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Incidence of Mucormycosis in Post-Covid Patients

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Abstract

Background and objectives: The majority of mucormycosis infections are fatal. It is mainly contracted when people come in touch with fungal spores in the environment. Mucormycosis is mainly associated with immunocompromising diseases or conditions. This study aims to ascertain and compare the outcomes of various treatment approaches for cases of mucormycosis.

Methods: This cross-sectional research was conducted in the Ear, Nose, and Throat (ENT) Department of Rizgary Teaching Hospital located in Erbil, Iraq. Data were collected over a one-year period, from January 2022 to August 2023. Participants in this study were individuals who were previously infected with COVID-19 and now presented with confirmed mucormycosis, diagnosed through biopsy of suspected lesions. Patients received treatment with amphotericin B, administered at a daily dose of 1 milligram per kilogram, given over four to six hours. Surgical debridement was performed in patients who gave approval. Clinical characteristics, treatment modality and outcome of these patients were assessed.

Results: Twenty-six patients were recruited for this study. The mean age of patients was 53.2±14.3. There were more males (57.7%) than females (42.3%). Around 85% of the patients were diabetic. In our study population, the overall mortality rate stood at 23%. The majority of the of them (80%) were among those who received Amphotericin B only. There was a significant association between treatment strategy and mortality ($p<0.05$).

Conclusions: In this study; rhino-orbital-cerebral cavities were the most typically involved, and diabetes was the primary underlying illness. There was a significant association between treatment modality and mortality rate in this study.

Keywords: Amphotericin B, Diabetes Mellitus, Mucormycosis, Surgical debridement

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Introduction

Mucormycosis is a deadly fungal infection, caused by a class of molds known as mycormycetes. These fungi are found in a wide variety of environments. They are found in soil and in organic debris that has decomposed, such as compost piles, rotten wood, and leaves.[1] The main pathogenic species in this group are Rhizopus species. Mucor, Apophysomyces, Cunninghamella, Saksenea, Lichtheimia, and Rhizomuc are the other mucormycosis-causing genera of microorganisms.[2,3]The majority of mucormycosis infections are fatal.[3] It is primarily acquired through contact with fungal spores present in the environment. Infections such as those affecting the lungs or sinuses can result from inhaling these spores. Such instances of mucormycosis are more prevalent among individuals with chronic diseases or patients whose body's ability to combat pathogens and diseases has weakened due to medications (e.g., Steroids, chemotherapy).[4,5] Mucormycosis is mainly associated with immunocompromising diseases or conditions. Patients with diabetes mellitus, neutropenic cancer patients who are on broad-spectrum antibiotics, and patients receiving immunosuppressive medications, such as tumor necrosis factor (TNF)-alpha blockers (rheumatoid disease patients), and intravenous or oral steroids are considered high-risk groups. Furthermore, graft versus host disease (GVHD) and opportunistic CMV infections raise the risk for patients with hematologic malignancies. Another risk factor for mucormycosis is having previously taken voriconazole.[6] Mucormycosis can manifest in various forms such as: Rhinocerebral mucormycosis: Primarily affects the nasal sinuses and can extend into the brain. This type is common in individuals with uncontrolled diabetes and kidney transplant recipients.[7,8] Pulmonary mucormycosis: The most prevalent type among stem cell or organ transplant patients, and cancer patients.[7,8] Gastrointestinal mucormycosis: this type is common in young children, particularly premature infants (<1 month old) who have undergone surgery, taken antibiotics, or used medications that weaken their immune system.[9,10] Cutaneous mucormycosis: Occurs when the fungus enters through a skin break, such as burns, scrapes, cuts, or surgical wounds. This form is most frequent in individuals with intact immune systems.[10] Disseminated mucormycosis: When the infection travels through the bloodstream to impact other organs, it typically targets vital organs like the brain, as well as other organs such as the, heart, spleen and skin.[10] Patients commonly present with severe sinusitis, accompanied by brain abscess, complicating the condition further. Pulmonary, cutaneous, and gastrointestinal (GI) infections are also recognized. In patients suspected of mucormycosis, timely diagnosis is critical.[11] Positive culture and histopathological changes are necessary for the diagnosis of mucormycosis. However, there are times when culture is unavailable or the results are inconclusive; in these cases, histopathology is used to make the diagnosis. [12] Individuals suspected or diagnosed with mucormycosis require immediate medical attention and should be directed to facilities equipped to provide the highest level of care.[13]Correcting the underlying problem, initiating liposomal amphotericin B therapy as soon as possible, and surgical excision are all crucial. Patient survival requires necrotic tissue removal in conjunction with medical therapy. Surgical treatment for rhinocerebral illness comprises sinus drainage and may need orbital contents and brain resection. Repeated surgery, particularly for rhinocerebral mucormycosis, may be required.[14,15,16] In these studies we aimed to ascertain and compare the outcomes of diverse treatment modalities for cases of mucormycosis.

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Patients and methods

This study was prospective cross-sectional research. It was conducted in the Ear, Nose, and Throat (ENT) department of Rizgary Teaching Hospital located in Erbil, Iraq. Data were collected over a one-year period, from January 2022 to August 2023. A questionnaire was developed for data collection, covering demographic details, medical history, concurrent immunosuppressive medications, clinical symptoms, treatment approaches, and the ultimate patient outcomes. Participants in this study were individuals with who had previously been infected with COVID-19 and now presented with confirmed mucormycosis diagnosed through biopsy of suspected lesions, showcasing distinctive characteristics of broad, wide-angled, ribbon-like, and non-septate hyphae, even if positive cultures and fungal hyphae invasion of tissue were absent. The exclusion criteria were human immunodeficiency virus (HIV) infected patients. Aeoxycholate amphotericin B was used as a treatment modality. It was administered at a daily dosage of 1mg/kg, given over 4-6 hours subsequent to a test dose of 1 mg infused in 100 mL of normal saline. All patients were advised for surgical debridement and underwent operation after giving approval. Those who did not approve to undergo surgical debridement were treated with antifungal medication alone. Figure (1) shows examples of signs and symptoms in our patients. The research received ethical approval from the Kurdistan Higher Council of Medical Specialties' ethics committee, and verbal consent was obtained from each patient or their legal guardian before their inclusion in the study. Data analysis was carried out using the SPSS statistical software package (SPSS Statistics version 25). Demographic characteristics were assessed using descriptive statistics, and differences between groups were determined through the chi-square or Fisher's exact test, as applicable. A threshold of $p<0.05$ was established for statistical significance.

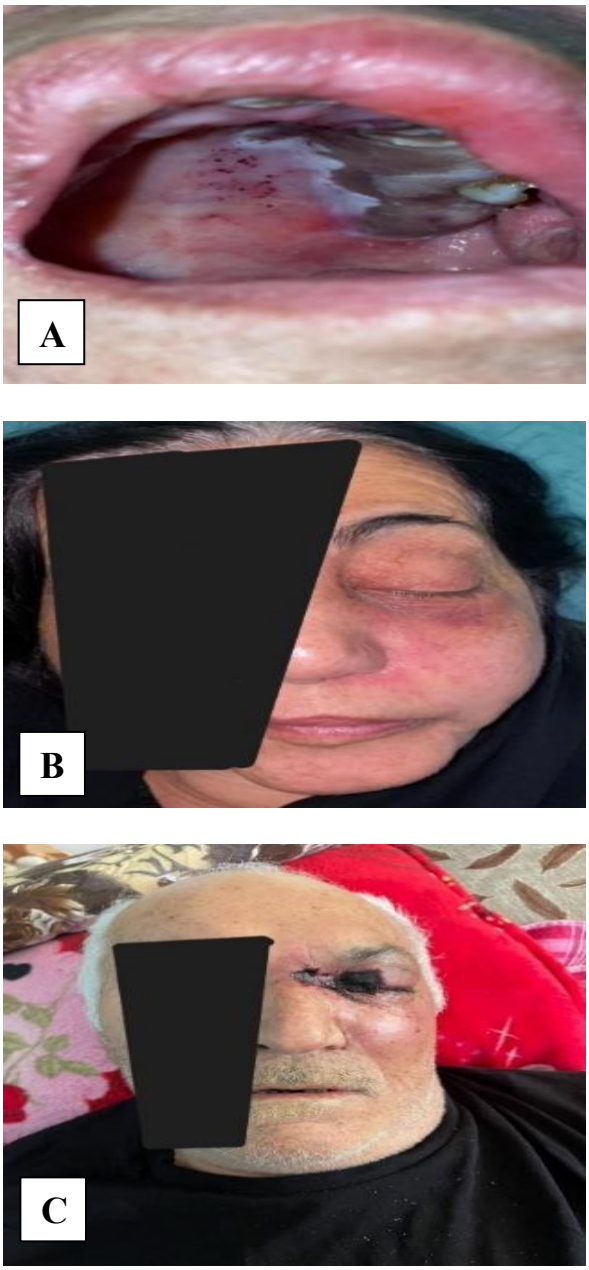

Figure (1): Examples of signs and symptoms of our case. A) intra-oral photo shows the ulcerative and necrotic lesion in the left hard palate; B) a photo that shoes left orbital swelling; B) a photo revealing erythema, black discoloration, and an ulcer on the nose and upper eyelid and of the left eye.

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Results

Twenty-six patients were recruited for this research. The mean age of patients was 53.2±14.3. The percentage of males (57.7%) was more than females (42.3%). The mean age for males was 54.13±13.4 and the mean age for females was 52±16.11. The majority of patients were from Urban areas (53.8%). Around 85% of the patients were diabetic and 23% had chronic kidney disease. Only a small portion of the patients (7.7%) were immunosuppressed or had history of organ transplant. Baseline characteristics of the patents are shown in Table (1).

Table (1): Baseline characteristics

Variables		
Mean age±SD (Median, [range])		53.2±14.3 (56.5[23-78])
Gender, n (%)	Male	15 (57.7%)
	Female	11 (42.3%)
Residency, n (%)	Rural	11 (46.2%)
	Urban	15 (57.7%)
Risk factors		
DM, n (%)		22 (84.6%)
CKD, n (%)		6 (23.1%)
Immunosuppressed, n (%)		2 (7.7%)
Organ transplant, n (%)		2 (7.7%)
Chemotherapy/steroid use, n (%)		1 (3.8%)
No risk factor		1(3.8%)
Extension as shown on MRI		
Orbital involvement on MRI		20 (76.9%)
Intracranial involvement on MRI		8 (30.8%)

Table (2) shows the prevalence of clinical presentations of the patients. Proptosis was found to be the most common clinical sign, identified in 61.5% of patients, followed by nasal obstruction found in 30.8%, facial pain and headache found in 15.4%, ophthalmoplegia in 11.5% of patients, and the least common presentation was nasal discharge and facial numbness which was recorded in only 7.7% of the cases.

Table (2): Clinical presentation

Symptoms	n (%)
Nasal discharge	2 (7.7%)
Nasal obstruction	8 (30.8%)
Facial pain	4 (15.4%)
Headache	4 (15.4%)
Facial numbness	2 (7.7%)
Ophthalmoplegia	3 (11.5%)
Proptosis	16 (61.5%)

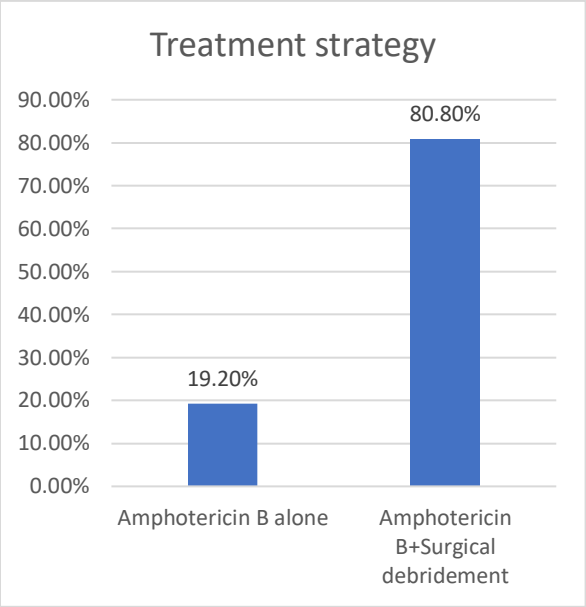

Figure (2): Treatment strategy

Figure (2) shows the prevalence of treatment modalities used in our study. The majority of our cases (80.8%) underwent surgical debridement and received amphotericin B. Only 19.2% of cases were treated with Amphotericin B only. Table (3) shows the prevalence of surgical procedures done. The most common surgical procedure was ethmoidal sinus surgical debridement (72%), followed by maxillary sinus surgical debridement (64%), sphenoidal sinus surgical debridement (44%), Maxillectomy (20%). Septectomy and frontal sinus surgical debridement was not performed in any of the patients.

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Table (3): Prevalence of surgical procedures performed on the study population

Surgical procedure	n (%) n= 25
Maxillary sinus surgical debridement	16 (64%)
Ethmoidal sinus surgical debridement	18 (72%)
Sphenoidal sinus surgical debridement	11 (44%)
Frontal sinus surgical debridement	0 (0%)
Septectomy	0 (0%)
Maxillectomy	5 (20%)

The mortality rate in the study population was 23%. The majority of them (80%) were among those who received Amphotericin B only. Table (4) shows the association of treatment modalities and the final outcome of the patient. Patients who were treated with antifungal Amphotericin B only, all passed away. Meanwhile, among patients who were treated with Amphotericin B and surgical debridement, only 1 passed away. It's worth mentioning that this association was statistically significant (p-value <0.05). Table (4) also shows the association between age and the extent of involvement with patient outcome. We found a statistically significant association between intracranial involvement and patient outcome (p-value <0.05). The majority of patients with intracranial involvement (75%) passed away. Figure (3).

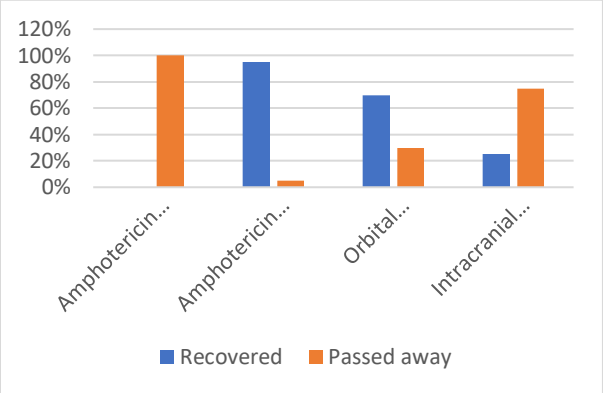

Figure (3): Association between patient outcome with treatment modalities and extent of involvement

Table (4): Association between Variables and outcome

Variables	Recovered	Passed away	p-value
Age, mean±SD	53.2 ± 14.4	53.3 ± 15.7	0.985
Orbital involvement, n (%)	14 (70%)	6 (30%)	0.280
Intracranial involvement, n (%)	2 (25%)	6 (75%)	0.000
Amphotericin B only, n (%)	0 (0%)	5 (100%)	0.000
Amphotericin B + Surgical debridement, n (%)	20 (95.2%)	1 (4.8%)	

Discussion

Our research has shown the clinical features, presentation, surgical procedures performed and outcome of mucormycosis in Erbil. We found a male predominance (57.7%) among our study population and this finding is in accordance with a study conducted by Abanamy et al.[17] in which they reported a higher prevalence of males (60.6%) compared to females. This is also similar to a global review of cases in which 929 patients were included and they reported that 65% of the cases were males. [18] Camara-Lemroy et al. also mentioned that the majority of their patients were males.[19]In this study, the mean age of our patients was 53.2 years. This is significantly higher than Abanamy et al. and Roden et al. and Camara_Lemroy et al.'s studies in which they reported the mean age of their patients as 42.23, 38.8 and 39.9 years, respectively. [17-19] Diabetes mellitus was the most common underlying condition in our study, this is in accordance with Abanamy et al., Roden et al., Camara-Lemroy et al., Chakrabarti et al.'s studies.[17- 20] Bhanuprasad et al. also reported that DM was the most common risk factor associated with mucormycosis even after COVID-19

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emergence.[21]Similar to the studies conducted worldwide including the studies in the middle east,[19,22,23] we found that the most common site of infection was rhino-orbital-cerebral mucormycosis. However, Abanamy et al. reported that the most common site of infection in their study population was cutaneous.[17] It's worth mentioning that, in our study there was a significant association between cerebral involvement and mortality. The majority of our cases with cerebral involvement passed away. This is comparable with Abanamy et al.'s findings in which the majority of their cases who passed away had cerebral involvement. In our study population, we found that the most common sign was proptosis, followed by nasal obstruction, facial pain and headache, respectively. Camara-Lemroy et al. reported that the most common symptoms and signs were fever, headache, nasal discharge.[19]Mucormycosis treatment continues to be challenging. universal guidelines currently propose the use of debridement and antifungal therapy in combination, using liposomal amphotericin B in high-dose as the first-line drug.[24] The majority of our cases were treated with both Amphotericin B and surgical debridement. The overall mortality rate in our study was 23%, this is much lower than Abanamy et al.'s finding in which their mortality rate was 50%.[17] In our study, there was a significant association between treatment modality and mortality, in which 80% of those who passed away were among those who had only received Amphotericin B without surgical debridement and 20% were among those who had received both amphotericin B and surgical debridement. This is in contrast to Abanamy et al. and Camara-Lemroy et al.'s studies in which they reported higher mortality rate among those who underwent surgical debridement along with receiving Amphotericin B.[17,19] This difference could be due to two factors, the first one is that in Camara-Lemroy et al's study, those who did not undergo surgical debridement had clinically milder forms of mucormycosis infection. The second factor is that in Abanamy et al.'s study, the majority of their cases had cutaneous involvement; and only patients who had rhino-orbital-cerebral underwent surgical debridement more commonly infection.

Conclusion

Mucormycosis is a potentially fatal infection that mostly affects people with weakened immunity and, in spite of intensive multimodal therapy, presents a considerable risk of death. To begin the right diagnostic workup and treatment, a strong index of suspicion is essential. In this study rhino-orbital-cerebral cavities were the most typically involved, and diabetes was the primary underlying illness. There was a significant association between treatment modality and mortality rate in this study. However, in order to come to such conclusions a higher number of patients should be included.

Conflict of interest: The authors declare no conflict of interest.

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