Original Article

Rhino-Orbital-Cerebral Mucormycosis During COVID-19 Pandemic Versus the Subsequent Period

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ABSTRACT

Objective: To compare the incidence of mucormycosis, its clinical features, and outcomes during the COVID-19 period versus the subsequent period.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted in Basra between May 2020 and the end of June 2025.

Methods: This retrospective study was undertaken in Basra from the onset of the COVID-19 outbreak until the end of June 2025. Rhino-orbito-cerebral mucormycosis (ROCM) cases were classified into two groups according to infection time (during COVID-19 vs. post-COVID). The total number of patients who were evaluated in this study was 20.

Results: The incidence of ROCM during the pandemic was approximately six-fold higher than that of the post-COVID period. The predominant predisposing factor was Diabetes mellitus. ROCM was more common in males and its clinical features were approximately similar in both groups. However, during the COVID-19 period, one patient died, four required ocular enucleations, and one developed a cerebrovascular accident (CVA). In the post-COVID period, only one patient experienced bilateral visual loss, but none required enucleation, and no deaths or CVA were reported.

Conclusion: The incidence of ROCM during COVID-19 was higher than that of the subsequent period. However, the clinical presentations were approximately similar in both periods.

Key Words: COVID-19, Rhino-orbito-cerebral mucormycosis, Basrah-Iraq

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INTRODUCTION

Mucormycosis is a serious fungal infection that can lead to increase morbidity and mortality.[1]

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It is predominantly caused by a variety of Mucorales species, such as Mucor, Rhizopus, Rhizomucor, and Lichtheimia.[2] The rhino-orbito-cerebral region was the most commonly involved region, with 90% of cases were infected with Rhizopus species.[3-5] Different other organs can be affected, including the lungs, skin, gastrointestinal system and kidneys.[6,7] The process of infection typically begins when the fungal spores inhaled from the environment and then colonize the respiratory mucosa of the nasal cavity and paranasal sinuses. Subsequently, hyphae developed, permitting the fungus to spread rapidly to adjacent tissues. The ability of these organisms to invade blood vessels enhance its spread and invasiveness.[8]

Several determinants contribute to the increased vulnerability to Mucormycosis. Before the COVID-19 pandemic, the most predominant predisposing factor was haematologic cancer, followed by diabetes mellitus (DM).[8-12] Other conditions that supress immunity, such as prolonged corticosteroid use, and chemotherapy and chronic renal impairment, significantly increase the susceptibility of infection. COVID-19 has recently arisen as a significant predisposing influence for mucormycosis, especially in developing countries. This risk increased in hypoxic patients who received

corticosteroid therapy and iron supplements which together facilitate *Mucorales* proliferation and invasion.[13] Basra confronted two serious waves of COVID-19, the first wave began at the end of May 2020 and the second in late January 2021.[14] Up to the present time, no articles have demonstrated the COVID-19 behaviour in Basra beyond these two waves. At the national level, however, Iraq encountered two additional waves: the third began in March and ended in July 2021, and the Omicron wave peaked in January 2022. However, these waves were associated with markedly lower severity and fewer hospital admissions.

This study examines the patterns of Mucormycosis and its associated outcomes during the COVID-19 pandemic and the subsequent period.

METHODS

This study is a retrospective study of patients who were infected with mucormycosis in Basra, southern Iraq. It covers cases that occurred during the COVID-19 outbreak, including all four waves (from May 2020 to February 2022), as well as the post-COVID period up to the late June 2025. All suspected cases of mucormycosis in Basra were referred to and admitted at Basra Teaching Hospital. Diagnosis of rhino-orbito-cerebral mucormycosis was confirmed depending on multiple clinical criteria. These include features of sinusitis and its complications, such as facial pain, nasal obstruction, nasal discharge, periorbital swelling, proptosis, and vision loss. Radiological evaluation was performed using computed tomography (CT) and/or magnetic resonance imaging (MRI) of the nose, sinuses, and brain to detect areas of bone destruction or infiltration of the orbit or cerebral region. In addition, histopathological assessment of biopsied tissue from affected regions was performed to confirm the diagnosis. All patients underwent radical debridement of necrotic tissue in a single operative session and received liposomal amphotericin type B, at a dose of 10mh/kg before and after the surgery. Antifungal therapy was continued postoperatively for 4-6 weeks, until complete clinical and radiologic improvement was achieved. In this study, we assessed 15 patients during the COVID-19 period and 5 patients between February 2022 and June 2025.

RESULTS

During the COVID-19 period (21 months), 15 cases of mucormycosis were recorded, compared with 5 cases during the post-COVID-19 period (41 months). The crude incidence rate was 0.71 cases per month during COVID-19 and 0.12 cases per month post-COVID, corresponding to an incidence rate ratio of approximately 6. Poisson regression analysis, using months as the offset, confirmed this significantly higher incidence during the COVID-19 period ($p < 0.001$) (see Table 1).

Of the five cases identified in the post-COVID period, four were diagnosed with mucormycosis in 2022; none had confirmed SARS-CoV-2 infection by PCR testing. The fifth case occurred in February 2023, after which no further cases were recorded.

Table No. 1: Incidence of mucormycosis during COVID-19 *vs.* post COVID period

Period	Observation time (months)	Cases (n)	Incidence rate (cases/ month)	Rate ratio (95% CI)
COVID -19	20	15	0.71	≈5.9
Post COVID -19	41	5	0.12	1.0 (Reference)

P-value<0.001, n: number, CI: Confidence interval

Mucormycosis was more common in males during both periods, with a total of 12 male cases (60%) compared to 8 female cases (40%). However, this difference was not statistically significant.

It can be observed that the prevalence of diabetes mellitus among patients with mucormycosis was very high during both COVID and non-COVID period, with no statistically significant difference between them (p value= 0.544). Table (2) shows that 93.3% of mucormycosis patients in COVID period had diabetes mellitus, compared to 100% of patients in the post COVID period.

Table No.2: Distribution of diabetes mellitus among patients with mucormycosis during COVID and non-COVID periods

Periods	No DM	DM	Total
COVID	1(6.7%)	14 (93.3%)	15
Non-COVID	0 (0%)	5 (100%)	5
Total	1 (5%)	19 (95%)	20

P value: 0.554, DM: Diabetes Mellitus

Regarding symptoms, there were no significant difference between symptoms during COVID-19 era and the period after that. The most noticeable symptoms were as following: facial pain happened in all patients, headache and nasal obstruction were complained by 16 patients, olfactory problems; including anosmia, hyposmia or cacosmia, perceived in 15 patients, facial disfigurement (facial swelling and or periorbital swelling) developed in 13 patients. Nasal discharge was not a common feature, only in 10 patients and only one patient complained of nasal bleeding (see table 3).

On examination, eschar was the most common finding in both the COVID and non-COVID periods. All five non-COVID patients presented with this feature, and

only one patient in the COVID group lacked eschar. Mucormycosis involved the turbinates and lateral nasal wall in 60% of patients (12 in total) across both groups. The nasal septum was the second most affected site, observed in 55% of all patients (60% in the COVID group and 40% in the non-COVID group). The pyriform fossa was not involved in any patient during either period (see Table 4).

The majority of severe complications of ROCM were observed during the COVID-19 outbreak. During this period, four patients underwent orbital exenteration. In addition, one patient developed a cerebrovascular accident, and one patient died. In the post-COVID period, a female patient presented with bilateral blindness, which did not necessitate orbital exenteration and no patient died of ROCM.

Table No. 3: Symptoms of mucormycosis during COVID-19 *vs* post COVID-19

	Facial pain	headache	Nasal obstruction	discharge	Olfactory problems	Epistaxis	Facial disfigurement
COVID	15	11	12	6	11	1	10
NON-COVID	5	5	4	4	4	0	3
TOTAL	20	16	16	10	15	1	13

Table No. 4: Signs of mucormycosis during COVID-19 *vs* post COVID-19

SIGNS (Site of involvement)	NASAL WALL AND TURBINATES	NASAL FLOOR	SEPTUM	Palate	ORBIT	PYRI-FORM	LOSS OF SENSITIVTY	ESCHAR
COVID	9 (60%)	2 (13.3%)	9 (60%)	1(6.7%)	5 (33.3%)	0	8 (53.3%)	14 (93.3)
NON-COVID	3 (60%)	1 (20%)	2 (40%)	0 (0%)	2 (40%)	0	1 (20%)	5 (100%)
TOTAL	12 (60%)	3 (15%)	11 (55%)	1 (5%)	7 (35%)	0	9 (45%)	19 (95%)

DISCUSSION

ROCM is a life-threatening fungal infection that can lead to serious complications and the death rate of this disease is relatively high.[1] DM and haematological disorders are the major predisposing factors for this condition.[8,10] Other conditions that can reduce immunity, such as prolong consumption of prednisolone, chemotherapy and chronic renal failure increase the susceptibility to develop this illness.[13] The link between mucormycosis and infection with COVID-19 was reported in several countries, such as India and Pakistan. However, the confirmed cases in Europe were very low.[15]

This study found that every patient who developed ROCM had diabetes, except one non diabetic patient who was infected with COVID 19 and received steroid for around two weeks. One of COVID patients in addition to diabetes mellitus he had thalassemia. All COVID patients and three non-COVID patients received steroid before developing mucormycosis. The lack of a statistically significant difference between groups likely reflects the high baseline prevalence of diabetes among patients with mucormycosis, rather than a differential effect of COVID-19 status. The risk of infection increases with diabetes mellitus, particularly in diabetic ketoacidosis because hyperglycaemia supresses neutrophil chemotaxis, leukocyte phagocytosis and local inflammatory response. In addition, a glucose-rich environment associated with diabetes, as well as the ketone reductase system of *Rhizopus*, provide optimal conditions for the fungal growth and invasion.

Andreescu et al reviewed case reports and series depending on Google scholar database from October 2021 to November 2022 and they concluded that Diabetes Mellitus plays a vital role in mucormycosis growth and this is in consistent with our findings.[15]

Noticeably, incidence of ROCM is nearly six times in COVID era compared to the post COVID period, 15 cases over 21 months as compared to 5 cases in 41 months.

The surge in mucormycosis cases during the COVID-19 pandemic is closely linked to disease-related hypoxia, prolonged corticosteroid therapy, and frequent iron replacement, all of which facilitate fungal growth and tissue invasion.[14]

Most of patients in both periods were males, 60% in total. Majority of reports were in agreement with this finding, for example, Pal et al found that 78% of patients were males.[16] Andreescu et al mentioned that most of reviewed patients were males.[15]

Our study showed that all patients experienced facial pain. sixteen patients reported headache and nasal obstruction, while olfactory disturbances, including anosmia, hyposmia, or cacosmia, were noted in 15 patients. Facial disfigurement (facial or periorbital swelling) occurred in 13 patients. Nasal discharge was less frequent, observed in only 10 patients, and epistaxis was documented in a single case. A COSMIC study in India reported that orbital and facial pain as the most common symptom. However, this was complained

by only 23% of patients. Facial and orbital oedema presented in 21%. Nasal discharge and nasal obstruction were observed in 10% and 9 % respectively.[17]

On clinical examination, eschar was the most common finding in both COVID-associated and non-COVID patients. All five non-COVID cases developed eschar, whereas it was absent in only one patient in the COVID group. COSMIC study showed that 48% of patients demonstrated eschar formation. The turbinates and lateral nasal wall were the most commonly involved structures, affected in 60% of the total cases (12 patients) in both groups. The nasal septum was the second most frequently involved site, observed in 55% of all patients (60% in the COVID group and 40% in the non-COVID group). The pyriform fossa was documented in either group.

This study reveals that 27% of COVID-19 patients required eye exenteration to survive the disease. However, from the five patients, only one patient developed bilateral blindness but did not require enucleation. Sen et al observed that 16% of COVID-19 patients with mucormycosis required eye exenteration. However, 63% of patients lost their vision.[17]

Malek et al reported a case with acute bilateral blindness developed in a young patient with COVID-19 and rhino-orbito-cerebral mucormycosis.[18]

This study also showed that one patient developed cerebrovascular accident (CVA) after being infected with COVID-19 and mucormycosis. This patient was previously complaint of Thalassemia which could be a predisposing factor to develop CVA. A prothrombotic state in patients with Thalassemia has been linked with increasing risk of CVA.[19]

The mortality rate of ROCM varies from 30-90% of cases with cerebral involvement.[20,21] For cases associated with SARS-COV-2, the estimated mortality was 14-31% .[17,22] Our study showed that only 7% of the patients died during the pandemic and no patient died in the post COVID period.

CONCLUSION

ROCM was approximately six times more common during the COVID-19 period compared to the subsequent post COVID phase, with diabetes mellitus recognised as the predominant predisposing factor. The clinical manifestations were largely similar in the two periods; however, patients without COVID-19 demonstrated better outcomes than those with coexisting infection.

Limitations of the study: Because the disease is rare, the sample size was relatively small. In addition, articles covering ROCM are very limited worldwide, therefore, it was difficult to compare our results with other studies.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Firas Baqir AL-Hameed, Firas T. Obeid
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