI	Computed tomography	Fluconazole tablets 200 mg for 12 days, Surgical debridement	Definitive obturator	5 months	Enhancing granulation in a postmucormycotic maxillectomy defect with honey: A review of literature and illustrative case. Niger J Basic Clin Sci 2018;15:156-60.
5.	Abrol et al./ 2019, India	44/ Male	Unspecified	Mucormycosis with osteomyelitis	Aramany Class IV	Not mentioned	Surgical debridement	Definitive maxillary obturator	2 months	Prosthodontic Management of Sub-Total Maxillectomy: A Case Report. Chronicles Dent Res 2019;8:61-5.

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Table 2 continued

6.	Bandari et al./2021, India*	65/ Male	Unspecified	Post covid mucormycosis	Aramany class IV	Not mentioned	Left maxillectomy	Hollow bulb obturator	Unspecified	Prosthetic Rehabilitation of A Post-Covid Mucormycosis Maxillectomy Defect Using A Fused Two-Piece Hollow Obturator: A Fabrication Technique. Eur J Mol & Clin Med 2021;7:8564-9.
7.	Rafique et al./ 2020, Pakistan	65/ Female	Unspecified	Type 2 Diabetes, Mucormycosis	Maxilla and extraoral defect**	Not mentioned	Partial maxillectomy, completely edentulous	Magnet retained defintive obturator	One week	Restoration of a post-surgical defect by magnetic maxillofacial prosthesis: A case report. J Univ Med \& Dent Coll 2020;11:44-8.
8.	Prakash M et al./ 2020, India	26/ Male	Unspecified	Kidney transplantation, Mucormycosis	Maxilla**	Unspecified	Partial maxillectomy	Cast metal maxillary definitive obturator	Unspecified	Prosthodontic Rehabilitation of Maxillary Defect in a Patient with Mucormycosis. J Evol Med Dent Sci 2020;9:3163-7.
9.	Mishra et al./ 2021, India	64/ Male	Unspecified	Rhinocerebral mucormycosis	Right maxilla, Aramany class II	Unspecified	Right maxillectomy	Cast metal maxillary defintive obturator	Unspecified	Prosthetic Rehabilitation of Maxillectomy Defects, with Single-Piece Open-Hollow Bulb Definitive Obturator. J Evol Med Dent Sci 2021;10:1169-74.
10.	Garde J et al./2021, India*	55/ Female	Broad, aseptate, ribbon shaped hyaline fungal hyphae seen.	Post covid mucormycosis	Aramany class IV	CT-PNS: MRI-PNS	Bilateral Subtotal Maxillectomy	Definitive maxillary obturator	1 month and at 8 months	Restoring a Smile Post Covid-19 Associated Mucormycosis: A Case Report. J Dental Sci 2021, 6(4): 000314.

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Table 2 continued

11.	Shilpa et al./ 2021, India	52/ Male	Unspecified	Diabetes mellitus	Aramany Class VI	Unspecified	Hemi maxillectomy	Cast metal hollow obturator	3 months	A case report on prosthetic rehabilitation of a patient with hemimaxillectomy: A modified technique. J Int Oral Heal. 2021;13:306-9.
12.	Chinta A et al./ 2022, India	24/Male	Unspecified	Diabetes mellitus Rhinosinomaxillary mucormycosis and right Mucormycosis	Aramany Class IV	Anterior diagnostic rhinoscopy	Left total maxillectomy and right hemimaxillectomy	Definitive hollow acrylic obturator	3 months	Prosthodontic rehabilitation of a mucormycosis patient: a case report
13.	Shalimon A et al./2023*, India	47/Male	Unspecified	Rhino orbital mucormycosis (Post COVID?)*8	Not clear**	Presented after resection	Right hemi maxillectomy	Cast metal obturator	Not specified	Prosthetic rehabilitation of post-COVID mucormycosis. J Interdiscip Dentistry 2023;13:43-7
14.	Nagpal A et al./ 2022, India	24/Male	Unspecified	Mucormycosis	Brown's class IIb**	Presented after resection	Unilateral maxillary defect not crossing midline	Cast metal obturator	Not specified	Prosthetic Rehabilitation of Mucormycosis Patient By Cast Partial Denture: A Case Report. Bull. Env. Pharmacol. Life Sci., Spl Issue[2] 2022 : 235-237

*Post covid mucormycosis, ***Difficult to decipher or classify according to Aramany's classification (1978)

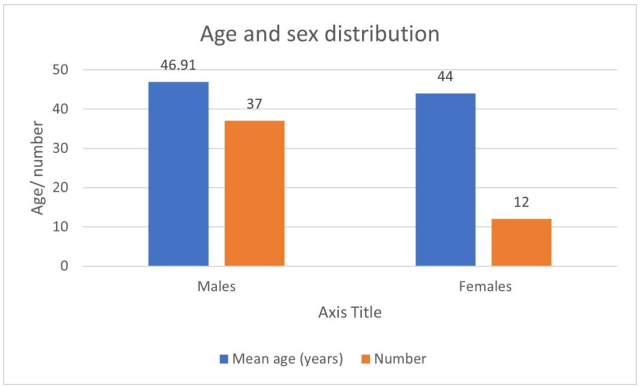

Fig. 1: Age and sex distribution of presented patients in Tables.

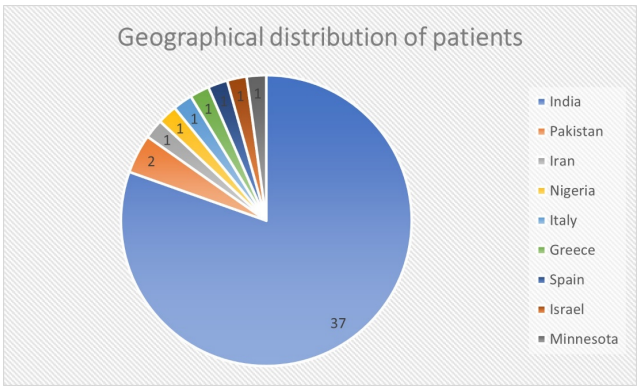

Fig. 2: Geographic distribution of presented cases.

2. Data Acquisition and Observations

Literature search was performed on PubMed and Google scholar/ Google for patients who had a history of Mucormycosis and underwent prosthodontic rehabilitation from 2007 to 18^{th} May 2023. 14 more cases could be found on PubMed (Table 1) and 5 on google scholar (Supplementary table with references) with same etiology and treatment during the same time frame (2007-2019).[4–16] In addition, Abu El-Naaj et al (2013) have reported 5 patients with history of mucormycosis who succumbed to the disease before they could be rehabilitated with maxillary obturator.[5]

I. E. Ali, et al reported prosthodontic rehabilitation of post mucormycosis defects from 30 case reports published between 2010 to 2021.[24] 18 more patients on PubMed[17–23] and 9 on google scholar [Table 2] were reported with history of mucormycosis followed by fabrication of palatal obturator from 2020 to May 2023. Mean age and gender wise distribution of patients who were rehabilitated after surgical management of mucormycosis has been depicted in Figure 1. A clear predilection of male patients is evident over females with age range between 18 months to 75 years.

As aptly emphasized by other authors that most of the cases were reported from India, a discussion about post covid mucormycosis is worth mentioning. Our data shows that approximately 80% of patients were reported from India. Previous literature has also reported global prevalence of mucormycosis to be 70 times more in India, though other countries also faced the heat of the situation.[2] Covid-19 virus infected patients with diabetes were predisposed at a higher rate to the invasion of fungus owing to a compromised host defence mechanism. One of the scientific rationales behind this could be existence of proviral and profungal cellular host factors in olfactory epithelium of diabetic patients, which makes them vulnerable to upper respiratory infections, owing to their higher glucose levels and lowered immunity.[25] In general, the spores of fungus find a favourable niche in pterygomandibular fossae from where they invade different structures.[26] Although the data is extensive on different manifestations of post covid mucormycosis, Moorthy et al have specifically documented history of 11 patients who underwent maxillectomy, out of which 4 patients did not survive this deadly fungal infection.[27] Recent case reports have documented 10 patients with history of post covid mucormycosis (PCM) who were efficiently rehabilitated with obturators (Table 1, Table 2).[19–23,28,29]

Diabetes mellitus was the most significant associated risk factor in 27 patients followed by Acute Myeloid Leukemia based on data reported here and earlier by Santos et al. Rhizopus oryzae has been reported to be the most common causative organism as high glucose levels, insulin resistance and ketoacidosis encourage its growth.[30] Amphotericin B remained the first-choice drug followed by Posaconazole. Follow up period was inconsistent in all the case reports with only one patient followed till 5 years by Shah et al.[10] Probable reasons for short term follow up could be because of aggressive nature of disease, poor general health of patients, uncertain family support and difficult accessibility to healthcare services, especially in developing countries.

Few authors performed extensive debridement in patient diagnosed with mucormycosis but did not mention any prosthetic rehabilitation.[31,32] So, here i would like to emphasize that diagnosis and management of patients with mucormycosis consist of a multidisciplinary team, where a huge onus lies on the maxillofacial prosthodontist. They play a crucial role by helping in social reintegration of patients by their functional and aesthetic rehabilitation. Various authors have provided either a hollow obturator, sectional prosthesis, or innovative designs to retain prothesis in orbito maxillary defects but there are many case reports in which the performance of obturator was not mentioned. Another critical aspect is reporting of patient satisfaction, which was measured subjectively with Oral health Impact Profile – 14 questionnaires in only two case reports and were found to be improved on Likert scale

after prosthodontic rehabilitation.[9,12] Artopoulou I et al used Obturator Functioning Scale and Distress Scale to evaluate the patient satisfaction and psychological status respectively.[23]

Early diagnosis of condition, treatment of underlying pathology, thorough debridement, antifungal drugs, local care of post debridement wound, psychological counselling and prosthodontic rehabilitation are integral components of a comprehensive treatment plan for such patients.[25] In a breakthrough research, Sharma et al have proposed the future of intranasal sprays with anti-inflammatory, anti-diabetic and antiviral action which would help in prophylactic control of mucormycosis in covid infected and/ or diabetic patients. Exact formulation of drugs is still unpublished, but it can be a promising therapy for preventing the spread of infection.[25]

I would like to highlight the huge discrepancy which was noticed among the references quoted in Table 1 and reference list given at the end of article by Santos et al.[3] So, the readers should follow correct references to prevent further error while quoting the literature. Last but not the least, this article has reported those case reports which have been already documented in literature, though the number of patients who might have suffered with PCM must be much larger. Data from large tertiary care hospitals from India need to be added for complete reporting of the evidence. Follow up of the patients should be provided by the authors as an integral part of comprehensive treatment plan. In view of incomplete reporting and lack of adequate follow up in most of the case presentations to report patient survival, improvement in quality of life or performance analysis of the prosthesis delivered in terms of functional, esthetic, or psychological benefit, I am unable to document any robust evidence on effect of prosthodontic rehabilitation of such patients.

Another interesting finding is that although maximum number of defects were classified as Class IV (n=12) according to Aramany's classification,[33] many authors did not classify the post resection defects. One of the reasons could be inability to fit the post mucor especially post covid mucor defects into any class of defects due to extensive and emergency management with overburdening of the system. Authors should ensure to consider this important component of presenting any case report and formulation of a more comprehensive single classification system to classify maxillofacial defects may be considered in future.

3. Conflict of Interest

There are no conflicts of interest in this article.

4. Source of Funding

None.

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Cite this article: Pruthi G. Prosthodontic rehabilitation of patients with Rhinocerebral mucormycosis: An update of evidence. *IP Ann Prosthodont Restor Dent* 2023;9(2):117-128.