

Original Research Article

Clinical profile of recent progressive illnesses in patients with mucormycosis: a comprehensive analysis

Shrikant Sharma, Mukul Singhal*, Sudhir Bhandari

Department of Medicine, SMS Medical College, Jaipur, Rajasthan, India

Received: 12 February 2022

Revised: 04 March 2022

Accepted: 11 March 2022

*Correspondence:

Dr. Mukul Singhal,

E-mail: mukul_1994@yahoo.in

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: The COVID-19 pandemic, in its omnipresence, descended an unprecedented blow on the reeling facilities nationwide, which at its stabilising junction posed another threat – mucormycosis. Potentially immunodeficient cases, diabetes and excessive rampancy of steroids propagated this neo-epidemic, currently challenging the fretting mortality rate. Aim of the study was to analyse the clinical profile elaborating the recent illnesses and progression in patients admitted with mucormycosis in a dedicated ‘mucor-care’ centre.

Methods: Total 195 admitted patients were evaluated based on their COVID protocol management and oxygen therapy administered with special emphasis on hygiene maintenance in view of mask support, oral care and hospitalisation course with duration and medications provided. Type and duration of glucocorticoids, injectable or oral, dispensed to the patients were duly logged and analysed.

Results: Half cases (50%) were found COVID reverse transcriptase-polymerase chain reaction (RT-PCR) positive with 69% patients suffering from moderate ailment and above. Patients averaged 25-30 days at onset of post-COVID mucormycosis symptomatology with 78% (172) cases having h/o hospitalisation. 90% patients required oxygen therapy in variable magnitudes with meagre 38% receiving ‘remdesivir’ complete course dosages. Despite being prudent, 58% did not maintain adequate sanitation while 72% denied having oxygen humidified. Steroids were pivotal with 84% affirmative prevalence; dexamethasone being commonest, averaging 15 days of therapy, which supplementing immune-compromised modalities, promulgated this epidemic.

Conclusions: The deadly trinity of diabetes, rampancy of steroids in a background of COVID-19 caused havoc in recent times. Only astute usage of resources and prudent education can curb this menace in a better way.

Keywords: Mucormycosis, Steroids, Oxygen, COVID-19, Remdesivir, Hospitalisation

INTRODUCTION

The pandemic of COVID-19 descended to every possible damage onto the grieving healthcare infrastructure of the nation and beyond, which on its reeling end has now propagated a dark nightmare. In recent times, as the second wave of COVID gained momentum, influx of cases of ‘COVID-induced black fungus’ has taken the world by storm. An angio-invasive disease characterized by tissue infarction and necrosis, ‘mucormycosis’ is an invasive

calamity caused by mold fungi belonging to genus *Mucor*, *Rhizopus*, *Rhizomucor* and *Absidia*, cross reacting in immune-compromised hosts.¹ As per Indian Council of Medical Research (ICMR) census, 24872 cases were reported as of 28 December 2021 with Gujarat leading the cascade with 8276 cases.² The first episode in Rajasthan was a 18 month old post COVID baby in Bikaner, diagnosed with the brutal ailment on 29 April 2021 post which the state has encountered an epidemic which stands at 4202 cases till date.³

This “coronavirus-associated mucor” (CAM) involvement presents in multiple anatomic localizations as of rhino-orbital-cerebral (ROCM), pulmonary, gastrointestinal, cutaneous, renal, and disseminated mucormycosis, with the first being the commonest entity in India.^{4,5} Patients with diabetes mellitus, hematological malignancies on chemotherapy, hematopoietic stem cells/organ transplant recipients, ones with iron overload or severely neutropenic, on antiretrovirals or any invasive procedures are at increased risk of contraction.⁵ Patients with retroviral disease, in adjunct or without TB are the worst affected.

Uncontrolled diabetes being the front player, mucor spores pathologically invades the vascular endothelium in the pulmonary vicinity, already compromised by the deadly coronavirus, which accounts for 54% all-cause mortality rate, as per Centre for Disease Control and Prevention (CDC), with this rate depending on the underlying medical condition, fungus type, and infected body location as it disseminated to organs mostly the eye, brain, heart, and spleen via the bloodstream.⁶ Clinically, it encompassed intense orbital pain, blackish discoloration of nasal bridge and eyes, severe headache, visual loss and significant prodrome in 55-60% cases.⁷ About 22% post COVID patients also c/o unilateral facial swelling with sinusitis along-with typical dyspnea and loss of sensations.⁸

Non contagious by nature, it was observed maximally in COVID-recovered patients who were exposed to self-medication, excessive steroidal intake, unrefined industrial oxygen inhalation in careless setups, wrong adhesive bandages, unclean wooden tongue depressors and hospital linens with unsterile negative pressure spaces and water leaks.⁹ Infection was widespread in patients on long term glucocorticoids or high dose prescriptions, for extensive pulmonary disease, including intravenous (IV) dexamethasone or IV MPS, used rampantly in ‘COVID-protocol’ management.^{10,11}

This neo-epidemic traversed everyone susceptible thus presenting with variable clinical profiles, defining high index of suspicion, early diagnosis and proper care required to conquer this mayhem, as documented in this study. This comprehensive analysis thereby aims to establish the variety of genre of symptomatology and clinical vignettes encountered in daily patient dealing that showed Mucor profiles in their follow up, thus opening up the realm of better understanding and approach towards its management.

METHODS

The study is a hospital based descriptive research conducted in Sawai Mansingh Hospital (SMS), Jaipur, India post the ravaging second wave of the “corona pandemic” from 30 April to 05 December 2021. The entire tertiary care multispecialty hospital, comprising of various medico-surgical and super-specialty branches was converted into a dedicated corona-care institution with

separate wing allotted for the newly-declared epidemic “mucormycosis”, in its bustling premises. This thriving wing was metamorphosed overnight as a single “mucor-care centre”, where all related branches operated as a single unit with health teams from every strata of the medical diversity.

Major departments Inc. medicine, ENT, ophthalmology with parental support from super-specialty departments’ viz. endocrinology and neurology, were integrated and all available wards were earmarked, thoroughly fumigated and intensified, as per ICMR guidelines, to tackle the epidemic.¹² All intensive care units (ICUs) and operation theaters in the premise were duly cleansed and carefully designated for different categories based on clinical status, which were then duly included in this study.

Patient selection

A total of 195 patients showing up at mucor OPD were filtered as per symptomatology and suspects, selected as per clinical diagnostic parameters on admission to various observation wards for further testing of dual sino-nasal swab or palatal scraping samples to be evaluated by potassium hydroxide (KOH) methods. These swabs were then examined microscopically or fungal spores or progressive growth and sent duly for culture and histopathological studies. These patients were subjected to radiological examination with NCCT/MRI studies of intracranial structures, paranasal sinuses orbits and facial anatomy to confirm the diagnosis.

Once selected to be included in this description, these patients were gauged on variable parameters defining their recent illnesses and their onset, whether or not related with COVID-19 ailments. Patients suffering from diagnosed active respiratory infections e.g. TB, and lung metastasis along with cases on active anti-fungal therapy were duly excluded from the scenario.

Routine laboratory tests including HbA1c, arterial blood gases, blood and urine ketones, electrolytes, renal and hepatic function tests, chest X-ray and ECG with importantly ‘COVID’ RT-PCR were sent and comprehensively compared with their due course of illness recently.

Since majorly patients belonged to the post-COVID genre, having suffered severe fibrosis and pulmonary compromise secondary to the disease, their thorough detailed history regarding the onset of COVID symptoms, the protocol management taken and hospitalization tenure was inquired and duly compiled. HRCT scans and corresponding severity scoring held major value apart from clinical severity documented giving special emphasis on triage protocols and aggressive therapy, if given.

Evidently, antiviral broad-spectrum medications viz. remdesivir and favipiravir were integrated as part of common anti-COVID protocol, supplemented by use of

monoclonal antibodies viz. tocilizumab in ICU setups. The receipt of their coercive therapy with duration of course was included and studied.

Incessant use of steroids especially glucocorticoids was seen in extensive genre of healthcare facilities, much aggravated both in dosage and duration. Patients gave testament on the type and tenure of steroids received during their illness, and follow up of oral steroids taken.

Oral hygiene proved immensely important in preventing breeding grounds of fungal spores in COVID-induced immune-compromise, thereby mandating analysis of the same.

Oxygen therapy played a major decisive role in the pandemic scenario, however rampant malpractices with mislabeled oxygen proved disastrous as evident in popular media. Special prominence was given to identify and categorize the patients those received significant oxygen therapy, elaborating the type of masks used and upgraded, requirements regarding invasive ventilation if any, or BIPAP support if provided. Details regarding authentic medical oxygen therapy used, proper sanitation, cleaning and usage of humidified water to eliminate microbial propagation, in case patients were previously admitted to private unlogged setups, if available were also underlined.

Particulars were collected regarding the variable clinical presentations of aforementioned 195 patients, their triage, illnesses and outcome for exploration.

RESULTS

The study involved a total of consecutive 195 cases admitted to SMS in its dedicated ‘mucor’ centre earmarked separately for epidemic mitigation as aforementioned. These patients were channelized and enquired as per their clinical characteristics, their COVID status, need for critical care and were traced as per history from recent illnesses leading to mucormycosis (CAM).

Table 1 exclaims the exhaustive details about the recent illness profile of the designated patients selected for this study. Majority of the ill victims of ‘the black calamity’ belonged to middle and old age group >40 years of age, out of which 50% were found COVID positive on subjected RT-PCR examination. In post COVID scenario, 53% of cases had suffered from Mild to moderate coronavirus disease in their recent past, with another 29% having a severe fate. In gross attrition, Ct severity scoring of 18% cases was found unknown.

As we evaluated the disease onset, majorly 93 patients (43%) had took >15 days with another 34% cases traversing more than a month for mucor symptomatic onset. A rare 3% cases had severe progression with redness and inflammation peaking in under 10 days’ time. Maximum people (59%) had been hospitalized beforehand in multiple government and private facilities for COVID pathology, including 28% cases with moderate symptoms like cough, dyspnea and episodic fever with intermittent oxygen requirements.

Table 1: Data depicting the clinical profile of patients.

Variables	No.	Percentage (%)
Demographics (population)		
Total	195	
Male	133	
Female	62	
Recent profile		
Age group		
Less than 20	4	2
20-30	11	6
30-40	30	15
More than 40	150	77
RTPCR		
Positive	98	50
Negative	88	45
Unknown	9	5
HRCT chest (score)		
Less than 8	25	13
8 to 15	78	40
More than 15	57	29
Unknown	35	18
Interval between onset of COVID and mucor symptoms (days)		
Less than 7	10	5
8 to 15	26	13
15 to 30	93	48

Continued.

Variables	No.	Percentage (%)
More than 30	66	34
Maximum severity of COVID (symptomatic)		
Nil	6	3
Mild	17	9
Moderate w/o IPD	56	29
Moderate with IPD	55	28
Severe with IPD	61	31
Oxygen support		
No		
Room Air	28	14
Yes		
Simple mask	116	59
High flow	33	17
NIV/invasive	28	14
Duration of hospitalisation (days)		
Nil	85	44
Less than 7	71	36
7 to 15	22	11
More than 15	17	9
Treatment profile		
Remdesivir		
Yes	74	38
No	121	62
Tocilizumab		
Yes	17	9
No	178	91
Oxygen mask profile (hygiene)		
Education received		
Yes	127	65
No	68	35
Proper sanitization		
Yes	82	42
No	113	58
Humidifier water		
Yes	54	28
No	141	72
Oral hygiene		
Education received		
Yes	125	64
No	70	36
Hygiene maintained		
Yes	92	47
No	103	53

About 61 patients had high-grade fever, breathlessness, fatigability and debilitating clinical status mandating round the clock heavy –load oxygen therapy, which on due treatment had recovered over time. The average duration of hospitalization was around 9-10 days with maximal staying for 15 days or less, in wards and ICU setups according to necessity. Every patient admitted to IPD services received optimum antibiotic and anticoagulant management owing to the disease specifications, out of which, wonder-drug ‘remdesivir’ was administered to

38% of total cases and patients suffering from cytokine storm with elevated IL-6 levels were concomitantly given monoclonal ‘tocilizumab’ drug as part of intensive therapy whom comprised 9% of the cases.

Medical oxygen was administered, documented on recall basis, with proper education regarding the usage, prevention of wastage and correct ways of consumption on personal guidance basis to 65% of total patients, out of which 42% maintained prudent sanitation in its working

and 28% managed to change humidifier water on a daily basis in order to ward away impurities that have led to successive ailments.

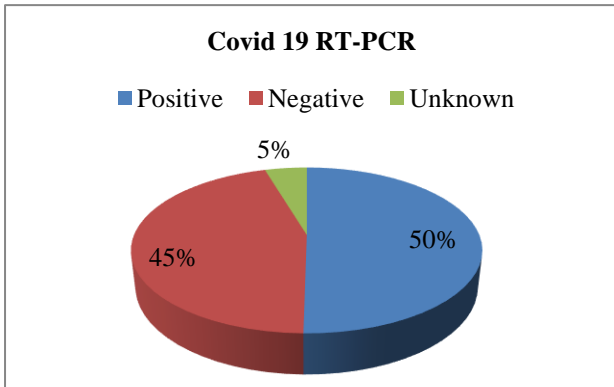


Figure 1: COVID status of the cases.

Education and awareness regarding oral hygiene comprising of daily brushing, mouth cleansing and mask care was also duly established in 64% cases but only 47% managed to keep the hygienic standards up to the mark.

Table 2: Therapeutic management details (in view of steroid predisposition).

Variables	No.	Percentage (%)
Demographics (population)		
Total	195	
Male	133	
Female	62	
Steroid used		
Yes	164	84
No	7	4
Unknown	24	12
Steroid duration (days)		
<7	52	27
8-14	83	43
>15	29	15
Type of steroid given		
Dexamethasone	97	50
Methylprednisolone	53	27
Prednisolone	11	6
Others	4	2
Unknown	0	0

As illustrated by Table 2, therapeutic steroids predominantly glucocorticoids were routinely observed as part of fixed anti-COVID protocol, with an astonishing 84% patients admitting to having received during their in-patient duration or outdoor visits. It usually depended on the clinical status; however 27% got jabs for less than 7 days while a majority 43% was administered for about 15 days. Only a meager 15% cases with thorough pulmonary tamper received steroidal therapy for a fortnight or more.

Elaborating the types, it was found that dexamethasone was most common with 97 cases (50%) while methylprednisolone and prednisolone followed with 27% and 6% prevalence respectively. Only 4% cases were sure of being steroid-free in their recent illness profile.

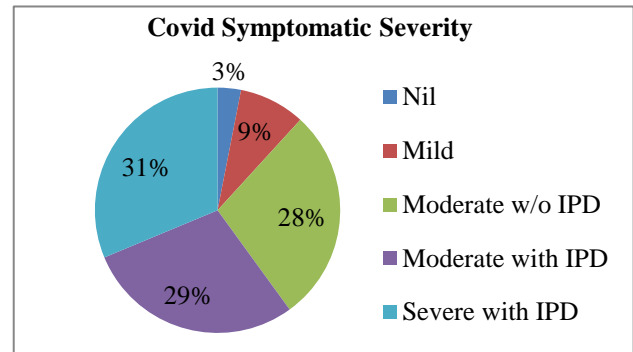


Figure 2: The symptomatic gravity of the cases.

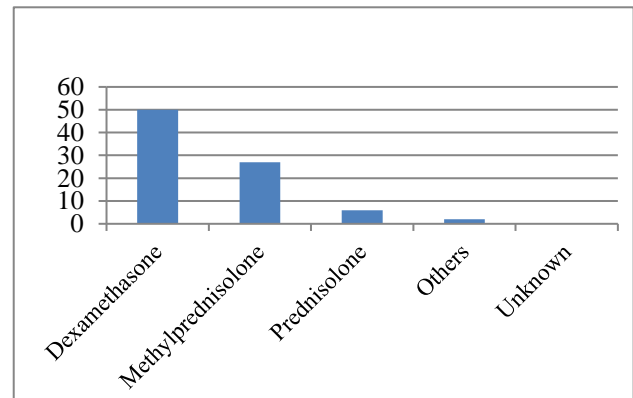


Figure 3: Steroid therapeutic status of the cases.

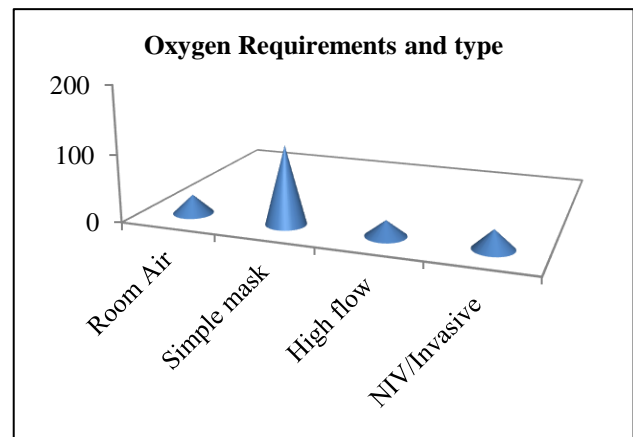


Figure 4: Oxygen necessity data of the cases.

These statistics signify how intricate and elaborate this institutionalized follow-up functioned, not only to accurately monitor the recent and present condition but also proving the minute links that amalgamated this outset in the admitted cohort of patients.

DISCUSSION

In this study regarding the recent ailment profiling leading to mucormycosis in these pandemic times, the singular goal was to reflect on the rationale, the impact and the potential of this type of exploratory module that not only explained the face of the theories lingering regarding the central causes or risk factors of developing mucormycosis but also proved useful for optimum patient care, withholder treatment protocol administered, already in mind.

CAM produced variable clinical presentations of patients that needed correct stratification and case profiling in view of secondary condition and prognosis, which otherwise could have proven disastrous.

Chenamchetty et al conducted a case study defining hypertensive, diabetic and severe acute respiratory distress syndrome (ARDS) patients suffering from COVID-19 who later high dose methylprednisolone for >15 days, with cases developing pulmonary soft tissue nodules and bilateral fungal invasion.¹³ Similarly, we encountered multiple patients with h/o steroidal intake for >7 days (58%) who later developed this ailment.

Song et al have suggested history profiling and early diagnosis as the best approach of managing invasive fungal infections viz. cryptococcosis, pulmonary aspergillosis and mucormycosis, which in comparison to our study, prove eccentric and true, as admitted patients, mostly suffering from post-COVID syndrome, were evaluated at early periods and as per their profiling, advocated correct treatment.¹⁴ Corticosteroid therapy and use of dehumidified oxygen, illustrated demeaning results in both studies concomitantly.

White et al in their study has scrutinized 135 post COVID patients treated with IPD services and defined protocols amid whom, 67% developed mucor while our study unlighted 50% cases of COVID positive individuals, leading to the disease.¹⁵

Mehta et al showed 56 patients with rhino-orbital mucormycosis having admitted to unlogged setups admitting to poor oxygen hygiene and care, in mucor follow up category, whereas similar mayhem was discovered in our analysis where 72% of patients (141) never used humidified oxygen or failed to highlight that while astonishing 58% cases maintain poor sanitation despite being made properly aware of its consequences through popular culture and education themes.¹⁶

This comprehensive discussion even showed majority of patients did not receive antibody and antiviral medications, either in view of low to moderate severity (41%), still contracting facio-orbital Mucor disease owing to poor hygiene, both oral and invasive, not to forget the diabetic, tubercular or chronic smoking status that rendered them immune-deficient at the first place.

In New York Presbyterian Hospital, protocols were developed for intubation, use of high flow oxygen, infectious disease consultation using technology to minimize staff exposure, encompassing a standardized protocol, which involved testing all patients attending COVID outdoor and inpatient services with the symptoms and signs of the fungal infection in accordance with their treatment history, if any.¹⁷

To conclude, it can be said that apt and quick integrated approach can make wonders in one of the biggest healthcare systems of the nation that showed solidarity in patient dealing, all over the epidemic, spotlighting the rationale behind the judicious and optimized use of antibiotics, steroids, oxygenation and supportive care to prevent newly emerging outbreaks.

Limitations

Since this study is a uni-centre mediated commission which lacks locational and social variations, it thereby mandates a need of multi centric studies involving large sample size of varied patients of different socio-economic and cultural strata.

Additionally, the presented study was of observational analytical type, aiming to ascertain past phenomena occurring in parallel with the natural course of a disease hence; it was not able to show a causal relationship between poor sanitation, gross rampancy of steroid exploitation and occurrence of mucormycosis. In concordance, critically ill patients who came to the hospital, directly intubated or worse could not be assessed for their illness profiling owing to the gravity of the condition.

CONCLUSION

COVID-19 propagated severe loss of functionality and health status in the people affected and with the second wave reeling down under, this new epidemic of mucormycosis is causing a setback. This study exclaimed the fact that multiple risk etiologies proved their presence in patient's recent history which secondary to COVID produced the deadly fungal invasion.

It was evident that widespread use of steroids and immune-compromised status with incessant oxygen therapy as times of hospitalization as a part of anti-COVID armamentarium developed this ailment. This enchants a message to worthy physicians and healthcare personnel to advocate judicious use of drugs, oxygen and supportive care to curb this menace.

The study also highlights the wrong on part of patients who despite of monumental education and training given regarding hygiene and care, practiced ill-cleanliness that gave this mayhem a breeding boost, which primarily should be broadcasted in order to achieve better control and effective management for future to come.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Frater JL, Hall GS, Procop GW. Histologic features of zygomycosis: Emphasis on perineural invasion and fungal morphology. *Arch Pathol Lab Med.* 2001;125:375-8.
2. Indian Council of Medical Research. Mucormycosis. Available at: www.icmr.gov.in/mucrmycosis/press-release. Accessed on 21 May 2021.
3. COVID19 India. Available at: www.COVID19india.org/rajasthan-newsrelease. Accessed on 21 May 2021.
4. Roden MM, Zaoutis TE, Buchanan WL, Knudsen TA, Sarkisova TA, Schaufele RL, et al. Epidemiology and outcome of zygomycosis: A review of 929 reported cases. *Clin Infect Dis.* 2005;41:634-53.
5. Chakrabarti A, Das A, Sharma A, Panda N, Das S, Gupta KL, Sakhuja V. Ten Years' Experience in Zygomycosis at a Tertiary Care Centre in India. *J Infect.* 2001;42:261-6.
6. Paltauf A. Mycosis mucorina: Ein Beitrag zur Kenntnis der menschlichen Fadenpilzkrankungen. *Virchows Arch Pathol Anat.* 1885;102:543-64.
7. Mandal J, Shivaprakash MR, George VK, Tarai B, Rao P, Panda N, et al. The rising trend of invasive zygomycosis in patients with uncontrolled diabetes mellitus. *Med Mycol.* 2006;44:335-42.
8. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. *Cureus.* 2020;12(9):e10726.
9. Prakash H, Chakrabarti A. Global Epidemiology of Mucormycosis. *J Fungi.* 2019;5:26.
10. Rawson TM, Moore LSP, Zhu N. Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis.* 2020.
11. Bottone EJ, Weitzman I HB. *Rhizopus rhizopodiformis*: emerging etiological agent of mucormycosis. *J Clin Microbiol.* 1979;9(4):530-7.
12. Indian Council of Medical Research. Mucormycosis. Available at: www.icmr.gov.in/mucrmycosis/press-release. Accessed on 21 May 2021.
13. Chennamchetty VK, Adimulapu S, Kola B. Post-COVID pulmonary mucormycosis- A case report. *Indian J Immunol Respiratory Med.* 2021;6(1):62-6.
14. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: A clinical and diagnostic perspective from China. *Mycopathologia.* 2020;1-8.
15. White PL, Dhillon R, Cordey A. National strategy to diagnose COVID-19 associated invasive fungal disease in the ICU. *Clin Infect Dis.* 2020.
16. Mehta S. Rhino-orbital mucormycosis associated with COVID-19. *Cureus.* 2020;12(9):e10726.
17. Griffin KM, Karas M. Available at: NY-PBT/ATSjournals.org. Accessed on 21 May 2021.

Cite this article as: Sharma S, Singhal M, Bhandari S. Clinical profile of recent progressive illnesses in patients with mucormycosis: a comprehensive analysis. *Int J Res Med Sci* 2022;10:898-904.