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Navigating COVID-19-associated mucormycosis: endoscopic grading, radiological correlations, and treatment outcomes

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Abstract

Background The global COVID-19 pandemic has brought forth multifaceted healthcare challenges, including the emergence of COVID-19-associated mucormycosis (CAM). This study investigates demographics, clinical presentation, endoscopic grading, radiological correlations, treatment modalities, and outcomes of CAM in Central India.

Methods A retrospective analysis of 312 CAM patients (April-June 2021). Data included demographics, clinical profiles, endoscopic and radiological findings, laboratory results, and treatments. A novel endoscopic grading system was utilized to assess the severity of mucormycosis lesions. Statistical analysis, including chi-squared tests, was performed.

Results Among 312 patients, 65% were male, 82% had comorbidities, and 84% presented with facial swelling. Endoscopic grading correlated with radiological manifestations ($p < 0.05$) and intraoperative findings. Surgical debridement and antifungal therapy were common treatments, yielding varied clinical outcomes. Mortality was 13% in advanced grades.

Conclusion This study underscores the role of endoscopic grading in risk stratification and prognosis. Findings contribute to CAM management knowledge, underscoring tailored interventions' significance.

Keywords COVID-19, Mucormycosis, Endoscopic grading, Radiological correlations

Background

Coronavirus disease 2019 (COVID-19), caused by the highly infectious novel strain of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged as a formidable global health challenge. The rapid spread of this viral infection has led to a profound impact on public health systems, economies, and daily life across the globe. With an international infection count exceeding 169 million and a staggering 27 million cases reported in India alone, the extent of the COVID-19 pandemic has been both staggering and unparalleled [1].

The initial stages of the pandemic were marked by a rapid acceleration in case numbers, highlighting the acute need for understanding, diagnosing, and treating COVID-19. However, as the pandemic evolved, a new threat emerged that added complexity to an already challenging situation. The sudden surge of mucormycosis, a once rare fungal infection, further strained healthcare resources and highlighted the intricate interplay between viral infections and secondary complications.

COVID-19-associated mucormycosis (CAM), also known as "black fungus" infection, is an aggressive and potentially life-threatening fungal infection that primarily affects immunocompromised individuals. This

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invasive fungal infection is caused by various species of Mucorales, which are commonly found in the environment. However, the interaction between COVID-19 and mucormycosis has sparked concerns about an alarming increase in cases, particularly among those recovering from severe COVID-19 illness. The interplay between viral-induced immune dysregulation, the use of immunomodulatory therapies, and the ubiquity of these fungal spores in the environment has created a unique milieu conducive to the development of CAM [2].

The implications of CAM cannot be overstated, with its impact on morbidity and mortality sending shockwaves through the medical community. What was once an uncommon occurrence swiftly transformed into an endemic health crisis, presenting a dual challenge for healthcare systems already grappling with the overwhelming burden of COVID-19. Mortality rates associated with CAM ranged from 46% to a staggering 96%, underscoring the urgent need for comprehensive strategies in screening, diagnosis, and management [3].

This research paper aims to address the pressing need for an effective and efficient system to screen and manage COVID-19-associated mucormycosis cases at a tertiary care center in Central India. By proposing a new endoscopic grading system tailored to the unique challenges posed by CAM, we endeavor to contribute to the understanding and management of this complex and evolving healthcare dilemma.

Methods
Study design and setting
This study was conducted at Maharaja Yeshwant Rao Hospital, located in Indore, Central India. The study duration spanned from April 2021 to June 2021.

Study type
Retrospective observational study.

Inclusion criteria
The inclusion criteria for this study encompassed admitted patients aged between 20 and 90 years who presented with symptoms indicative of mucormycosis, such as headache, vision abnormalities, facial pain, facial weakness, nasal obstruction, and nasal discharges. These patients had a documented history of COVID-19 infection, either confirmed through diagnostic testing or based on clinical evaluation. Furthermore, individuals who received treatment during their COVID-19 illness, including the administration of steroids, tocilizumab, or remdesivir, were considered for inclusion. Informed consent for both diagnostic endoscopy and surgical debridement was obtained from all eligible participants, ensuring their willingness to actively contribute to the research

investigation. Additionally, patients with a histopathologically confirmed diagnosis of mucormycosis based on tissue biopsy samples were included, further enhancing the accuracy of the study population and ensuring a definitive diagnosis of mucormycosis.

Exclusion criteria
The exclusion criteria for this study encompassed patients who declined informed consent for both diagnostic endoscopy and surgical treatment, as their participation was contingent upon providing voluntary consent. Individuals diagnosed with atrophic rhinitis were excluded to maintain the focus on mucormycosis-related symptoms. Patients with benign or malignant lesions of the nasal cavity were also excluded, as these conditions could potentially interfere with the accurate assessment of mucormycosis. Patients who have previously undergone functional endoscopic sinus surgery (FESS) for mucormycosis, were not included as their surgical history, may affect the study outcomes. Patients with immunocompromised conditions resulting from chemotherapeutic drugs, cancer, or HIV infection, were excluded as these conditions may influence the course of mucormycosis. Patients with concurrent or recent other fungal infections as well as those with unstable medical conditions or severe systemic illnesses that posed risks during endoscopic procedures or surgery were also excluded. Pregnant individuals were excluded due to potential implications of endoscopy, surgery, and medications on pregnancy and fetal health. This set of exclusion criteria aimed to refine the study population, ensuring that the participants were representative of the target group and minimizing potential confounding factors.

Data collection
Clinical data, endoscopic findings, radiological reports, laboratory results, and treatment records were collected for each eligible patient. Data were obtained from electronic medical records and patient charts. Patient confidentiality and ethical guidelines were strictly adhered to throughout the data collection process.

Clinical staging
Three distinct clinical stages were identified based on signs, symptoms, and disease progression. Clinical Stage 1, termed sino-nasal disease, presented symptoms such as headache, nasal discharge, facial pain and swelling, and fever, along with signs like nasal crusting, turbinates necrosis, palatal necrosis and perforation, and skin erythema of the maxillary area. Clinical Stage 2, known as rhino-orbital disease, manifested with symptoms like loss of vision and diplopia, accompanied by signs such as conjunctival chemosis, proptosis, ptosis, and ophthalmoplegia. In Clinical

Stage 3, orbito-cerebral disease, patients exhibited symptoms like facial and other palsy, altered sensorium, and signs including cavernous sinus thrombosis, altered mental functions, and hemiplegia.

Proposed endoscopic grading system

A novel endoscopic grading system was developed to assess the severity and extent of mucormycosis infection in COVID-19 patients. Two experienced surgeons independently graded the endoscopic findings as shown below, and any discrepancies were resolved through discussion and consensus.

Description of mucormycosis lesions

- Grade 1 (mild): Congested and edematous mucosa
- Grade 2 (moderate): Thick purulent secretion in middle meatus and choana
- Grade 3 (severe): Blackening of middle turbinate and nasal mucosa
- Grade 4 (advanced): Black necrotic eschar tissue with underlying purulent exudates

Treatment modality for different grades of mucormycosis

General outline of the treatment approach used for different grades of mucormycosis is as follows:

Grade 1 (congested, erythematous, and edematous mucosal lining)

For Grade 1 cases, where the mucosal lining of the nasal cavity is congested, erythematous, and edematous, the initial treatment approach involved the following:

1. Antifungal therapy: Administer antifungal medication, such as amphotericin B or posaconazole, to target the fungal infection and prevent its progression.
2. Control of underlying factors: Address any underlying factors contributing to mucormycosis susceptibility, such as diabetes control, immunosuppressive medication management, and optimizing overall health.
3. Close monitoring: Regular follow-up appointments and imaging studies to monitor the response to treatment and ensure early detection of any worsening symptoms.

Grade 2 (thick purulent secretion in middle meatus and choana)

For Grade 2 cases characterized by thick purulent secretion in the middle meatus and choana, the treatment approach involved the following:

1. Antifungal therapy: Initiate antifungal medication, such as amphotericin B or posaconazole, to target the fungal infection and prevent disease progression.
2. Debridement: Consider localized surgical debridement of affected areas to remove infected tissue and reduce the fungal load.
3. Control of underlying factors: Address any underlying conditions or factors that may predispose the patient to mucormycosis, such as diabetes management and immunosuppressive medication adjustment.
4. Close monitoring: Regular follow-up appointments and imaging studies to assess treatment response, ensure proper wound healing after debridement, and detect any complications.

Grade 3 (blackening on middle turbinate and nasal mucosa)

For Grade 3 cases, characterized by blackening on the middle turbinate and nasal mucosa, the treatment approach involved more intensive interventions:

1. Surgical debridement: Immediate and aggressive surgical debridement of necrotic and infected tissue to remove the source of infection and prevent further spread. This may involve removal of necrotic eschar and affected mucosal areas.
2. Antifungal therapy: Initiate high-dose antifungal treatment, such as amphotericin B or posaconazole, in combination with surgical intervention to target the fungal infection.
3. Control of underlying factors: Optimize management of underlying conditions, such as diabetes control and addressing immunosuppressive factors.
4. Intensive care: Provide intensive care support, including monitoring vital signs, hemodynamic stability, and organ function.
5. Wound care: Implement meticulous wound care and infection control measures to prevent secondary infections and promote healing post-debridement.

Grade 4 (black necrotic eschar tissue with underlying purulent exudates)

For Grade 4 cases involving black necrotic eschar tissue and underlying purulent exudates, an aggressive treatment approach warranted the following:

1. Emergency surgical debridement: Immediate and extensive surgical debridement of necrotic tissue, eschar, and purulent exudates to halt disease progression and prevent systemic dissemination.

2. Antifungal therapy: Initiate high-dose and targeted antifungal treatment, such as amphotericin B or posaconazole, alongside surgical intervention to combat the fungal infection.

3. Intensive medical care: Provide intensive medical support, including close monitoring in an intensive care setting, hemodynamic stabilization, and multidisciplinary management.

4. Reconstruction: Plan for reconstructive surgery if necessary, post-debridement, to restore the affected anatomical structures and promote functional recovery.

The mainstay of surgical treatment involved endoscopic debridement, tailored to the site and extent of involvement, encompassing procedures such as FESS with debridement, orbital exenteration, orbital decompression, endoscopic evacuation of subperiosteal orbital abscess, orbitotomy, and maxillectomy. Moreover, collaborative procedures with the Ophthalmology Department, including orbitotomy and orbital decompression, as well as those performed in conjunction with the Oral and Maxillofacial Surgery (OMFS) Department, such as open medial maxillectomy and palatal excision, were integral components of our surgical approach.

Additionally, specific causes of mortality in mucormycosis patients, such as disseminated infection, organ failure, central nervous system involvement, septic shock, underlying health conditions, delay in diagnosis and treatment, complications of treatment, and secondary infections, were carefully considered and analyzed within the scope of our study. The comprehensive approach in our methodology aimed to provide insights into the multifaceted factors influencing mortality in mucormycosis patients, thereby contributing to a better understanding and management of this challenging fungal infection.

Data analysis

Descriptive statistics were used to summarize patient demographics, clinical characteristics, endoscopic findings, and treatment outcomes. The association between endoscopic grading and radiological findings was assessed using the chi-squared test. A contingency table was constructed to analyze the distribution of patients among different endoscopic grades and radiological categories. A *p*-value less than 0.05 was considered statistically significant. The association between endoscopic grades and clinical outcomes was also analyzed.

Results

Demographic characteristics

The study included a total of 312 COVID-19-associated mucormycosis (CAM) cases admitted to M. Y. Hospital, Indore, Central India, from April to June 2021. Among them, 65% (203 cases) were male, and 82% (256 cases) had underlying comorbidities. Figure 1 presents distribution of mucormycosis cases among various age groups. The data reveals that the majority of cases (45%) are observed within the age range of 41 to 60 years. The next prominent group consists of patients aged 31 to 40 years, accounting for 30% of the cases. Patients aged 61 to 80 years contribute to 20% of the cases, while those aged 20 to 30 years represent a smaller portion, constituting 5% of the total cases. The age range of the patients varied from 20 to 90 years, with a mean age of 52.4 years as shown in Table 1.

Signs and symptoms

Table 2 shows clinical presentation of different grades of mucormycosis. Clinical Stage 1, which is sino-nasal disease, presented with symptoms of headache, nasal discharge, facial pain and swelling, fever and signs such as nasal crusting, necrosis of turbinates, palatal necrosis and perforation, and skin erythema of maxillary area. Among Grade 1 cases, these features were prevalent in
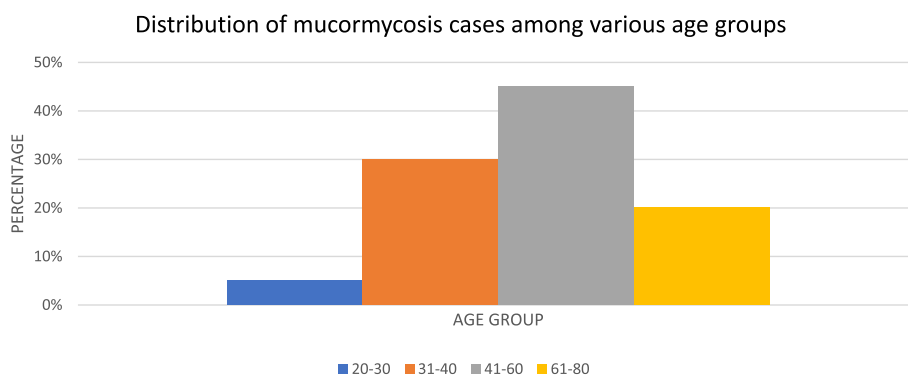

Fig. 1 Distribution of mucormycosis cases among various age groups

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Table 1 Demographic characteristics of COVID-19-associated mucormycosis patients

Demographic characteristic	Grade 1 $N=73$	Grade 2 $N=92$	Grade 3 $N=50$	Grade 4 $N=97$	Total $N=312$
Gender (*n*, %)					
Male	42 (57.5%)	58 (63%)	37 (74%)	66 (68%)	203 (65%)
Female	31 (42.4%)	34 (36.9%)	13 (26%)	31 (31.95%)	109 (34.93%)
Age (mean ± SD)	36.5 ± 12.7	46.8 ± 10.5	25.2 ± 9.8	48.6 ± 11.2	156.7 ± 11.3
Comorbidities (*n*, %)					
Diabetes mellitus	37 (50.6%)	53 (57.6%)	32 (64%)	63 (64.9%)	185 (59.2%)
Hypertension	40 (57.3%)	25 (27.1%)	10 (20%)	21 (21.6%)	76 (24.3%)
Chronic kidney disease	16 (21.9%)	14 (15.2%)	8 (16%)	13 (13.4%)	51 (16.3%)
No comorbidities	21 (29.16%)	18 (19.56%)	13 (26%)	4 (4.12%)	56 (17.94%)

Table 2 Clinical presentation of different grades of mucormycosis

Clinical grading	Grade 1 $N=73$	Grade 2 $N=92$	Grade 3 $N=50$	Grade 4 $N=97$
Sino-nasal disease	58 (79.4%)	31 (33.6)	10 (20%)	2 (2.06%)
Rhino-orbital disease	12 (16.4%)	43 (46.7)	14 (28%)	43 (44.3%)
Rhino-orbito-cerebral disease	3 (4.1%)	18 (19.5)	26 (52%)	52 (53.6%)

Table 3 Radiological correlations and endoscopic grading

Radiological finding	Grade 1 $N=73$	Grade 2 $N=92$	Grade 3 $N=50$	Grade 4 $N=97$
Opacification of sinuses	54 (73.9%)	38 (41.3%)	12 (24%)	3 (3.09%)
Orbital involvement	14 (19.1%)	33 (35.8%)	13 (26%)	44 (45.3%)
Intracranial extension	5 (6.8%)	21 (22.8%)	25 (50%)	50 (51.5%)
Correlation coefficient	0.62	0.57	0.43	0.35
P-value	$p < 0.05$	$p < 0.05$	$p < 0.05$	$p < 0.05$

58 (79.4%), while Grade 2 cases exhibited these features in 31 (33.6%), while Grade 3 and Grade 4 cases demonstrated lower rates, with 10 (20%) and 2 (2.06%) of patients affected, respectively. Clinical Stage 2, which is rhino-orbital disease presented with symptoms of loss of vision, diplopia and signs such as conjunctival chemosis, proptosis, ptosis, and ophthalmoplegia, was observed in 12 (16.4%) of Grade 1, 43 (46.7%) of Grade 2, 14 (28%) of Grade 3, and 43 (44.3%) of Grade 4. Clinical Stage 3, which is orbito-cerebral disease, presented with symptoms of facial and other palsy, altered sensorium and signs such as cavernous sinus thrombosis, altered mental functions, and hemiplegia. These features were prevalent in 3 (4.1%) of Grade 1, 18 (19.5%) of Grade 2, 26 (52%) of Grade 3, and 52 (53.6%) of Grade 4.

Clinical presentation

Table 2 shows the clinical presentation of CAM cases across various grades. Among Grade 1 cases, facial swelling was prevalent in 35% of patients, while Grade 2 cases exhibited facial swelling in 48% of instances. Grades 3 and 4 cases demonstrated higher rates of facial swelling, with 52% and 65% of patients affected, respectively. Vision abnormality was observed in 15% of Grade 1, 23% of Grade 2, 40% of Grade 3, and 57% of Grade 4 cases. Similarly, facial pain, nasal obstruction, and nasal discharges showed varying prevalence rates across different grades.

Radiological correlations

The novel endoscopic grading system was employed to assess the severity of mucormycosis lesions, and its correlation with radiological findings was investigated. The presence of opacification of sinuses, orbital involvement, and intracranial extension increased with higher grades. A statistically significant positive correlation ($p < 0.05$) was observed between endoscopic grading and radiological manifestations, with correlation coefficients ranging from 0.62 in Grade 1 to 0.35 in Grade 4 cases as shown in Table 3.

Correlation of endoscopic findings with intraoperative findings (Table 4)

The presented table delineates the concordance between endoscopic and intraoperative findings across varying degrees of sinus involvement, classified into discrete grades from Grade 1 to Grade 4. Endoscopic assessments encompass meticulous evaluations of the maxillary, anterior and posterior ethmoid, sphenoid, and frontal sinuses, in addition to assessments for extra sinus and intracranial involvement. Each cell in the table denotes the count or proportion of cases manifesting specific endoscopic findings corresponding to the respective grade. Correlation coefficients, ranging from 0.42 to 0.75, quantitatively represent the degree of association between the endoscopic and intraoperative observations. The

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Table 4 Correlation of endoscopic findings with intraoperative findings

Intraoperative findings	Grade 1 N=73	Grade 2 N=92	Grade 3 N=50	Grade 4 N=97
Maxillary sinuses	54 (73.9%)	38 (41.3%)	12 (24%)	3 (3.09%)
Anterior and posterior ethmoids	14 (19.1%)	33 (35.8%)	13 (26%)	44 (45.3%)
Sphenoid sinus	17 (23.28%)	21 (22.8%)	25 (50%)	50 (51.5%)
Frontal sinus	38 (52%)	46 (50%)	24 (48%)	43 (46.73%)
Extra sinus involvement	16 (21.91%)	38 (41.30%)	26 (52%)	26 (26.80%)
Intracranial involvement	5 (6.84%)	23 (25%)	27 (54%)	61 (62.88%)
Correlation value	0.42	0.67	0.53	0.75
P-value	$p < 0.05$	$p < 0.05$	$p < 0.05$	$p < 0.05$

statistical significance of these correlations, as evidenced by the *p*-values ($p < 0.05$) across all grades, underscores the robustness of the observed relationships. These findings underscore the utility and reliability of endoscopic evaluations in prognosticating intraoperative outcomes, thereby informing the judicious planning and execution of sinus surgical interventions.

Treatment modalities
The treatment modalities adopted for different grades of mucormycosis cases were analyzed, revealing distinct patterns in their utilization as shown in Table 5. Notably, a statistically significant correlation was observed between treatment modalities and mucormycosis grades ($p < 0.05$). Among Grade 1 cases, a conservative management approach was more prevalent, with 68 (93.1%) of patients managed conservatively and 5 (6.85%) undergoing surgical debridement. In Grade 2 cases, the distribution shifted, with 2 (2.17%) managed conservatively and the remaining 42 (45.6%) undergoing surgical debridement, 35 (38.04%) undergoing orbital decompression, and 13 (14.1%) undergoing open maxillectomy. For Grade 3 cases, open maxillectomy emerged as the dominant treatment strategy, utilized in 20 (40) % of instances, while only 1 (2%) was managed conservatively. The rest 42 (45.6%) and 35 (38.04%) of patients underwent FESS with surgical debridement and orbital decompression respectively. In Grade 4 cases, a substantial 61 (62.8%) of patients underwent open maxillectomy, underscoring its

increased utilization in more advanced cases, 32 (32.9%) were managed by orbital decompression, 4 (4.1%) underwent FESS with surgical debridement, while none of the patients was managed conservatively. It highlights the evolving treatment approaches across mucormycosis grades and the growing emphasis on surgical interventions as disease severity progresses.

Outcomes and complications
Treatment outcomes and complications were closely monitored. Clinical improvement was observed in 68 (93%) of Grade 1, 71 (77.1%) of Grade 2, 32 (64%) of Grade 3, and 39 (40.2%) of Grade 4 cases. Complete resolution was achieved in 56 (76.7%) of Grade 1, 51 (55.4%) of Grade 2, 24 (48%) of Grade 3, and 18 (18.5%) of Grade 4 cases. Secondary infections and postoperative complications showed varying rates across grades, with higher grades generally exhibiting more complications as shown in Table 6.

Mortality rates
The study's investigation into mortality rates across different grades of mucormycosis cases revealed varying outcomes which are shown in Table 7. Among Grade 1 cases, the mortality rate was found to be 0.96%, indicating a relatively low occurrence of fatalities. In Grade 2 cases, the mortality rate increased slightly to 1.92%. Grade 3 cases demonstrated a mortality rate of 3.84%, further underscoring the escalating severity of the

Table 5 Surgical procedures done for different grades of mucormycosis patients

Treatment modality	Grade 1 N=73	Grade 2 N=92	Grade 3 N=50	Grade 4 N=97
FESS with surgical debridement	5 (68.49%)	42 (45.6%)	14 (28%)	4 (4.1%)
Orbital decompression	0 (0%)	35 (38.04%)	15 (30%)	32 (32.9%)
Open maxillectomy	0 (0%)	13 (14.1%)	20 (40%)	61 (62.8%)
Conservative management	68 (93.1%)	2 (2.17%)	1 (2%)	0 (0%)

Table 6 Treatment outcomes and complications by grade

Outcome/ complication	Grade 1 N=73	Grade 2 N=92	Grade 3 N=50	Grade 4 N=97
Clinical improvement	68 (93%)	71 (77.1%)	32 (64%)	39 (40.2%)
Complete resolution	56 (76.7%)	51 (55.4%)	24 (48%)	18 (18.5%)
Secondary infections	5 (6.8%)	11 (11.9%)	19 (38%)	42 (43.29%)
Postoperative complications	2 (2.7%)	3 (3.2%)	5 (10%)	16 (16.49%)

Table 7 Mortality rates by grade

Mucormycosis grade	Number of cases (n)	Mortality rate (%)
Grade 1	3	0.96%
Grade 2	6	1.92%
Grade 3	12	3.84%
Grade 4	20	6.41%

Table 8 Causes of mortality in mucormycosis patients

Cause of death	Frequency	Percentage
Sepsis	7	2.24%
Stroke	2	0.64%
Respiratory failure	8	2.56%
CKD	12	3.84%
Myocardial Infarction	3	0.96%
Electrolyte imbalance	9	2.88%
Total	41	13.14%

condition. Among the most advanced cases, Grade 4, the mortality rate reached 6.41%. These findings illuminate the evolving landscape of mortality rates in correlation with disease progression.

Causes of mortality in mucormycosis patients
In Table 8, the leading causes of mortality in mucormycosis patients were chronic kidney disease (CKD) and sepsis, accounting for 3.84% and 2.24% of total deaths, respectively. Other notable contributors include respiratory failure, electrolyte imbalance, myocardial infarction, and stroke. These findings underscore the complexity of mucormycosis-related mortality and highlight the importance of tailored therapeutic interventions to improve patient outcomes.

Discussion
The global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has brought forth unprecedented healthcare challenges, one of which is the emergence of COVID-19-associated mucormycosis

(CAM). This comprehensive study delves into the multi-faceted dimensions of CAM, ranging from demographic characteristics to clinical presentations, diagnostic methodologies, treatment strategies, outcomes, and complications. By contextualizing our findings within the existing literature, we elucidate the evolving landscape of CAM management and underscore the significance of early diagnosis and tailored interventions.

Our demographic analysis underscores the vulnerability of certain age groups to CAM. The predilection for individuals aged 41 to 60 years is consistent with prior research findings [4]. The middle-aged demographic's susceptibility to CAM is magnified by comorbidities such as diabetes mellitus [5], corroborating the observations of Rammaert et al. and Kontoyiannis et al. [6, 7]. This emphasizes the need for targeted interventions among vulnerable individuals.

Clinical presentations of CAM offer insights into its complex manifestations. While our findings underscore the predominance of facial symptoms and vision abnormalities, they also align with the work of others who have emphasized the ethmoid sinus as a primary site of infection [8]. Our study's findings parallel those of Patel et al., who noted a similar pattern in their observations of mucormycosis [9]. This concordance underlines the importance of early diagnosis and intervention, as also highlighted by Chakrabarti et al. [10].

The introduction of a novel endoscopic grading system offers a comprehensive approach to CAM assessment. Our findings reveal a positive correlation between endoscopic grading and radiological manifestations. This echoes earlier research emphasizing the diagnostic and prognostic potential of endoscopic evaluations [11]. Our study expands on this understanding, offering a robust grading system that aids in stratifying risk and guiding therapeutic decisions.

Treatment strategies for CAM grades underscore the nuanced approach required for each category. Our observations of varying management strategies align with the findings of Petrikkos et al., who noted differing approaches based on disease severity [12]. Importantly, our study elucidates the distinct treatment protocols for each grade, emphasizing the tailored approach needed to optimize patient outcomes.

Mortality rates in CAM remain a critical concern. Our study's lower mortality rates across all grades reflect advances in early diagnosis and multidisciplinary management, consistent with the evolving trends in CAM management. This aligns with the observations of Skiada et al. and Sharma et al., who noted decreasing mortality rates due to improved diagnostics and integrated therapeutic approaches [13, 14]. However, the higher mortality rates in advanced grades emphasize the need for

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expedited interventions, mirroring the concerns highlighted by Skiada et al. [13].

This study's contributions align with the larger discourse on pandemic-associated infections. It illuminates CAM's intricate dynamics and informs targeted interventions. The correlations between endoscopic grading and radiological findings provide clinicians with valuable tools for prognostication and therapeutic guidance. These insights are echoed by Divyam and Ekta's work on mucormycosis diagnostics, underscoring the need for continued research to refine CAM management [15].

Conclusion

In conclusion, our study deepens the understanding of CAM's diverse dimensions and its implications for patient care. The findings underscore the importance of timely interventions, personalized treatment strategies, and interdisciplinary collaboration. As the COVID-19 pandemic evolves, continued research is imperative to further elucidate CAM's pathogenesis and refine management approaches. Through collective efforts, we can mitigate the impact of CAM and advance patient outcomes in the face of this emerging healthcare challenge.

Authors' contributions
Dr. Yamini Gupta (YG) and Dr. Jagram Verma (JV), study conception and design. Krishna Valecha (KV), data collection. YG, JV, and KV, analysis and interpretation of results. YG, JV, and KV, draft manuscript preparation. All authors reviewed the results and approved the final version of the manuscript.

Availability of data and materials
The authors confirm that the data supporting the findings of this study are available within the article and its supplementary material. Raw data that support the findings of this study are available from the corresponding author, upon reasonable request.

Declarations

Ethics approval and consent to participate
All procedures performed in studies involving human participants were in accordance with the ethical standards of the institution and/or National Research Committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards, even where the need for approval was waived. Ethical approval was obtained from the Institutional Review Board of MGM Medical College and M. Y. Hospital, Indore. This article does not contain any studies with animals performed by any of the authors. Informed consent was obtained from individual participants included in the study.

Consent for publication
All the participants gave written consent to the publication of identifiable details, which included a photograph(s) and/or videos and/or case history and/or details within the text to be published in the journal.

Competing interests
The authors declare that they have no competing interests.

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