• Clinical Research •

Prognostic factors and clinical features of rhino-orbital-mucormycosis cases: an update for patient and visual survivals

Mustafa Aksoy, Altan Atakan Ozcan, Burak Ulas

Department of Ophthalmology, Cukurova University Faculty of Medicine, Saricam, Adana 01330, Türkiye

Correspondence to: Mustafa Aksoy. Cukurova University Faculty of Medicine, Saricam, Adana 01330, Türkiye. mustfaksy@gmail.com

Received: 2023-03-09 Accepted: 2024-02-02

Abstract

● **AIM:** To determine the frequency of patients' vision survival and prognostic factors and evaluate clinical features in rhino-orbital mucormycosis.

● **METHODS:** Forty-three eyes of 43 patients followed up with orbital mucormycosis infections were included in the study. Demographic characteristics of the patients, symptoms at admission, ophthalmologic and non-ophthalmologic examination findings, clinical findings during follow-up, medical and surgical procedures, and complications were recorded. Patient survival was determined by assessing the incidence of mortality, and vision survival was defined as achieving a final visual acuity of at least light perception.

● **RESULTS:** Twenty-seven (62.8%) patients were male, and 16 (37.2%) were female. When the underlying disease status of the patients was examined, it was observed that all patients had an underlying disease and diabetes constituted the majority (65.2%). Periorbital swelling (69.8%) and ophthalmoplegia (53.5%) were the most common symptoms and findings at the admission of patients with mucormycosis infection. The disease resulted in death in 22 (51.2%) patients. The presence of fever and shorter duration of antifungal therapy were associated with lower patient survival. Exenteration surgery was not found to be associated with the survival of the patients. Frozen eye, loss of pupillary light reflex, and development of central retinal artery occlusion were associated with lower vision survival.

● **CONCLUSION:** This study presents one of the most extensive patient series in the literature on rhino-orbital mucormycosis. Knowing the patients' symptoms at the time of admission and the clinical findings during the infection process will increase awareness about the disease.

● **KEYWORDS:** mucormycosis; rhino-orbital-mucormycosis; orbital apex syndrome; retinal arterial occlusion

DOI:10.18240/ijo.2024.05.17

Citation: Aksoy M, Ozcan AA, Ulas B. Prognostic factors and clinical features of rhino-orbital-mucormycosis cases: an update for patient and visual survivals. *Int J Ophthalmol* 2024;17(5):916-923

INTRODUCTION

Mucormycosis is an uncommon but highly aggressive fungal infection. It is caused by the filamentous fungi in the order Mucorales[1]. A distinguishing feature of mucormycosis infection is the presence of extensive angioinvasion with resultant vessel thrombosis and tissue necrosis. Mucormycosis is known to affect patients who are immunocompromised. Uncontrolled diabetes mellitus is the most common risk factor identified in patients with mucormycosis. Hematologic malignancies such as lymphomas and leukemias, long-term corticosteroid and immunosuppressive therapy, and chronic renal failure are other important predisposing factors. Rhino-orbital mucormycosis is characterized by the extension of the infection from the paranasal sinuses into the orbital wall[1-2]. The management of mucormycosis involves control of systemic conditions, prompt initiation of active antifungal agents, and surgical debridement of infected tissues. Despite antifungal agents, aggressive surgical debridement and hyperbaric oxygen therapy, mortality related to mucormycosis infections is relatively high[3]. Early diagnosis and aggressive management play pivotal roles in the management of this invasive infection. The most challenging decision of orbital mucormycosis management in the follow-up is to decide whether to perform an aggressive intervention, orbital exenteration.

This study aims to determine the frequency and influencing factors of patient and visual survival in patients with mucormycosis with orbital involvement and to evaluate the treatment schemes, clinical features, and treatment responses.

SUBJECTS AND METHODS

Ethical Approval The study was approved by the

Institutional Review Board of Cukurova University, and it adhered to the tenets of the Declaration of Helsinki (approval No.21.05.2021/111/105). The written informed consent was obtained.

The diagnosis of mucormycosis was confirmed through histopathologic examination in all patients in the study. In this retrospective study, 43 patients who were diagnosed as having mucormycosis with ophthalmologic manifestations at Cukurova University between August 2012 to December 2021 were analyzed.

All patients underwent a comprehensive ophthalmologic examination, including the status of visual acuity, anterior segment, fundus, pupillary light reflex, and eye movements. The patients were evaluated with a multidisciplinary approach by the ophthalmology, otorhinolaryngology, and infectious diseases clinics. The treatment protocol applied to all patients primarily included strong control of the underlying disease, intravenous liposomal amphotericin B treatment at the discretion of the Infectious Diseases Clinic, and endoscopic surgical debridement performed by the Otorhinolaryngology Clinic. As deemed necessary by the infectious diseases clinic, oral posaconazole was introduced to the treatment in instances of resistance. The decision to perform exenteration lacked a distinct indication. In light of the infection's cerebral dissemination and the disease's continued progression despite medical and surgical interventions, a collaborative evaluation involving the ophthalmology, otorhinolaryngology, and infectious diseases clinics was conducted to determine the need for exenteration, considering the patient's current visual acuity.

The admission times of patients, demographic characteristics, symptoms at admission, ophthalmologic and non-ophthalmologic examination findings, laboratory results, clinical findings during follow-up, radiologic imaging, duration of antifungal drugs used, surgical procedures, and complications were recorded. In patients, a temperature of 38°C and above is considered as the presence of a fever. A decrease in best corrected visual acuity of two lines or more was considered vision loss. Survival of patients was determined by assessing the incidence of mortality, and vision survival was defined as achieving a final visual acuity of at least light perception. In assessing the outcomes related to vision and patient survival, observations were documented for surviving patients after a minimum of one year of follow-up. Survival time was evaluated by recording the time from symptom onset to death in patients who died.

Statistical Analysis The SPSS 20.0 software was used for the statistical analysis of the data. Categorical measurements are summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum-maximum where appropriate). The categorical variables between the groups were analyzed using the Chi-square test. Comparisons between groups were performed using Student's *t*-test for normally distributed data, and the Mann-Whitney *U* test was used for data non-normally distributed. The Log-rank test was performed under Kaplan-Meier analysis to compare survival distributions between groups. Cox regression analysis was used to model the survival time, and the corresponding hazard ratios were obtained. A *P*-value of <0.05 was considered statistically significant.

RESULTS

Forty-three eyes of 43 patients were included in the study. There were no patients with bilateral involvement. The mean age of the patients was 47.6±20.1y. Twenty-seven (62.8%) patients were male, and 16 (37.2%) were female.

When the cases were evaluated seasonally, the patients were admitted with mucormycosis infection in the summer (34.6%) and autumn (30.2%) periods; only four patients presented in the spring period. More than half of the patients (53.4%) presented to the clinic between August-September-October.

When the underlying disease status of the patients was examined, it was observed that all patients had an underlying disease and diabetes constituted the majority (65.2%; Table 1). Ketoacidosis was also present in 10 patients with diabetes. In nine patients with no known comorbidities, diabetes was diagnosed during the initial assessments conducted upon admission. Diabetes was uncontrolled in all patients. Among the patients, 11 had previously been diagnosed as having coronavirus disease 2019 (COVID-19) and only one among them had a documented history of corticosteroid treatment specifically for managing this infection. All 11 patients whose disease may have been related to COVID-19 also had diabetes as an underlying disease.

When the outpatient clinic presentations of the patients were examined, 18 (42%) patients presented to the emergency department, 10 (23.2%) to infectious diseases, 10 (23.2%) to otorhinolaryngology, and five (11.6%) to ophthalmology clinics. Periorbital swelling (69.8%), ophthalmoplegia (53.5%), and decreased vision (46.5%) were the most common symptoms and findings at the admission of patients with mucormycosis infections (Table 2).

All patients underwent brain-orbital and maxillofacial computed tomography (CT) examinations. When the paranasal sinuses were evaluated using CT scans, the most common sinus involvement was observed as ethmoid (97.7%) and maxillary (95.3%). Pansinusitis was present in 11 (25.6%) patients.

When the laboratory findings at the time of admission were examined, the mean white blood cell level was 12.6±11.3 (range, 0.04-54.2) $10^3/\mu L$, and 11 (25.6%) patients had pancytopenia. The mean C-reactive protein (CRP) level was

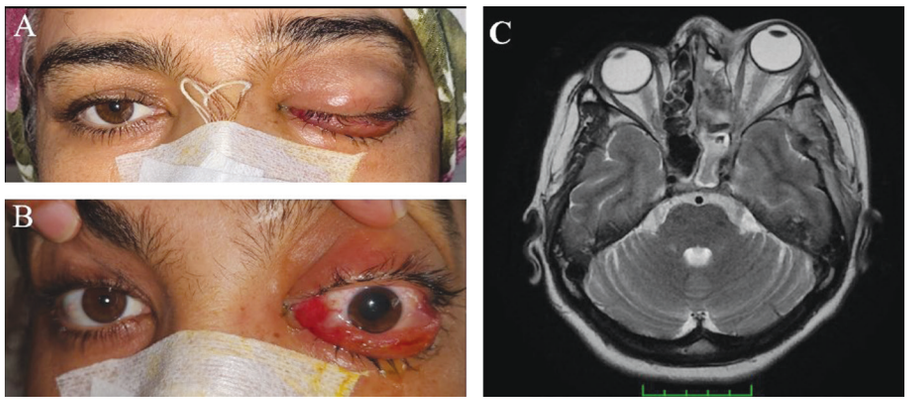

Figure 1 Clinical findings A female diabetic patient in her early 30s with mucormycosis with left eye involvement had periorbital edema, proptosis, chemosis, ptosis, and frozen eye (A and B). MRI shows left eye proptosis with involvement of the left orbital apex secondary to ethmoid sinusitis (C). MRI: Magnetic resonance imaging.

Table 1 Distribution of the patients according to the underlying disease *n* (%)

Underlying disease	Data
Diabetes mellitus	28 (65.2)
Hematological malignancy	11 (25.6)
Corticosteroid use	1 (2.3)
Organ transplantation	1 (2.3)
Chemotherapy	2 (4.6)
Total	43 (100)

Table 2 Symptoms of the patients at admission *n* (%)

Symptoms on admission to the clinic	Data
Periorbital swelling/pain	30 (69.8)
Ophthalmoplegia	23 (53.5)
Decreased vision	20 (46.5)
Ptosis	19 (44.2)
Proptosis	16 (37.2)
Facial swelling/pain	14 (32.6)
Toothache	9 (20.9)
Headache	8 (18.6)
Facial palsy	7 (16.3)
Numbness in the face	6 (14)
Hemiparesis/hemiplegia	3 (7)
Nasal pain/congestion	2 (4.7)
Earache	2 (4.7)
Epistaxis	2 (4.7)

115.9±131.9 (range, 0.2–443) mg/L. The majority (86%) of the patients had hypoalbuminemia at presentation.

When the clinical findings of the patients during mucormycosis infection were evaluated, the most common ophthalmologic findings were periorbital edema (88.4%), ophthalmoplegia (88.4%), vision loss (76.7%), and proptosis (76.7%; Figure 1). The most common non-ophthalmic finding was mucosal necrosis (67.4%). Loss of light reflex, frozen eye (total ophthalmoplegia), chemosis, ptosis, optic disc edema, facial nerve palsy, fever (body temperature >38°C), corneal edema, and trigeminal anesthesia were among the other clinical findings encountered (Table 3).

Table 3 The clinical findings of the patients during the infection process *n* (%)

Clinical findings	Data
Periorbital edema	38 (88.4)
Ophthalmoplegia	38 (88.4)
Vision loss	33 (76.7)
Proptosis	33 (76.7)
Mucosal necrosis	29 (67.4)
Frozen eye	28 (65.1)
Loss of light reflex	28 (65.1)
Chemosis	26 (60.5)
Ptosis	26 (60.5)
Optic disc edema	12 (27.9)
Facial nerve paralysis	11 (25.6)
Fever	8 (18.6)
Trigeminal anesthesia	7 (16.3)
Corneal edema	6 (14)

All patients included in the study had orbital involvement. Rhino-orbital involvement was observed in 20 (46.5%) and rhino-orbital-cerebral involvement in 23 (53.5%) patients. Orbital apex syndrome (OAS) was the most common complication (67.4%). Other common complications were cavernous sinus thrombosis (30.2%) and central retinal artery occlusion (25.5%).

All patients underwent surgical debridement with functional endoscopic sinus surgery (FESS) by the otorhinolaryngology clinic. In addition to surgical debridement with FESS and intravenous liposomal amphotericin B treatment, 9 (20.9%) patients underwent exenteration surgery.

The mean follow-up period was 5±6.7 (range, 0.3–33)mo. The disease resulted in death in 22 (51.2%) patients. In 9 (52.9%) of 17 patients who were alive and did not undergo exenteration, visual acuity was at least at the level of perception, and there was visual survival.

Table 4 Comparison of demographic data, clinical, laboratory and examination findings and treatment parameters in deceased and surviving patients *n* (%)

Parameters	Total	Deceased patients	Survived patients	*P*
Age, mean±SD (range)	47.6±20.1 (1–76)	44.3±22.9 (1–74)	51±16.4 (5–76)	0.543
Gender				0.907
Male	27/43 (62.8)	14/22 (63.6)	13/21 (61.9)	
Female	16/43 (37.2)	8/22 (36.4)	8/21 (38.1)	
Underlying disease				0.055
Diabetes mellitus	28/43 (65.1)	11/22 (50)	17/21 (81)	
Non-diabetes mellitus	15/43 (34.9)	11/22 (50)	4/21 (19)	
Frozen eye	28/43 (65.1)	14/22 (66.7)	14/21 (63.6)	>0.99
Central retinal artery occlusion	11/43 (25.5)	5/22 (22)	6/21 (28,5)	>0.99
Loss of light reflex	28/43 (65.1)	13/22 (59.1)	15/21 (71.4)	0.526
Initial best-corrected visual acuity				0.745
20/50≤BCVA<20/20	8/43 (18.6)	5/22 (22.7)	3/21 (14.2)	
20/200≤BCVA<20/50	5/43 (11.6)	2/22 (0.09)	3/21 (14.2)	
LP≤BCVA<20/200	18/43 (41.8)	10/22 (45.4)	8/21 (38)	
No light perception	12/43 (27.9)	5/22 (22.7)	7/21 (33.3)	
Final visual acuity				
20/50≤BCVA<20/20	2/43 (0.04)	-	2/21 (0.09)	-
20/200≤BCVA<20/50	2/43 (0.04)	-	2/21 (0.09)	
LP≤BCVA<20/200	5/43 (11.6)	-	5/21 (23.8)	
No light perception	8/43 (18,6)	-	8/21 (38)	
Exenterated or died	26/43 (60.4)	-	4/21 (19)	
Facial nerve paralysis	11/43 (25.6)	6/22 (27.3)	5/21 (23.8)	>0.99
Mucosal necrosis	29/43 (67.4)	14/22 (63.6)	15/21 (71.4)	0.747
Bilateral sinus involvement	17/43 (39.5)	11/22 (50)	6/21 (28.6)	0.215
Cerebral involvement	23/43 (53.5)	13/22 (59.1)	10/21 (47.6)	0.547
Fever	8/43 (18.6)	7/22 (31.8)	1/21 (4.8)	0.046
White blood cell count (10^3/μL), mean±SD (range)	12.6±11.3 (0–54)	12.5±14.2 (0–54)	12.7±7.6 (0–29)	0.958
HbA1c (%), mean±SD (range)	11.1±1.9 (7.2–14)	11.1±1.8 (9–14)	11±2 (7.2–13.8)	0.942
Pancytopenia	11/43 (25.6)	8/22 (36.4)	3/21 (14.3)	0.162
CRP (mg/L), mean±SD (range)	115.9±131.9 (0–443)	144.3±150.3 (0–443)	87.5±106.7 (2.4–335)	0.166
Antifungal treatment duration (d), mean±SD (range)	78.8±79.1 (5–300)	48.9±57.3 (5–240)	123.7±87.6 (45–300)	<0.001
FESS count, mean±SD (range)	1.4±0.5 (1–3)	1.3±0.4 (1–2)	1.5±0.5 (1–3)	0.222
Exenteration	9/43 (20.9)	5/22 (22.7)	4/21 (0.19)	>0.99

BCVA: Best-corrected visual acuity; LP: Light perception; CRP: C-reactive protein; FESS: Functional endoscopic surgery.

The relationship between demographic data; underlying diseases; clinical, laboratory and examination findings; treatment parameters, and survival was evaluated (Table 4). The prevalence of diabetes as an underlying condition was notably greater among surviving patients (81%) in comparison with deceased patients (50%) but it was not statistically significant. A significant difference was observed between the patients who died and those who survived in terms of fever and duration of antifungal treatment. The presence of fever and shorter duration of antifungal therapy were associated with lower patient survival. A meaningful relationship between exenteration and survival was not identified.

The time between symptom onset and death (survival time) was compared according to demographic data, underlying diseases, clinical and laboratory findings, and treatment parameters. In univariate analyses, a significant difference was observed between survival time and vision loss (+)/visual loss (-). The existence of visual loss in a patient was associated with earlier death (Figure 2).

Visual survival was analyzed using the same variables in 17 patients who survived and did not undergo exenteration surgery. A significant difference was observed between the presence of frozen eye, loss of light reflex, central retinal artery occlusion, and visual survival. Frozen eye, loss of light reflex, and development of central retinal artery occlusion were associated with lower visual survival (Table 5).

Table 5 Parameters associated with visual survival in univariate analysis *n* (%)

Parameters	Total	Total vision loss (+)	Total vision loss (-)	*P*
Loss of light reflex	11/17 (64.7)	8/8 (100)	3/9 (33.3)	0.009
Frozen eye	10/17 (58.8)	8/8 (100)	2/9 (22.2)	0.002
Central retinal artery occlusion	4/17 (23.5)	4/8 (50)	0	0.029

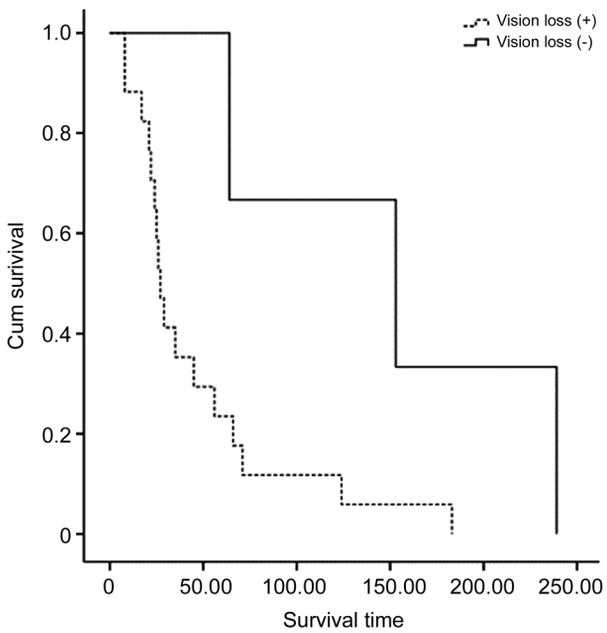

Figure 2 Kaplan-Meier survival graph associated with visual loss and patient survival time (d).

DISCUSSION

Rhino-orbital-cerebral mucormycosis is the most crucial clinical picture of mucormycosis and has a high mortality rate. The disease begins with clinical manifestations in the form of sinusitis or periorbital cellulitis. As a result of the spread of the infection to the orbit, loss of function in the extraocular muscles and proptosis develop[4-5]. Progressive vision loss and blindness can be seen due to direct invasion of the infection into the retinal artery, optic nerve involvement, or cavernous sinus thrombosis. Due to the rarity of mucormycosis and the lack of comprehensive studies on this subject, approaches regarding the prognosis and treatment methods are limited. The excess of male patients in the patient population in our study is similar to the literature[6-7]. The higher prevalence of the infection in men has not been clearly explained. The potential protective role of estrogen in fungal infections is discussed in previous studies[8], and the mean age in our study was close to the literature at 47y[9].

Seasonal changes can be observed in the frequency of mucormycosis infection throughout the year. In the study of Talmi *et al*[10] on 19 patients with mucormycosis, 16 (84%) were hospitalized between August and November. In the study by Shpitzer *et al*[11] with 36 patients, the incidence of the disease increased in the autumn and summer, and 58% of the patients presented between August and October. In our study, in line with the literature, patients mainly presented in summer and autumn, and 53.4% of all pateints were infected in August-October. Although the reason for the seasonal variation in the incidence of the disease cannot be clearly explained, it is thought that temperature and humidity may contribute. A large case series was investigated in our study, and because our study covers the south of Turkey, it has a hot and humid climate, and the region also has a central referral hospital.

Mucormycosis usually occurs in individuals with a suppressed immune system. The most common predisposing factor is diabetes, but hematologic diseases, corticosteroid use, organ and bone marrow transplantation, and antineoplastic agents used in chemotherapy are also included in the etiology[12]. In the Meta-analysis of Jeong *et al*[9], in which 851 cases of mucormycosis were evaluated, diabetes was found to be the underlying disease in 40% of the patients. In Yohai *et al*'s[13] series of 145 cases, diabetes (60%) was the most common predisposing factor. In line with the literature, our study's most common predisposing factor was diabetes (65.2%), followed by hematologic malignancies (25.6%).

COVID-19 has become a global public health crisis associated with mortality and morbidity worldwide as of 2020. The advent of the COVID-19 pandemic has led to predictions suggesting that coronavirus infection could potentially serve as a risk factor for mucormycosis. Research indicates that individuals, particularly patients with poorly managed blood sugar levels and those who have received corticosteroid treatment, are susceptible to developing mucormycosis infection following a COVID-19 infection[14-16]. In a multicenter study conducted by Dave *et al*[15], the authors documented a cohort of 58 patients who developed mucormycosis following COVID-19 infection. Further, Srivastava *et al*[16] evaluated the clinical findings and postoperative results of 89 mucormycosis cases associated with COVID-19. In our study, consistent with existing literature, it was observed that mucormycosis cases increased after the COVID-19 pandemic and 11 patients had a history of COVID-19. Only one of these patients had a history of corticosteroid use, and all had uncontrolled diabetes.

In mucormycosis, patients most frequently present with symptoms of fever, headache, periorbital swelling, decreased vision, and ophthalmoplegia. In the study of Yohai *et al*[13] with 149 patients, fever (44%), periorbital and facial swelling (34%), decreased vision (30%), and ophthalmoplegia (29%) were the most common presenting symptoms. In the Meta-analysis

study of Vaughan *et al*[17], patients most frequently presented with periorbital swelling (27%), fever (26%), decreased vision (20%), ptosis (18%), and ophthalmoplegia (15%). In our study, the most common symptoms at presentation were periorbital swelling and pain (69.8%), ophthalmoplegia (53.5%), decreased vision (46.5%), and ptosis (44.2%), which was consistent with the literature.

In our study, all patients had orbital involvement, rhino-orbital involvement was observed in 46% of the patients, and rhino-orbital-cerebral involvement was observed in 54%. In the study of Abdollahi *et al*[18], the maxillary sinuses (67%) were most frequently involved, followed by the ethmoid sinuses (53%). In the study by Gupta *et al*[19], ethmoid sinus involvement was present in all cases, and followed by maxillary sinus (55%) involvement. In our study, the most frequently involved paranasal sinuses were the ethmoid (97.7%) and maxillary (95.3%) sinuses.

During the course of the infection, ophthalmic and non-ophthalmic findings may occur at any stage of the disease. Clinical findings vary according to the extent of the disease and organ involvement. In the study of Yohai *et al*[13], ophthalmoplegia (67%), decreased vision (65%), proptosis (64%), and periorbital edema (43%) were the most common ophthalmic findings. Mucosal necrosis (80%) was the most common non-ophthalmic finding[13]. In our study, similar to the literature, periorbital edema (88.4%), ophthalmoplegia (88.4%), decreased vision (76.7%), ptosis (76.7%) were the most common ophthalmic findings, and mucosal necrosis (67.4%) and facial nerve palsy (25.6%) were the most common non-ophthalmic findings.

OAS is a loss of function, including ophthalmoplegia, ptosis, and vision loss due to infection, vasculitis, ischemia, or mechanical compression. In the study performed by Jiang *et al*[20], 11 patients with mucormycosis presenting with OAS were defined. In our study, OAS was present in 67% of the cases and was the most common complication. Other common complications were cavernous sinus thrombosis (30.2%) caused by the spread of the infection to the brain cavity and central retinal artery occlusion (25.5%) caused by invasion of retinal vessels.

The mortality rate of mucormycosis infection is very high, and it is reported in the literature as between 15%–85%[6,13]. In the study of Yohai *et al*[13], the survival rate was reported as 60%. In the study of Peterson *et al*[21], orbital involvement, cerebral involvement, ketoacidosis, and nondiabetic underlying disease were associated with lower patient survival. In the study of Kashkouli *et al*[7] with a series of 63 patients, the survival rate was determined as 57%. The mean time from symptom onset to death is 50.4d; frozen eye, elevated body temperature, and short duration of antifungal therapy were associated with lower patient survival in this study[7]. Our study's survival rate was 48.8%, and the mean survival time was 59.4d. In our study, fever and shorter duration of antifungal therapy were associated with lower patient survival. Although it did not reach statistical significance, the rate of diabetes as an underlying condition was notably higher in surviving patients than in deceased patients. The development of vision loss during the follow-up period was also associated with a shorter survival time. The association with a shorter duration of antifungal therapy may be due to the shorter lifespan of patients with more severe diseases. High diabetes rates as an underlying condition in surviving patients are thought to be due to the ability to reverse the underlying hyperglycemia.

Antifungal therapy combined with surgical debridements, particularly amphotericin B and posaconazole, plays a key role in the successful treatment of mucormycosis. If accessible, the preference is for the liposomal formulation of amphotericin B to minimize the risk of infusion-related reactions and nephrotoxicity. In our study, the liposomal form of liposomal amphotericin B was used in all cases. In three patients resistant to treatment, the decision from the infectious diseases clinic was to incorporate posaconazole into the treatment regimen, but only one of these patients survived. Seventeen cases of mucormycosis with orbital involvement were managed successfully without exenteration. The belief is that early detection and prompt initiation of treatment prove effective in such instances.

The decision of exenteration is one of the most challenging stages in orbital mucormycosis cases. Exenteration surgery has long-term ophthalmic, cosmetic, and psychological effects on patients. A balance exists between protecting the eye and preventing the intracranial spread and eventual death. In the study of Hargrove *et al*[22], which compiled 113 articles and was conducted with 292 cases, exenteration indications were evaluated, and a standard algorithm could not be established. Shah *et al*[23], in their study with 15 cases, developed a scoring system for exenteration decisions based on clinical signs and symptoms, ophthalmoscopic examination, and imaging methods. Ulas *et al*[24] showed in their studies that this scoring system could help ophthalmologists in the preliminary evaluation and the decision of exenteration. Exenteration was not associated with survival in the study of Kashkouli *et al*[7], and no significant correlation was found between exenteration and survival in our study.

In addition to being a fatal disease, mucormycosis can result in loss of vision in the affected eye, even if recovery is achieved. Unlike most studies in the literature, visual survival was also evaluated in our study. In 52.9% of 17 patients who did not undergo exenteration surgery and recovered, visual acuity was at least at the level of perception, and visual survival was

available. In a similar study by Kashkouli *et al*[7], only younger age was associated with lower vision survival. In our study, loss of light reflex, frozen eye, and presence of central retinal artery occlusion were associated with lower vision survival but age was not associated with vision survival. Patients without light reflex loss, frozen eye, and central retinal artery occlusion are important candidates for vision survival. These indicators must be taken into account in the treatment process.

In the diagnosis, treatment, and follow-up of mucormycosis infection, which is of vital importance, ophthalmologists, otorhinolaryngologists, and infectious diseases physicians should act together in a multidisciplinary approach. Daily follow-up of these patients, who have a high risk of morbidity and mortality, is of great importance.

In conclusion, mucormycosis is a multisystemic problem that needs to be addressed *via* multidisciplinary collaboration. Various therapeutic modalities used to treat the disease have been described. With this study, we aimed to increase ophthalmologists' awareness of mucormycosis clinical findings and prognostic factors. However, due to the aggressive nature of the disease, none of these treatments has proven to be completely effective in eradicating the disease, and the mortality rate is still high. Detection of prognostic factors in mucormycosis infection is critical in evaluating the course of the disease and planning treatment. Nevertheless, augmentation of the host's immune response is key to successful therapy and may offer a more favorable outcome whenever possible.

ACKNOWLEDGEMENTS

Conflicts of Interest: Aksoy M, None; **Ozcan AA,** None; **Ulas B,** None.

REFERENCES

1 Kancharu FK, Viswam V, Sreeram P, Warrier A, Karunakaran A. Mucormycosis of neck a rare presentation. *Indian J Otolaryngol Head Neck Surg* 2022;74(2):2681-2685.

2 Werthman-Ehrenreich A. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. *Am J Emerg Med* 2021;42:264.e5-264264.e8.

3 Madhavan Y, Sai KV, Shanmugam DK, Manimaran A, Guruviah K, Mohanta YK, Venugopal DC, Mohanta TK, Sharma N, Muthupandian S. Current treatment options for COVID-19 associated mucormycosis: present status and future perspectives. *J Clin Med* 2022;11(13):3620.

4 Murthy R, Bagchi A, Gote YS. Role of medial orbital wall decompression in COVID-19-associated rhino-orbital mucormycosis management. *Indian J Ophthalmol* 2021;69(12):3795-3796.

5 Swain SK, Lenka S, Das SR. Rhino-orbital mucormycosis—a dreaded clinical entity. *Int J Curr Res Rev* 2020;12(24):197-203.

6 Roden MM, Zaoutis TE, Buchanan WL, *et al*. Epidemiology and outcome of zygomycosis: a review of 929 reported cases. *Clin Infect Dis* 2005;41(5):634-653.

7 Kashkouli MB, Abdolalizadeh P, Oghazian M, Hadi Y, Karimi N, Ghazizadeh M. Outcomes and factors affecting them in patients with rhino-orbito-cerebral mucormycosis. *Br J Ophthalmol* 2019;103(10):1460-1465.

8 Restrepo A, Salazar ME, Cano LE, Stover EP, Feldman D, Stevens DA. Estrogens inhibit mycelium-to-yeast transformation in the fungus Paracoccidioides brasiliensis: implications for resistance of females to paracoccidioidomycosis. *Infect Immun* 1984;46(2):346-353.

9 Jeong W, Keighley C, Wolfe R, Lee WL, Slavin MA, Kong DCM, Chen SC. The epidemiology and clinical manifestations of mucormycosis: a systematic review and meta-analysis of case reports. *Clin Microbiol Infect* 2019;25(1):26-34.

10 Talmi YP, Goldschmied-Reouven A, Bakon M, *et al*. Rhino-orbital and rhino-orbito-cerebral mucormycosis. *Otolaryngol Head Neck Surg* 2002;127(1):22-31.

11 Shpitzer T, Keller N, Wolf M, *et al*. Seasonal variations in rhino-cerebral Mucor infection. *Ann Otol Rhinol Laryngol* 2005;114(9):695-698.

12 Mohanty A, Gupta P, Varshney S, Kabi A, Angral S. Breaking the mold: a brief review on the diagnostic and treatment approaches of mucormycosis. *Int J Otorhinolaryngol Head Neck Surg* 2021;7(7):1207.

13 Yohai RA, Bullock JD, Aziz AA, Markert RJ. Survival factors in rhino-orbital-cerebral mucormycosis. *Surv Ophthalmol* 1994;39(1):3-22.

14 Sundaram N, Bhende T, Yashwant R, Jadhav S, Jain A. Mucormycosis in COVID-19 patients. *Indian J Ophthalmol* 2021;69(12):3728-3733.

15 Dave TV, Nair AG, Hegde R, Vithalani N, Desai S, Adulkar N, Kamal S, Mittal R, Bradoo RA. Clinical presentations, management and outcomes of rhino-orbital-cerebral mucormycosis (ROCM) following COVID-19: a multi-centric study. *Ophthalmic Plast Reconstr Surg* 2021;37(5):488-495.

16 Srivastava SR, Ganguly P, Barman D, *et al*. Clinical outcome of orbital apex syndrome in COVID associated mucormycosis patients in a tertiary care hospital. *Int J Ophthalmol* 2022;15(4):527-532.

17 Vaughan C, Bartolo A, Vallabh N, Leong SC. A meta-analysis of survival factors in rhino-orbital-cerebral mucormycosis-has anything changed in the past 20 years? *Clin Otolaryngol* 2018;43(6):1454-1464.

18 Abdollahi A, Shokohi T, Amirrajab N, *et al*. Clinical features, diagnosis, and outcomes of rhino-orbito-cerebral mucormycosis- a retrospective analysis. *Curr Med Mycol* 2016;2(4):15-23.

19 Gupta S, Goyal R, Kaore NM. Rhino-orbital-cerebral mucormycosis: battle with the deadly enemy. *Indian J Otolaryngol Head Neck Surg* 2020;72(1):104-111.

20 Jiang N, Zhao GQ, Yang SS, Lin J, Hu LT, Che CY, Wang Q, Xu Q. A retrospective analysis of eleven cases of invasive rhino-orbito-cerebral mucormycosis presented with orbital apex syndrome initially. *BMC Ophthalmol* 2016;16:10.

21 Peterson KL, Wang M, Canalis RF, Abemayor E. Rhinocerebral mucormycosis: evolution of the disease and treatment options. *Laryngoscope* 1997;107(7):855-862.

22 Hargrove RN, Wesley RE, Klippenstein KA, Fleming JC, Haik BG. Indications for orbital exenteration in mucormycosis. *Ophthalmic Plast Reconstr Surg* 2006;22(4):286-291.

23 Shah K, Dave V, Bradoo R, Shinde C, Prathibha M. Orbital exenteration in rhino-orbito-cerebral mucormycosis: a prospective analytical study with scoring system. *Indian J Otolaryngol Head Neck Surg* 2019;71(2):259-265.

24 Ulas B, Kursun E, Turunc T, Demıroglu YZ, Pelıt A. Scoring system evaluation for orbital exenteration in patients with rhino-orbito-cerebral mucormycosis. *J Fr Ophtalmol* 2022;45(1):47-52.