

Clinical Profile, Risk Factors and Visual Outcome of Orbital Mucormycosis in COVID-19 Patients in a Tertiary Care Hospital

V. Ramalakshmi, M. Rita Hepsi Rani, T. Vedhavalli

Abstract: Rhino orbital mucormycosis (ROCM) which is a life threatening disease has emerged as a serious problem in COVID-19 patients during the second wave. This study was conducted to analyse the various risk factors, ocular manifestations, management and the visual outcome of orbital mucormycosis in COVID-19 positive patients. This is a retrospective, record based, single centered, cross sectional study conducted in a tertiary care hospital between may2021 to October 2021. Of these 138 mucormycosis patients 89 had invasive ROCM stage 3 and 4. Among these patients 93% are diabetic, 79% were on steroids, 26% were on oxygen therapy during COVID, 13% had increased serum ferritin levels. 64% patients were actively managed with intravenous injection amphotericin B, 8% of patients received retro bulbar injection amphotericin B, FESS was done in 72% patients, exenteration was done in 2% patients. A multidisciplinary approach of management was done by a team of ophthalmologist, ENT surgeon, physician, neurologist and microbiologist, in reducing the mortality and morbidity.

Keywords: Rhino Orbital Mucormycosis, ocular manifestations, risk factors, multidisciplinary approach

1. Introduction

Rhino orbital mucormycosis has emerged as a serious problem in COVID-19 positive patients during the second wave. During this pandemic period there was an alarming rise in the number of mucormycosis cases. It is caused by fungi of class zygomycetes, including the genera *Absidia*, *Mucor*, *Rhizomucor* and *Rhizopus* [3]

2. Materials and Methods

This study undertaken is a retrospective record based study conducted in the Department of Ophthalmology, during the period of April 2021 to October 2021. Ethical committee approval obtained and proper informed consent obtained in the patients enrolled.

Inclusion Criteria

All patients tested positive for COVID-19 RTPCR or with CT chest findings suggestive of COVID-19.

All patients presenting with symptoms suggestive of mucormycosis and positive for either KOH (clinical cases) or culture positive (laboratory confirmed cases).

Exclusion Criteria

KOH and culture negative for mucormycosis.

3. Methodology

All patients suspected as mucormycosis were subjected to ophthalmological examination. A detailed history regarding the onset, progression and duration of symptoms such as swelling of eyelids, pain, protrusion of eyeball, drooping of eyelids, restriction of movement of eyeball, visual impairment, double vision, headache, symptoms of sinusitis-facial swelling, pain, sinus tenderness, epistaxis, history of trauma, previous orbit or sinus surgery, tooth extraction with dental pain

Mucormycosis patients were subjected to the following examinations-Best corrected visual acuity, colour vision, visual fields by confrontation, extraocular movements, ptosis measurement, proptosis measurement, tonometry, anterior segment examination, corneal sensation, supra and infraorbital sensation, posterior segment examination by indirect ophthalmoscope. Complete neurological profiling done and significant cases underwent expert neurological consultation.

Mucormycosis is best treated by a multi-specialty team of physician, orbital surgeon, ENT surgeon neurologist and microbiologist.

Patients with rhino-orbito-cerebral mucormycosis were received in a separate zero delay ward. Baseline investigations done for all patients. CT orbit and PNS is taken for all patients. Treatment of COVID infection and metabolic control was done by physician.

DNE is done, specimens collected were send for culture and histopathological examination.

Empirical antibiotics is started for all patients. Intravenous injection amphotericin B is started in KOH positive patients at the dose of 1 to 1.5 mg/kg body weight per day [8].

Based on CT PNS findings if sinusitis is present FESS is done with extensive and repeated debridement of the sinuses, orbit and other infected areas. The aim is to remove all unhealthy tissue. ROCM stage 3A patients if KOH positive started on injection amphotericin B and observed. For Stage 3B –stage 4 patients with sinus involvement FESS with orbital wall decompression and sinus wash was done. Specimens were sent for histopathological examination. Patients were reviewed daily and repeat radiological investigation done. If the condition is not improving retrobulbar injection amphotericin was given. Retrobulbar inj. amphotericin B was given in 11 patients. Orbital exenteration was done in 3 cases.

Volume 11 Issue 1, January 2022

www.ijsr.net

Licensed Under Creative Commons Attribution CC BY

4. Results

Among 138 mucormycosis patients 83 were male and 55 were female (chart 2).119 patients were of age more than 40 years, 19 patients were of age less than 40 years (chart 1).128 patients were diabetic and 10 were non diabetic.44 patients had right eye involvement, 32 had left eye involvement and 9 had both eyes involvement (chart 3).

The most common primary symptoms were facial/orbital pain in 69 patients, facial or orbital edema in 46 patients, defective vision in 40 patients and nasal blockage in 12 patients (chart 4). Other symptoms were headache, diplopia, drooping of eyelid, protrusion of eye, deviation of angle of mouth and inability to close the eyelids^[2].

ROCM patients presented with the following signs facial edema in 46 patients, ptosis in 44 patients, proptosis in 44 patients, decreased vision in 44 patients, EOM restriction in 37 patients, facial palsy in 9 patients, nasal eschar in 8 patients^[2] (chart 5).

Among the 138 patients, 30 patients presented with preseptal cellulitis, 44 presented with orbital cellulitis, 20 presented with orbital apex syndrome, 4 presented with panophthalmitis, 3 presented with cavernous sinus thrombosis, 2 presented with superior orbital fissure syndrome, 1 presented each with orbital ischaemic syndrome, papilledema, optic neuritis and central retinal artery occlusion (chart 7).

Among the 138 patients, 20 patients had optic nerve involvement, 46 patients had Oculomotor nerve involvement both isolated and combined, 38 patients had trochlear nerve involvement, 44 patients had abducent nerve involvement both combined and isolated, 9 patients had facial nerve involvement, 2 patients had trigeminal nerve involvement, and 38 patients had total external ophthalmoplegia (chart 8).

About 128 patients were diabetic, 109 patients were on steroid therapy during COVID infection, 36 patients were on oxygen therapy and 18 patients had increased serum ferritin level (chart 8).

10 patients expired and 43 patients had no ocular manifestations.3 patients had cutaneous mucormycosis and 1 patient had pulmonary mucormycosis.

Among 138 patients 20 patients had no perception of light, 3 patients had only perception of light, 14 patients had vision less than 20/200, 23 patients had VA between 20/40 and 20/200, 79 patients had vision better than 20/40 (chart 9).89 patients received intravenous amphotericin B injection and 11 patients received retrobulbar injection amphotericin B. FESS was done in 59 patients, exenteration was done in 3 patients.

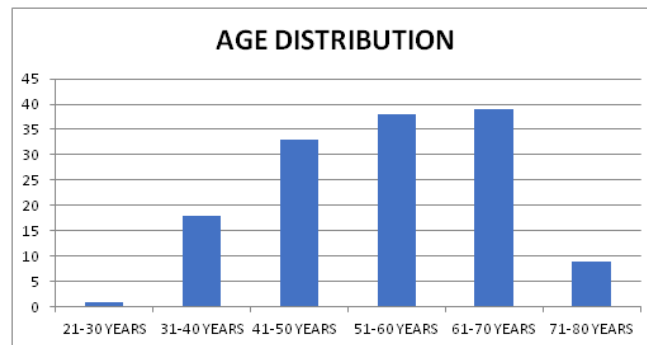


Chart 1: Showing Age Distribution of Mucormycosis Patients

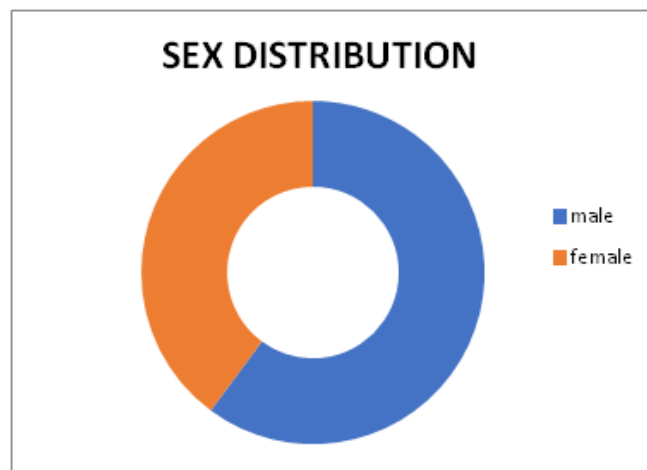


Chart 2: Showing Sex Distribution of Mucormycosis Patients

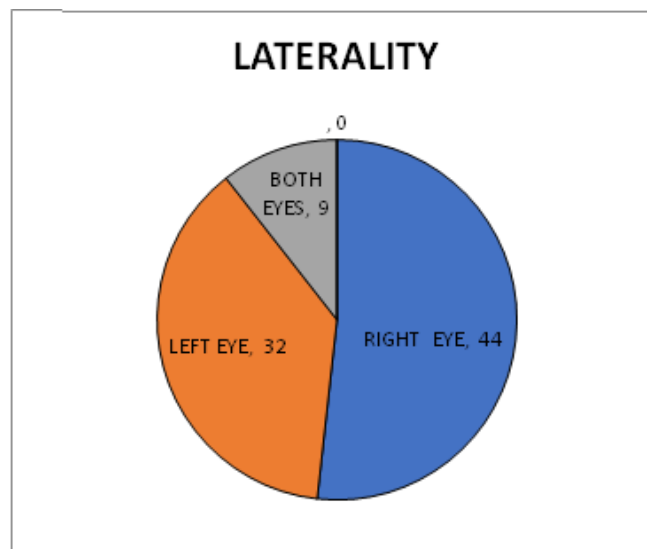


Chart 3: Showing Eye Involvement in Mucormycosis Patients

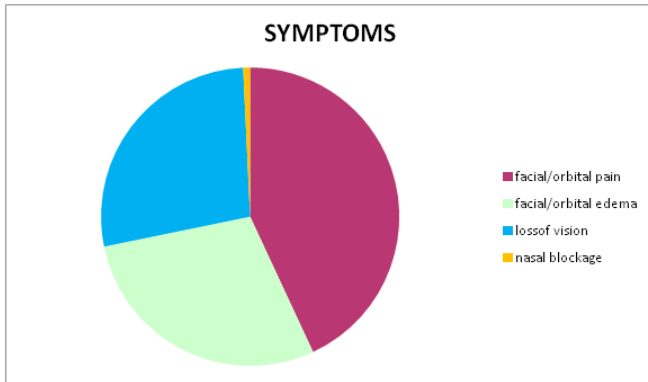


Chart 4: Showing the Symptoms of Mucormycosis

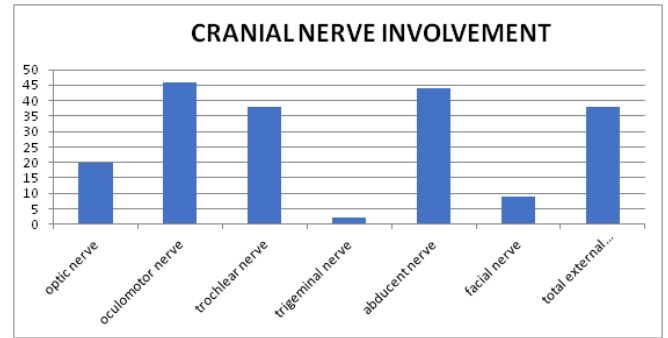


Chart 7: Showing Cranial Nerve Involvement in Mucormycosis Patients

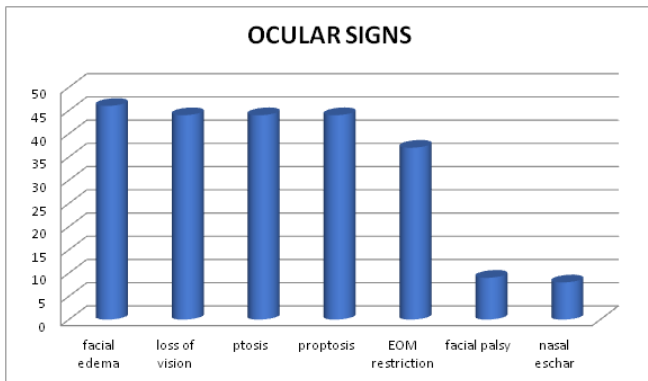


Chart 5: Showing the Signs of Mucormycosis

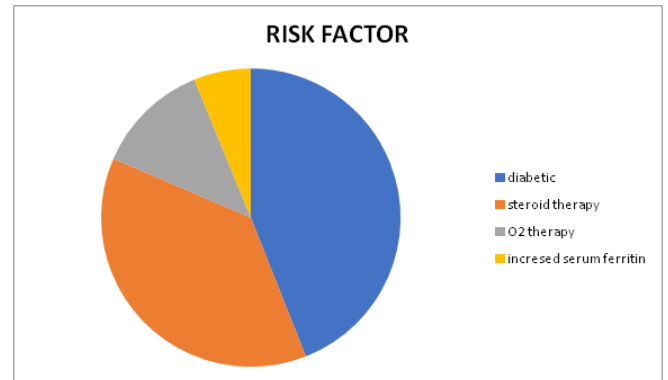


Chart 8: Showing the Various Risk Factors in Mucormycosis Patients

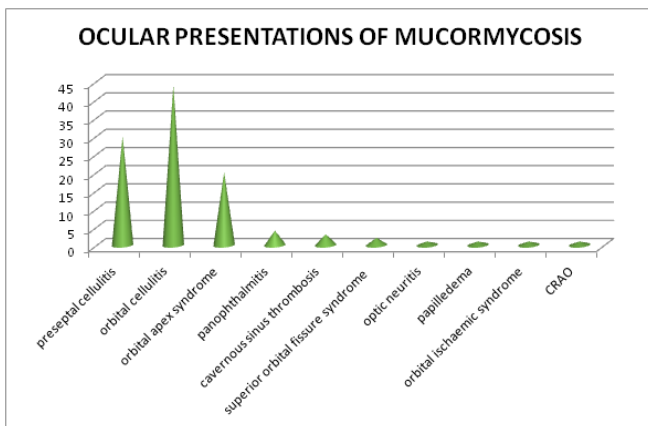


Chart 6: Showing Various Ocular Presentations of Mucormycosis

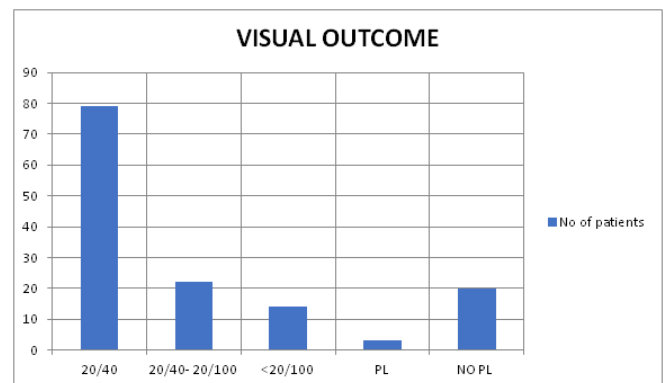


Chart 9: Showing the Visual Outcome in Mucormycosis Patients





Clinical pictures of Rhino Orbital Mucormycosis patients in our hospital

5. Discussion

ROCM is a fulminant disease caused by organisms of the family Mucoraceae. It is a life-threatening systemic fungal infection caused by members of the class Zygomycetes which is ubiquitous in nature^[4].

The mean age of presentation in our study is 54.62 years. Males were commonly affected than females. Unilateral presentation is more common than bilateral presentation. Most commonly seen in patients of age more than 40 years.

This disease most commonly occurs in immune compromised and diabetic patients. The disease originates in nasal and paranasal sinuses, spreads to orbit, cavernous sinus and ultimately results in death.

The common risk factors are increased prevalence of COVID-19 positive patients, uncontrolled diabetes especially in diabetic ketoacidosis, long term steroid therapy, patient on mechanical ventilation, long standing oxygen therapy, immunocompromised patient, and iron overload^[2].

Patients were profiled into categories as:

- Preseptal cellulitis
- Orbital cellulitis
- Panophthalmitis.
- Cavernous sinus thrombosis
- Multiple cranial palsy
- Central retinal artery occlusion
- Orbital apex syndrome
- Superior orbital fissure syndrome
- Cutaneous mucormycosis
- Antibiotoma

According to Honaveret al ROCM has been classified into 4 stages^[2]

Stage 1 Involvement of nasal mucosa

1a: Limited to middle turbinate

1b: Involvement of inferior turbinate or ostium of the nasolacrimal duct.

1c: Involvement of the nasal septum

1d: bilateral nasal mucosal involvement

Stage 2: Involvement of paranasal sinuses

2a: one sinus

2b: Two ipsilateral sinuses

2c: >2 ipsilateral sinuses and/or palate/oral cavity.

2d: Bilateral paranasal sinus involvement or involvement of the zygoma or mandible

Stage 3: Involvement of the orbit

3a: Nasolacrimal duct, medial orbit, vision unaffected

3b: Diffuse orbital involvement (>1 quadrant or >structures) vision unaffected

3c: Central retinal artery or ophthalmic artery occlusion or superior ophthalmic thrombosis, involvement of the superior Orbitalfissure, inferior orbital fissure, orbital apex, loss of vision.

3d: bilateral orbital involvement

Stage 4: Involvement of the CNS

4a: Focal or partial cavernous sinus involvement and/or involvement of the cribriform plate

4b: Diffuse cavernous sinus involvement and /or cavernous sinus thrombosis

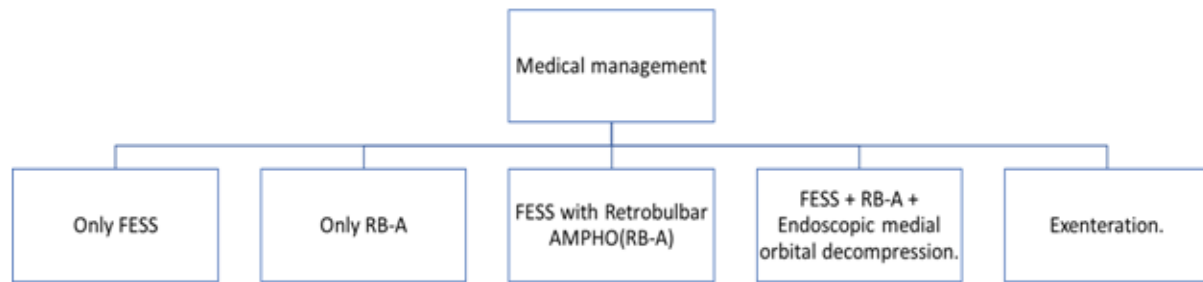
4c: Involvement beyond the cavernous sinus, involvement of the skull base, internal carotid artery occlusion, brain infarction

4d: Multifocal or diffuse CNS disease.

In our hospital, based on ROCM staging treatment protocol was planned.

All patients were done diagnostic nasal endoscopy and nasal mucosa biopsy sampling for microbiological

diagnostics. Based on clinical and radio imaging findings, with zero delay, Inj. L-AMPHO-B was started. For patients with raised RFT, Inj. Posoconazole was instituted. All suspected mucormycosis patients were started on empirical antibiotics.



Surgical treatment:

Only FESS was done in stage 2 and 3a patients. Only retrobulbar injection amphotericin B was given in stage 3 and 4 patients whose general condition doesn't fit for anesthetic fitness. FESS with retrobulbar injection amphotericin B+endoscopic medial orbital wall decompression was done in patients with stage 3b and above.

All patients are subjected to ophthalmic examination daily. Repeat DNE is done in all patients before discharge to ensure the sinus is free of infective debris. inj. amphotericin wash is given. Tablet posaconazole 300mg OD was given for 1month after discharge. Periodical review of mucormycosis patients were done in post COVID OPD to look for sequele.

During follow up exposure keratitis was seen in 5 orbital cellulitis patients and tarsoraphy was done for those patients. Exenteration which is the surgical treatment of mucormycosis was done only in 3 patients (2.1%) in our hospital. This is less when compared to the study of Honavar S G et al (17%) and Seiff et al (14%). Thus reducing the mortality and morbidity.

This was achieved by the team of doctors by zero delay in diagnosis and treatment, repeated sinus debridement with amphotericin wash, retrobulbar injection amphotericin B and regular follow up of patients.

6. Conclusion

ROCM an opportunistic fulminant disease seen most commonly in patients with the following predisposing factors such as diabetes mellitus, steroid supplementation, oxygen therapy and increased serum ferritin level. Early diagnosis and treatment with timely intervention is most important in the management of ROCM. There was improvement in visual outcome. A multidisciplinary approach of management was done by a team of ophthalmologist, ENT surgeon, physician, neurologist and microbiologist, in reducing the mortality and morbidity. Follow up of patients after discharge aids in the management of post COVID sequele.

Financial support and sponsorship:

Nil.

Conflicts of interest:

There are no conflicts of interest.

References

- [1] Rootman J, editor. Inflammatory diseases. In: Diseases of the Orbit. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2003.
- [2] Santosh G Honavar. Code Mucor: Guidelines for the Diagnosis, Staging and Management of Rhino-Orbito-Cerebral Mucormycosis in the Setting of COVID-19; IJO Volume 69 (6).
- [3] Salil Mehta, Abha Pandey – Rhino-Orbital Mucormycosis Associated With COVID-19; DOI: 10.7759/cureus.10726.
- [4] Nurettin Bayram, CemalOzsaygili, HafizeSav, YucelTekin, MedineGundogan, EminePangal, AyseCicek, Ibrahim Ozcan. Susceptibility of severe COVID-19 patients to rhino orbital mucormycosis fungal infection in different clinical manifestations; Japanese Journal of Ophthalmology (2021) 65: 515–525.
- [5] SD Mathebula. Rhino-orbital mucormycosis, a case report; S AfrOptom 2006; 65 (2) 78 – 81.
- [6] A. M. Sugar Mucormycosis. Clin Infect Dis, 14 (1992), pp. S126-S129
- [7] George Petrikos, Anna Skiada, Olivier Lortholary, Emmanuel Roilides, Thomas J. Walsh, and Dimitrios P. Kontoyiannis. Epidemiology and Clinical Manifestations of Mucormycosis; CID 2012: 54 (Suppl 1).
- [8] SP Dhir, VP Munjal, Amod Gupta, IS Jain. Rhino-orbito-cerebral, mucormycosis; Indian J Ophthalmol 1983; 31: 425-427.
- [9] M. V. S. Prakash, P. Ashok Kumar, T. G. Umamaheswari, V. Harivanzan. The Clinical Pattern of Orbital Mucormycosis in a Tertiary Eye Care Hospital; TNOA J
- [10] Sen, M., Honavar, S. G., Bansal, R., Sengupta, S., Rao, R., Kim, U., Sharma, M., Sachdev, M., Grover, A. K., Surve, A., Budharapu, A., Ramadhin, A. K., Tripathi, A. K., Gupta, A., Bhargava, A., Sahu, A., Khairnar, A., Kochar, A., Madhavani, A., Shrivastava, A. K., ... members of the Collaborative

- OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC) Study Group (2021). Epidemiology, clinical profile, management, and outcome of COVID-19 associated rhino-orbital-cerebral mucormycosis in 2826 patients in India – Collaborative OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. Indian journal of ophthalmology, 69 (7), 1670–1692.
- [11] Karadeniz Ugurlu S, Selim S, Kopar A, Songu M. Rhino-orbital Mucormycosis: Clinical Findings and Treatment Outcomes of Four Cases. Turk J Ophthalmol. 2015; 45 (4): 169-174. Doi: 10.4274/tjo.82474.
- [12] Ferry AP, Abedi S. Diagnosis and management of rhino-orbitocerebral mucormycosis (Phycomycosis). A report of 16 personally observed cases. Ophthalmology. 1993; 90: 1096–1104.
- [13] Yohai RA, Bullock JD, Aziz AA, Markert RJ. Survival factors in rhino-orbital-cerebral mucormycosis. Surv Ophthalmol. 1994; 39: 3–22. 13. Seiff SR, Choo PH, Carter SR. Role of local amphotericin B therapy for sino-orbital fungal infections. Ophthal Plast Reconstr Surg. 1999; 15: 28–31.
- [14] Mucormycosis in COVID-19: A systematic review of cases reported worldwide and in India July–August 2021, Page undefined Awadhesh Kumar Singh, Ritu Singh, Shashank R. Joshi Anoop Misra
- [15] K. L. Peterson, M. Wang, F. R. Canalis, E. Abemayor Rhinocerebral mucormycosis: evolution of the disease and treatment options Laryngoscope, 107 (1997), pp.855-862
- [16] H. Prakash, A. K. Ghosh, S. M. Rudramurthy, et al. A prospective multicenter study on mucormycosis in India: epidemiology, diagnosis, and treatment Med Mycol, 57 (2019), pp.395-402
- [17] A. Patel, H. Kaur, I. Xess, et al. A multicentre observational study on the epidemiology, risk factors, management and outcomes of mucormycosis in India Clin Microbiol Infect, 26 (7) (2020) 944. e9-944. e15
- [18] K. Bala, J. Chander, U. Handa, et al. A prospective study of mucormycosis in north India: experience from a tertiary care hospital Med Mycol, 53 (3) (2015 Apr), pp.248-257