ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 8, Issue – 2, April - 2025, Page No. : 01 – 14

The Success of Zygomatic Implant in Rehabilitation of Post-Mucormycosis Cases: A Systematic Review

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How to citation this article: Dr. Kanchan Shah, Dr. Jayant Landge, Dr. Sunny Singh, Dr. Asma Fruitwala, "The Success of Zygomatic Implant in Rehabilitation of Post-Mucormycosis Cases: A Systematic Review", IJMACR- April - 2025, Volume – 8, Issue - 2, P. No. 01 – 14.

Type of Publication: Review Article

Conflicts of Interest: Nil

Abstract

Introduction: Maxillectomy, performed in mucormycosis cases can significantly disrupt critical oral functions and lead to severe facial deformity. Zygomatic implants offer a remote bone anchoring solution for severe maxillary atrophy or defects resulting from resection. However, there remains a scarcity of studies addressing the success of zygomatic implants in mucormycosis cases. Therefore, our systematic review aims to provide a comprehensive analysis of the effectiveness of zygomatic implants (ZI) in the prosthetic rehabilitation of patients recovering from mucormycosis.

Methods: The systematic search used PubMed, Embase, Scopus and Google Scholar to retrieve articles. Publications addressing ZI for COVID-19-associated mucormycosis (CAM) or non-CAM studies with a minimum follow-up period of 3–12 months were considered for inclusion.

Results: A total of nine publications were reviewed. All studies showed that prosthesis rehabilitation with ZI improved phonation, chewing, deglutition, aesthetics, and satisfactory bone deficit management function. Only one study observed a significant reduction in stress and anxiety levels after ZI surgery. Complications such as moderate soft tissue infections, prosthesis loosening,

occlusal discrepancies, and one implant failure were reported.

Conclusions: Zygomatic implants seem to be a reliable, safe, and effective treatment option for enhancing the functional and psychological recovery of facial deformity caused by mucormycosis. Nonetheless, this conclusion is founded on a small number of studies. Hence, prospective large-scale cohort studies or clinical trials are recommended.

Keywords: Mucormycosis; zygoma; dental implants

Introduction

Mucormycosis, known colloquially as black fungus, is an Angio invasive fungal infection caused by Mucorales with fungus Rhizopus Oryzae in the majority of cases. Currently, Mucorales fungi are the next most common Mold pathogens after Aspergillus, leading to invasive fungal disease[1]. This life-threatening condition predominantly afflicts individuals with compromised immune systems, such as those with uncontrolled diabetes, renal failure, liver failure, prolonged treatment with immunosuppressive therapy, leukaemia, organ transplants, polytrauma, AIDS, or tuberculosis, making them susceptible to the disease[2,3]. The incidence of mucormycosis has notably increased in diabetic patients (60-80%) and those undergoing immunosuppressive therapy, with a global prevalence rate ranging from 0.005 to 1.7 per million population[4]. Globally, Mucormycosis has been seen among high risk patients in countries like India which contributes to 44% of cases followed by Israel and Turkey[5]. while European nations reported haematological malignancy (acute myeloid leukaemia, acute lymphoblastic leukaemia, non-Hodgkin's lymphoma, myelodysplastic syndrome) as common underlying diseases[6]. Drug-related MM like chronic corticosteroid use and nosocomial MM have also been reported. Association of MM in 88% of covid 19 patients was reported to be due to the use of systemic corticosteroids [7].

Mode of contamination occurs through the inhalation of fungal spores[2]. The disease manifests in various forms, with rhino-orbital-cerebral mucormycosis (ROCM) being the most common. ROCM caused by the direct spread of the infection from the sinus to the hard palate, results in sudden tooth mobility, perforation of the hard palate, pus secretion, painful necrotic ulcerations, gingival thickening, and halitosis which can lead to severe complications, including facial bone necrosis and potential cranium penetration[8]. A definitive diagnosis is typically achieved through histological examination, which can identify Mucorales as hyaline filaments in tissue samples. Treatment for mucormycosis primarily involves the administration of intravenous antifungals and surgical debridement. The prognosis depends significantly on prompt medical intervention and the extent of surgical resection [9].

Maxillectomy, the surgical removal of the maxilla, is usually performed in mucormycosis cases [10]. and can significantly impact life by disrupting critical functions such as mastication, speech, and swallowing, and lead to severe facial deformity [11]. The stigma associated with such disfigurement can adversely affect the patient's psychological well-being. Early detection of mucormycosis allows for limited resection, preserving the zygomatic arch and enabling the use of zygomatic implants for reconstruction. Developed in 1998, zygomatic implants offer a remote bone anchoring solution for severe maxillary atrophy or defects resulting from resection [12]. Their high survival rates and avoidance of bone graft-related complications make them a favourable option for prosthetic rehabilitation in

cases where conventional implants are not feasible due to extensive maxillary resection [13]. The zygomatic implant technique allows for immediate reconstruction, minimizing the need for additional bone grafting procedures and reducing donor site morbidity. The success of these implants is not solely attributed to their structural advantages but also to their role in restoring facial aesthetics and function, which are crucial for psychological well-being and social reintegration [12].

However, there remains a scarcity of studies with larger sample sizes specifically addressing the success of zygomatic implants in mucormycosis cases. Therefore, our systematic review seeks to fill this gap by consolidating existing literature and providing a comprehensive analysis of the effectiveness of zygomatic implants in the prosthetic rehabilitation of patients recovering from mucormycosis, with an emphasis on their impact on patient outcomes and quality of life.

Study Search

This systematic review was conducted in conformity with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA)[14] standards and was documented apriori in the Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD42024507217.

This systematic review focuses on patients requiring zygomatic implant insertion due to a condition known as Mucormycosis. The systematic search used the electronic databases -PubMed, Embase, and Scopus to retrieve articles published from conception until February 28th, 2024. The search technique included a combination of medical search terms (MeSH) and keywords for zygomatic implants and mucormycosis, along with the Boolean operators "OR" and "AND" [Supplementary Table 1]. Only peer-reviewed articles, regardless of the language of publication, were considered.

Supplementary table 1: Search terms

Keywords	Key terms	MeSH terms
Zygomatic	zygomatic OR zygoma OR zygomaticus OR Zygomatic Arch OR Cheek Bone OR quad zygoma	"Zygoma"[Mesh]
Implant	implant OR implants OR fixture OR fixtures	"Dental Implants"[Mesh]
Mucormycosis	Mucormycos* OR Mucorales Infection*	"Mucormycosis" [Mesh]

*Indicates wild card

Article selection

Two reviewers individually screened the articles. To locate relevant studies, abstracts and titles were reviewed first, followed by full-text articles. Any differences between the decisions of the two reviewers were settled by discussion and mutual agreement.

Inclusion and Exclusion Criteria

Publications addressing the zygomatic implant for COVID-19-associated mucormycosis (CAM) or non-CAM studies were considered for inclusion. Research types deemed suitable for inclusion included case studies, cross-sectional, cohort, and case series studies. Studies reporting the following outcome variables were considered eligible: zygomatic implant success in the form of patient satisfaction, improvement in mastication function/aesthetic improvement, implant survival/failure, and any complications (surgical/prosthetic) within a minimum follow-up period of 3–12 months.

Letters to editors, laboratory modelling or in vitro investigations, review papers and conference proceedings were among the exclusion criteria. Studies in which the patient was not followed up were also omitted.

Data extraction

Two reviewers independently extracted and reviewed data in a spreadsheet. The variables included were authors/year of publication, study design, study settings, patient data (age, gender, total number of participants), follow-up durations, surgical approach and outcome reported.

Data analysis

The extracted study information was synthesized under categories and described using a narrative approach.

Risk of bias assessment

The risk of bias in the listed papers was assessed using the Joanna Briggs Institute's critical evaluation criteria for case series, case reports, and cohort studies (15). These checklists evaluated the report's thoroughness, risk of bias, and reporting accuracy. Two reviewers reviewed each report separately, and any disputes were handled by mutual discussion or consultation with a senior reviewer.

Result

Figure 1 depicts the selection procedure for relevant studies. The systematic search approach found 110 papers, six of which were duplicates. Two reviewers separately selected titles and abstracts that addressed the focus subject matter. Of the 104 studies, 14 were requested for full-text reading, one of which could not be obtained. Out of the remaining 13 studies, one was removed owing to a lack of follow-up data, one was in a non-English language and two were unrelated to zygomatic implants. Thus, a total of nine publications were reviewed [12,16,23].

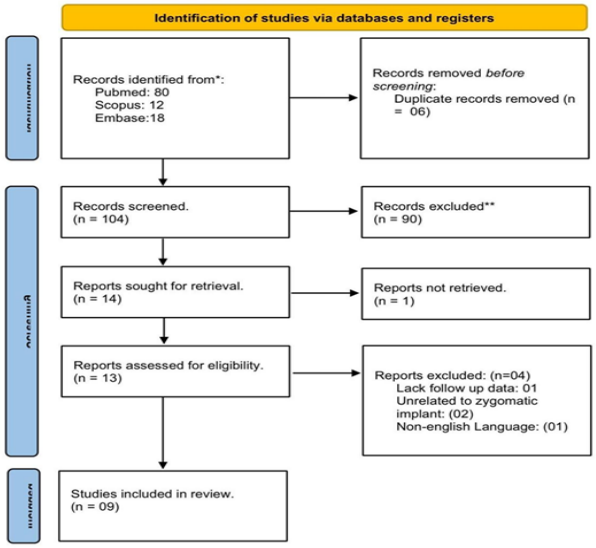

Figure 1: Study selection process

Study Characteristics

One prospective cohort study and 8 case reports/ series were included. The included studies were performed in India (n=8) and Pakistan (n=1). Five studies were conducted among the COVID-19-associated mucormycosis (CAM) whereas the remaining four were among non-CAM patients. The investigations included 77 individuals, ranging from 1 to 26 samples across studies. The average of patients in the studies was 47±12.18 years (Table 1). The follow up duration was 3-4 months in two studies, 6-12 months in five studies, 2 years in 1 study, and 5 years in another study (Table 1).

Table 1: Characteristics of included studies

Authors/ Year	Location	Study Type	Follow up Duration	Study population	Total Number of Cases	Patient age	Surgical approach
Gaur et al. 2022(16)	India	case report	6-12 months.	rhino-orbital-cerebral mucormycosis (ROCM)	1	55	bilaterally placed pterygoid and zygomatic implants
Beri et al. 2023(17)	India	case report	up to 2 years	Post-COVID-19 mucormycosis patient	1	32	zygomatic implants placed following the exposure of the zygomatic bone through full-thickness flap elevation and subperiosteal dissection f
Kumar et al. 2023(12)	India	Prospective cohort	6-12 months.	Post-COVID-19 mucormycosis patient	20	58	Four zygomatic implants were placed in the zygomatic process of maxilla, splinted to distribute the occlusal load to apical threads
Singh et al. 2023(23)	India	Case series	4 months	COVID associated mucormycosis and non-CAM patients	26	47	ZIP Temporalis Flap technique, combined with zygomatic implants
Patel et al. 2023(19)	India	case series	6–12 months.	Post-COVID-19 mucormycosis patient	21	NM	sub-periosteal undermining on the zygoma to place bilateral implants, secured with a titanium bar and screws
Pandya et al. 2023(18)	India	case report	6-12 months.	non-COVID mucormycosis	3	46	four zygomatic implants, two on each side
Abbasi and Alam, 2023(20)	Pakistan	case report	upto 5 years	non-COVID mucormycosis	1	65	Two zygomatic implants were placed in the right zygomatic bone and one each in the left zygomatic bone and infraorbital rim,

							using a modified Lefort 1 incision and mucoperiosteal flap elevation
Gupta et al. 2023(22)	India	Case Series	6-12 months.	non-COVID mucormycosis	3	43	Full thickness mucoperiosteal flap was raised and subperiosteal dissection was done palatially and labially. 4 zygomatic implants were placed at 45-degree angulation
Basavaraju et al. 2024(21)	India	case report	3 months	Post-COVID-19 mucormycosis patient	1	30	subperiosteal implant attached to an implant-bridge prosthesis by titanium screws

Functional Improvement

All of the studies included in this review showed that prosthesis rehabilitation improved function. Patel et al.[19] confirmed the structural resilience of the prosthetic implant under masticatory forces, while Kumar et al.[12] reported improved mastication and speech post-rehabilitation, with significant increases in retained particle weight and reduced auditory perception scores from 11.100 ± 0.640 before surgery to 4.250 ± 0.444 after 1 year[12], indicating enhanced oral function. Remaining seven studies [16, 18, 20-23]. documented high patient satisfaction after one year of treatment, with improved phonation, chewing, deglutition, aesthetics, and satisfactory bone deficit management.

Psychological Well-being

There is only one study that examined the effect of zygomatic implant surgery on patients' psychological well-being. Kumar et al.[12] observed a significant reduction in stress and anxiety levels after zygomatic implant surgery, as evidenced by lower diurnal salivary cortisol slopes (from 22.750 ± 0.966 before surgery to 8.500 ± 1.277 after one year and decreased depression and anxiety scores from 27.350 ± 3.030 before rehabilitation to (8.950 ± 0.887) after 1 year.

Complications

Only two studies documented complications related to zygomatic implants. Patel et al.[19] observed postoperative problems such as moderate soft tissue infections managed by irrigation and antibiotics, prosthesis loosening necessitating fresh fabrication, occlusal discrepancies repaired post-surgery, and a gummy smile resolved by prosthesis re-construction. Singh et al. [23] reported minimal donor site morbidity in ZIP flap patients, with one implant failure and one fibula flap failure requiring a secondary temporalis ZIP flap treatment, as well as a case of recurrent mucormycosis. Seven studies[12,16–18,20–22] reported no complications in their studies.

Quality assessment of included studies

The included case series [19,22,23] used explicit inclusion criteria, standard, reliable procedures for condition measurement, and valid methods for identifying the conditions. Except for Patel et al., all studies supplied comprehensive participant demographics as well as precise data on presenting locations' demographics and follow-up outcomes. Two of the three studies included consecutive participants. All three studies were deemed to follow suitable statistical analysis protocols (Table 2A). The included case reports. [16–18, 20, 21] mainly met all quality evaluation criteria. However, two of them [17, 18] exhibited inconsistencies in their descriptions of diagnostic procedures, and Pandya et al. failed to offer an overview of the patient's history (Table 2B). The prospective cohort study [12] also met key research quality standards. Overall, the studies exhibit a low level of bias (Table 2C).

Table 2A: Quality assessment of included case Series

	Case Series									
Author/ Year	clear criteria for inclusion	condition measured in a standard, reliable way for all participants	valid methods used for identification of the condition	consecutive inclusion of participants	complete inclusion of participant	clear reporting of the demographics of the participants	clear reporting of clinical information of the participants	outcomes or follow up results of cases clearly reporte	clear reporting of the presenting site(s)/clinic (s) demographic information	statistical analysis appropriate?
Singh et al., 2023(23)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Patel et al, 2023(19)	Y	Y	Y	Y	Y	N	U	Y	U	Y
Gupta et al., 2023(22)	Y	Y	Y	U	U	Y	Y	Y	Y	Y

Table 2B: Quality assessment of included case Reports

	Case Reports							
Author/ Year	Were patient's demographic characteristics clearly described?	Was the patient's history clearly described and presented as a timeline?	Was the current clinical condition of the patient on presentation clearly described?	Were diagnostic tests or assessment methods and the results clearly described?	Was the intervention(s) or treatment procedure(s) clearly described?	Was the post-intervention clinical condition clearly described?	Were adverse events (harms) or unanticipated events identified and described?	Does the case report provide takeaway lessons?
Gaur et al., 2022(16)	Y	Y	Y	Y	Y	Y	Y	Y
Beri et al., 2023(17)	Y	Y	Y	N	Y	Y	Y	Y
Pandya et al., 2023 (18)	Y	N	Y	N	Y	Y	Y	Y
Abbasi and Alam, 2023(20)	Y	Y	Y	Y	Y	Y	Y	Y
Basavaraju et al., 2024 (21)	Y	Y	Y	Y	Y	Y	Y	Y

Table 2C: Quality assessment of included cohort study

		Cohort study									
Author/ Year	two groups similar and recruited from the same population	exposures measured similarly	exposure measured in a valid and reliable way	confounding factors identified	strategies to deal with confounding factors stated	Participants free of the outcome at the start of the study	Outcomes measured in a valid and reliable way	follow up time reported	follow up complete	strategies to address incomplete follow up utilized	statistical analysis appropriate?
Kumar et al., 2023(12)	NA	Y	Y	Y	Y	Y	Y	Y	Y	NA	Y

Discussion

Zygomatic implants, also known as ZIs, are recognised for their ability to provide a graft-free rehabilitation option for patients experiencing severe maxillary atrophy due to trauma, cancer, infection, or other medical conditions[24]. They are also a viable option for patients unable to undergo extensive augmentation procedures for traditional maxillary implant therapy,

cleft palate patients, and, more recently, COVID-associated mucormycosis [25–27]. This systematic review focuses on the outcome of ZIs in patients with mucormycosis following maxillectomy. Although there are fewer occurrences of mucormycosis, it is expected that reconstructive demands among COVID-19-associated mucormycosis survivors, particularly in India, will rise in the coming months, underlining the significance of this review[28].

Oral structures are vital for swallowing, chewing, and phonation. The loss of oral elements has a substantial impact on these processes, resulting in nutritional deficiencies, functional musculoskeletal asymmetries, facial disorders, and speech problems. Studies [29–31] have consistently shown that prosthetic interventions improve oral functionality in individuals who have had surgical excision of oral tissues for cancer therapy or maxillary abnormalities. Zygomatic implants are essential for both supporting dental prostheses and aiding in the rehabilitation of edentulous arches that have experienced considerable bone loss. ZIs can induce masticatory muscle hyperactivity, as demonstrated by electromyography tests, even in the absence of periodontal receptors [32,33]. The fixed prosthesis attached to the zygomatic bone provides the fundamental benefit of a robust occlusal surface necessary for a well-balanced stomatognathic system. Consistent with this, our review shows that ZIs can improve oral functionality in individuals with mucormycosis and improve overall patient outcomes.

The psychological effects of apparent disfigurement trauma are profound. Researchers have extensively investigated how physical appearance shapes everyday interactions and perceptions. Research conducted on people with physical and facial disfigurements has repeatedly demonstrated that self-esteem and quality of life are highly impacted by one's physical appearance and body image[34]. Mucormycosis-related facial deformities lead to social isolation and persistent psychological distress, which manifests itself as anxiety and stress. Moreover, functional deficits such as trouble speaking and chewing food aggravate these psychological problems. Srivastava et al.[35] found that individuals with Rhino-Orbital Mucormycosis had significant rates of severe depression (28%), as well as high levels of anxiety (26%). Maravi et al.[36] also discovered sleep disorders, stress and trauma-related disorders depression, and anxiety in mucormycosis patients. Only one study in this review has assessed and found a reduction in stress and anxiety following zygomatic implant (ZI) treatment (12). Comparable psychological benefits were observed by Ahuja et al.[37] in patients with mucormycosis after surgical procedures such as exenteration, retrobulbar amphotericin B injection, or functional endoscopic sinus surgery. These findings indicate that the stress and anxiety experienced by these patients are strongly linked to the functional losses and facial deformity associated with maxillectomy, emphasizing the importance of physical looks and functioning on mental health.

While ZIs are generally associated with positive outcomes, there is a possibility of immediate complications such as pain, paraesthesia, hematoma, and orbital penetration. These complications have a positive prognosis; however, there is also a possibility of late complications such as diminished osseointegration, oroantral communication, chronic sinusitis, and soft tissue infections, which require meticulous treatment due to their complexity and the delicate anatomical sites involved[24]. The majority of the analysed studies reported

no complications, while one reported only minor difficulties such as mild soft tissue infections, prosthesis loosening, occlusal discrepancies, and gummy smile. This is consistent with Chrcanovic et al.[38,39] findings, which showed a 2% occurrence of soft tissue infection. Unlike our study, sinusitis has been identified as a common concern in systematic reviews[24,31,40] and if left untreated for too long, it can contribute to ZI failures. Goiato et al.[31] emphasised the need of maintaining a clean oral environment since soft tissues can harbour bacteria such as Prevotella spp. and Porphyromonas gingivalis, which can compromise implant integrity. Only one study in our review[23] reported specific examples of flap and implant failures, as well as a recurrence of mucormycosis. Corresponding to this, a recent systematic review [25] found that the overall yearly rate of ZI failure is only 0.7%. Overall, even though ZIs can result in a variety of complications, most of them are mild, controllable, and uncommon, suggesting that ZIs are a dependable treatment option with a generally safe profile when carried out carefully and taking into account specific patient factors.

Strengths, limitations, and recommendations of the review

The PRISMA reporting requirements were adhered to in this systematic review in order to perform the review and analysis of the pertinent literature. But even with a thorough investigation, it's possible that some pertinent studies might get overlooked. However, no controlled trials, whether randomized or non-randomized, met our inclusion criteria. As a result, the majority of the research evaluated in this review were case reports or case series, which do not constitute high-quality data. Also, the majority of studies had a one-year follow-up period. Furthermore, the utilization of diverse surgical procedures for ZI implants may influence overall patient outcomes and complications. As such, care should be taken while interpreting the data. Furthermore, the majority of the included studies did not report psychological well-being. The success of ZI may be overestimated or underestimated as a result of these gaps in the literature. Therefore, it is necessary to conduct large-scale cohort studies or clinical trials with standardized surgical techniques in the future to assess the success rate and patient satisfaction of ZI implants.

Conclusion

Zygomatic implants seem to be a reliable, safe, and effective treatment option for enhancing the functional and psychological recovery of facial deformity caused by mucormycosis. Additionally, the complications are generally minimal and are manageable. Nonetheless, this conclusion is founded on a small number of studies, the majority of which are case reports/series. Hence, prospective large-scale cohort studies or clinical trials to examine the success rate and patient satisfaction with ZI implants in mucormycosis cases are recommended.

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