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COVID-19-associated Mucormycosis: A clinico-epidemiological study☆

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ABSTRACT

Background: There was an unprecedented increase in COVID-19-associated-Mucormycosis (CAM) cases during the second pandemic wave in India.
Methods: This observational study was done to know the epidemiological profile of CAM cases andincluded all patients admitted with mucormycosis between May 2021 and July 2021.
Results: Out of the enrolled 208 CAM cases (either SARS-CoV-2 RT-PCR or serology positive), 204, three and one had rhino-orbital-cerebral, pulmonary and gastrointestinal mucormycosis, respectively. 95.7 % of the patients had diabetes, out of which 42.3 % were recently diagnosed. Mean HbA1c was 10.16 ± 2.56 %. 82.5 % of the patients were unvaccinated. During their COVID-19 illness, 86.5 % were prescribed antibiotics, 84.6 % zinc preparations, 76.4 % ivermectin, and 64.9 % steroids, while only 39.5 % required oxygen therapy. The frequency of blood groups A, B, O and AB in our CAM patients was 29.5 %, 18.9 %, 38.9 % &12.6 %, respectively. At three months follow up, 60 (28.8 %) patients died, four (1.9 %) stopped antifungal treatment, and 144(69.23 %) were on antifungal treatment. 55 % (n = 33) of deaths occurred within 15 days of admission. Mortality was significantly associated with higher age, RT-PCR positive for SARS-CoV-2, raised serum creatinine and alkaline phosphatase during treatment. At 6 months follow-up, eight more patients died, three due to chronic kidney disease, four patients who had stopped treatment and one patient who was on a ventilator due to COVID-19 associated pneumonia and the rest 140(67.3 %) survived.
Conclusion: Uncontrolled hyperglycemia, SARS-CoV-2 infection, rampant use of antibiotics, zinc supplementation and steroids were some of the risk factors for mucormycosis. Despite the overwhelming number of patients with an uncommon disease like mucormycosis, the six months mortality was much lower than expected.

1. Introduction

Mucormycosis, a rare and life-threatening fungal infection, had an unprecedented upsurge amidst the pandemic of *Coronavirus* disease 2019 (COVID-19) worldwide. India, with a vast burden of SARS-CoV-2 affected population (32,036,511 cases as of Aug 11, 2021), reported the highest number of cases of mucormycosis, especially during the second wave of COVID-19.[1,2]According to reports from the Union Health Ministry, India reported 40,845 cases of mucormycosis as of June 28, 2021.[3]The impact of the disease was such that the government declared "mucormycosis", a notifiable disease under the Epidemic Diseases Act, 1897.[4]

Interestingly, mucormycosis cases were higher in the Indian subcontinent as compared to other parts of the globe even before the

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pandemic. This variation has been explained by the high diabetic population of the country.[5] This sudden increase in the number of COVID-19-associated mucormycosis (CAM) cases has been explained by the combination of hyperglycemic state induced by the SARS-CoV-2 as well as drugs used during its therapy (especially steroids), hypoxic conditions in affected patients, severe acidosis, higher levels of iron in the form of raised ferritin levels and other factors supporting the immunosuppressed condition of the host.[6–8] Furthermore, the ubiquitous presence of the spores, especially in tropical countries, facilitated the growth of this opportunistic pathogen in an ideal COVID-19 affected host.[7]

In a recent systematic review of the CAM cases in India and worldwide during the pandemic, 82 cases have been reported from India against only 19 cases from other parts of the world.[2] Among these, hyperglycemia either due to pre-existing or new-onset diabetes or deranged glucose metabolism has been implicated as the single most important risk factor, supported by the findings of another recent review.[9]

Mucorales group of fungi can penetrate the blood vessels and disseminate hematogenously to distinct body organs.[10]The rapid progressive nature of Mucorales entails its early and prompt diagnosis followed by efficient management by a multidisciplinary team, which is one of the major limitations in resource-limited countries. However, even with the best management, the mortality is high. There have been few reports of the rising mucormycosis cases in the literature; however, most published data on CAM are case reports/series, with a limited description of risk factors. With this background, this study was specifically designed to present the epidemiological profile of the CAM cases admitted and managed in our tertiary care centre during the second wave of COVID-19 pandemic in India. Being of immense public health importance, this epidemiological study will add to the existing scarce data available in the global literature to better understand the pathogen and the disease.

2. Material and methods

2.1. Study design

This observational study was done in the Mucor ward, SS Hospital, IMS BHU Varanasi, from May 2021 to July 2021. The Institute Ethics Committee (ECR/526/Inst/UP/2014/RR-20 dt 19.5.20) approved the study protocol. Informed and written consent was taken for the admitted patients and data was extracted from the hospital records and was analyzed anonymously. The objectives of the study were to describe the epidemiology, risk factors, and treatment outcome at six months of the patients with CAM admitted to our centre.

2.2. Study population

Patients with probable/putative mucormycosis were included in this observational study. Probable mucormycosis cases were defined as the presence of broad aseptate hyphae observed on direct microscopic examination by potassium hydroxide (KOH) wet mount or histopathological examination of the excised sterile tissue in individuals with clinically compatible disease.[11]In contrast, putative cases were defined with clinical features with demonstration of broad aseptate hyphae in non-sterile samples (gastric lavage, sputum/bronchoalveolar lavage (BAL).[11,12] In addition, data of baseline demographic details, COVID-19 status at the time of admission, previous history and clinical features; both related to SARS-CoV-2infection and mucormycosis, COVID-19vaccination status, predisposing risk factors (diabetes mellitus, glucocorticoid therapy, transplant, malignancy, immunosuppression), other co-morbid illness like hypertension, ischaemic heart disease, chronic kidney disease, chronic liver disease, chronic respiratory illnesses, were obtained from hospital records. Hypertension was defined according to the Eighth Joint National Committee (JNC-8); obesity was defined by body mass index (BMI) according to WHO guidelines, diabetes mellitus was defined as per the latest ADA guidelines published in 2017.[13–15] Investigations were done as per the Institution's protocol and at treating physicians discretion and included a complete hemogram, liver function tests, creatinine, serum potassium, blood sugar, HbA1c, and CD4 count. Localization of the Mucorales infected site was determined by clinical and radiological examination, by contrast enhanced computed tomography (CECT)scan of paranasal sinuses, orbit and MRI brain with contrast. In cases of suspected pulmonary mucormycosis, high-resolution computed tomography (HRCT) thorax was done. CECT abdomen with endoscopy was performed in case of suspected gastrointestinal mucormycosis, where it was possible.

RT-PCR for SARS-CoV-2 was done for all patients at the time of admission except those who had a previous SARS-CoV-2 RT-PCR positive report, and 15 days had elapsed since the positive report, and the patient did not have any COVID-19 related symptoms. COVID-19 IgG antibodies were estimated quantitatively by LIAISON® SARS-CoV-2 TrimericS IgG assay in the patients negative for SARS-CoV-2 by RT-PCR, done at admission as virus-specific antibody detection for COVID-19as serological testing may be helpful for the diagnosis of suspected patients with negative RT-PCR results as reported by Long et al.[16] We also collected the details of the treatment given (antifungal agent, dose and duration of antifungal agent); and analyzed the association of risk factors with mortality at 180 days.

Excised tissue samples were subjected to microbiological and histopathological examination. Direct microscopy with KOH wet mount was done to determine the fungal element in tissue samples; concomitantly. The tissue samples were inoculated on two sets of Sabouraud's Dextrose agar (SDA) with subsequent incubation at 25 °C in a Biological oxygen demand (BOD) incubator. Once there was growth over the medium, the identification of the causative Mucorale was made by standard mycological procedures, including their growth characteristics and lactophenol cotton blue (LPCB) wet mount. The tissue samples submitted for histopathological examination were examined using haematoxylin & eosin, periodic acid Schiff or Grocott methenamine silver stain.

All the enrolled patients were managed by a multidisciplinary team (COVID-19 associated fungal study group) constituted by the Institution. The patients received treatment as per Institutional protocol and availability of amphotericin B and posaconazole. Patients underwent extensive surgical debridement of the affected tissue. Nasal endoscopy was done between 2 and 3 weeks after initial surgery; if positive, meaning the presence of necrotic material, it was repeated after 2–3 weeks and at discharge. Diabetes was managed with insulin in the initial phase of treatment which was then converted to oral hypoglycemic agents. In addition, a low dose of atorvastatin (10 mg) was given where indicated.

2.3. Statistical analysis

The statistical analysis was performed using a statistical package for the social sciences (SPSS), Version 23.0. IBM Corp., NY). Simple descriptive statistics (mean ± standard deviation) were used for quantitative variables, and frequency with percentage distribution for categorized variables. The statistical analysis was carried out for various categorical parameters using the chi-square test and Fischer's Exact Test. In addition, for comparing two groups of mean or median, Student's *t*-test and Mann Whitney *U* test were used. P-value <0.05 was considered statistically significant.

3. Results

During the study period 219 cases of mucormycosis were admitted in our Centre. All 219 cases of mucormycosis were assessed for previous/concomitant SARS-CoV-2 infection either by RT-PCR or antibody detection. A total of 135 patients had a positive SARS-CoV-2 RT-PCR report while 84 patients were SARS-CoV-2 RT-PCR negative. Out of these 84mucormycosis cases, 73 had high antibody titres against SARS-CoV-2 estimated quantitatively by LIAISON® SARS-CoV-2 TrimericS

IgG assay. Antibody test could not be done in 11 cases as ten patients expired and one patient refused. Thus, only 208 cases (135 + 73) were designated as CAM (COVID-19-associated mucormycosis), and rest 11 cases were excluded from the study.

Baseline data of 208 enrolled CAM cases (probable 204 and putative 4) has been shown in Table 1. Our patients were predominantly male.95.7 % of enrolled patients had Type 2 diabetes; out of these, 88 (42.3 %) were diagnosed recently during their illness. Two patients had concomitant HIV-1 infection. 38.9 % of the patients had blood group O, followed by blood group A in 29.5 % of the enrolled patients.

88.46 % of our patients had symptoms of COVID-19 before the onset of mucormycosis symptoms, but 27.88 % (n = 58) did not get themselves tested. Fever was present in 85 % (n = 177), cough in 73 % (n = 152), shortness of breath in 37.44 %, and loss of taste in 7.2 %. The interval between SARS-CoV-2 positivity/COVID-19 symptoms and the onset of mucormycosis symptoms was 20.73 ± 12.65 days. Steroids were taken by 64.9 % of participants with a mean duration of 7.78 days.

The rhino-orbital- cerebral presentation of mucormycosis was noted in 204 patients, three had pulmonary and one had gastrointestinal mucormycosis, presenting as upper GI bleed. The commonest presentation of mucormycosis was rhino-orbital (n = 160; 76.9 %), followed by rhino-orbito-cerebral (*n* = 57; 27.4 %) and only nasal/sinus involvement was seen in 23.55 % (n = 49) patients. The predominant clinical presentation of these patients were facial swelling in (n = 201, 96.6 %) of cases, followed by facial pain (n = 183; 88 %), nasal discharge (n = 111; 53.4 %), blindness (n = 44; 21.5 %), and neurological manifestation in form of ophthalmoplegia (n = 30; 13.7 %), 7th nerve palsy (n = 20; 9.1 %) and altered sensorium in 7.3 % (n = 16).

Out of these enrolled208patients, 189 underwent extensive surgical debridement in our hospital. The excised tissue samples, one from each were sent for microbiological and histopathological examination. On KOH wet mount, broad aseptate hyphae with right-angle branching were observed in 166 samples. Rest 23 samples were diagnosed histopathologically. Mucorales were isolated in 79 excised tissue samples, with a preponderance of *Rhizopus arrhizus* (n = 76) (Figs. 1, 2). Follow up samples were taken from 135 patients who had necrotic tissue in there repeat endoscopy after 2-3 weeks. Among these 135 patients, 113 had broad aseptate hyphae in the excised tissues (10 samples were initially negative), with culture-positive in seven samples. Subsequently, 2-3 weeks later, nasal endoscopy showed necrotic material in 98 patients, out of which 54 had broad aseptate hyphae without any culture positivity. Again after 15 days, nasal endoscopy was done to look for necrotic material, but no necrotic material was observed.

Treatment was provided free of cost by the government and prescribed as per Institute guidelines and availability of drugs. Various formulations of amphotericin B (AmB) were given-liposomal, lipid-associated and conventional as per the availability. During the initial phase of treatment, due to the unavailability of regular AmB, gastro-resistant posaconazole tablet were given along with AmB.

Fever with chills, rigor and hypokalemia were the commonest side effects of conventional amphotericin B. Eleven patients had hypotension, out of which two expired. Sixty-seven patients had fever unrelated to amphotericin B during treatment for which they received antibiotics. In addition, 58 patients taking oral posaconazole had raised alkaline phosphatase (n = 58), out of which 12 patients had levels >3 times, and 4 patients had levels >5 times for which oral posaconazole was stopped. The mean alkaline phosphatase value was 428.79 ± 368.51 IU/L. Sixteen patients (7.3 %) had posaconazole induced diarrhea, for which the drug was stopped in one patient. Injectable posaconazole resulted in severe thrombophlebitis in 15 patients. Four patients had chickenpox, one had Herpes zoster, and six patients had dengue infection during their stay in hospital.

Out of the 208 patients, 189 (90.86 %) underwent surgical intervention, nine expired before surgery, surgery was not done in three cases of pulmonary mucormycosis, and seven patients refused surgery. All 189 patients underwent extensive sinonasal debridement, with orbital

Table 1
: Baseline characteristics of CAM cases.

Characteristics	Total	Positive	Negative	p-value
Age (mean ± SD) (n = 208)	52.84 ± 14.07	52.82 ± 11.61	52.88 ± 12.83	0.973
Sex (n = 208)				0.542
Male	136 (65.4 %)	81 (63.8 %)	55 (67.9 %)	
Female	72 (34.6 %)	46 (36.2 %)	26 (32.1 %)	
Rural/Urban (n = 194)				0.064
Rural	99 (51.0 %)	67 (56.3 %)	32 (42.7 %)	
Urban	95 (49.0 %)	52 (43.7 %)	43 (57.3 %)	
Vaccinated (n = 194)				0.223
No	160 (82.5 %)	95 (79.8 %)	65 (86.7 %)	
Yes	34 (17.5 %)	24 (20.2 %)	10 (13.3 %)	
Vaccine doses given (n = 34)	30 (15.4 %)	19 (16.0 %)	11 (13.3 %)	0.28
One	04 (2.1)	4 (3.4 %)	0 (0)	
Two				
Blood Group (n = 181)				0.901
A	55 (30.4 %)	35 (31.3 %)	20 (29.0 %)	
B	35 (19.3 %)	20 (17.9 %)	15 (21.7 %)	
O	69 (38.1 %)	44 (39.3 %)	25 (36.2 %)	
AB	22 (12.2 %)	13 (11.6 %)	9 (13.0 %)	
BMI kg/m^2(mean ± SD),(n = 181)	24.57 ± 1.82	24.59 ± 1.81	24.55 ± 1.85	0.892
Diabetes (n = 208)	200 (96.2 %)	124 (97.6 %)	76 (93.8 %)	0.163
Duration of diabetes (months) (n = 113)	6.90 ± 4.95	7.06 ± 5.32	6.69 ± 4.46	0.698
Hypertension (n = 207)	61 (29.5)	38 (30.2 %)	23 (28.4 %)	0.786
Chronic kidney disease (n = 206)	8 (3.9)	4 (3.2 %)%	4 (3.2 %)	0.509
Admission during COVID (n = 200)	90 (45.0 %)	56 (46.3 %)	34 (43.0 %)	0.652
Yes	110 (55.0 %)	65 (53.7 %)	45 (57.0 %)	
No				
Drugs taken during COVID-19 infection				
Steroid intake(n = 202)	131 (64.9 %)	81 (65.9 %)	50 (63.3 %)	0.710
Ivermectin intake (n = 199)	152 (76.4 %)	96 (78.7 %)	56 (72.7 %)	0.335
Antibiotics intake (n = 200)	173 (86.5 %)	108 (87.8 %)	65 (84.4 %)	0.495
Zinc intake (n = 201)	170 (84.6 %)	107 (87.0 %)	63 (80.8 %)	0.234
Ayurveda medications (n = 190)	109 (57.4 %)	69 (54.3 %)	40 (63.5 %)	0.229
Inhalational O_2 given (n = 200)	79 (39.5 %)	47 (38.5 %)	32 (41.0 %)	0.724
Steam inhalation (n = 180)	123 (68.3 %)	70 (64.8 %)	53 (73.6 %)	0.214
Gargling (n = 179)	104 (58.1 %)	58 (54.2 %)	46 (63.9 %)	0.198
Baseline investigations				
Total WBC Count (n = 204)	11,550.17 ± 11,817.55	10,638.96 ± 5573.34	12,991.97 ± 17,625.07	0.167
Neutrophil (n = 204) %	73.48 ± 11.046	73.20 ± 10.976	73.92 ± 11.212	0.649
Lymphocyte (n = 204) %	17.175 ± 10.0045	17.509 ± 10.3753	16.646 ± 9.4286	0.550
CD4 count (n = 167)	538.43 ± 233.404	536.33 ± 238.349	541.72 ± 227.220	0.885
Fasting blood sugar (n = 206)	184.20 ± 87.597	191.39 ± 95.230	172.88 ± 73.143	0.140
Total Protein (n = 204)	6.655 ± 0.8863	6.683 ± 0.8723	6.610 ± 0.9117	0.567
Albumin (n = 204)	3.099 ± 0.5044	3.094 ± 0.5259	3.108 ± 0.4714	0.847
Serum glutamic-oxaloacetic transaminase (n = 204)	40.267 ± 32.1565	40.259 ± 34.3758	40.278 ± 28.5055	0.997
Serum glutamic-pyruvic	45.065 ± 32.3662	44.850 ± 32.1088	45.405 ± 32.9726	0.905

(*continued on next page*)

Table 1 (*continued*)

Characteristics	Total	Positive	Negative	p-value
transaminase (n = 204)				
Serum Creatinine(n = 204)	1.109 ± 0.9021	1.116 ± 0.9359	1.099 ± 0.8518	0.894
Serum Ferritin (n = 166)	126.7550 ± 161.85323	147.5863 ± 172.86456	97.4704 ± 141.02900	0.049
HbA1c (n = 201)	10.1626 ± 2.56382	10.4528 ± 2.55264	9.7049 ± 2.53030	0.044

exenteration in 48, and palatal surgery in 23 patients. The mean duration of follow-up of patients who expired was 21.11 ± 21.95 days, while among those who survived, it was54.41 ± 20.35 days. At three months follow up, 60 (28.8 %) patients died, 4 (1.9 %) patients stopped treatment, whereas 144 (69.23 %) were on treatment. Thirty-three (55 %) patients died within 15 days of admission. The risk factors for mortality are given in Table 2. At 6 months follow-up, eight more patients died, 3 due to chronic kidney disease, 4 patients who had stopped treatment and one patient who was on ventilator due to COVID-19 associated pneumonia and 140(67.3 %) were survived. All patients who were surviving had weight loss, 85 % received at least one dose of COVID-19 vaccine, and only 7 % had uncontrolled blood sugar levels.

4. Discussion

Uncontrolled diabetes mellitus is the most common underlying risk factor for CAM in the patients admitted to our tertiary care hospital (96 %), similar to other studies from India, varying between 66 and 80 %.[17–19] The postulated mechanism is that hyperglycemia increases the expression of glucose-regulated 78 kDa protein (GRP78) on the human endothelial cell and the spore coat protein (CotH) of Mucorales, which binds with it and results in vascular invasion and damage to nasal epithelial cells.[20–22]

Our patients were predominantly male with uncontrolled diabetes. Almost 42.3 % of our patients were recently diagnosed with diabetes either during their COVID-19 or mucormycosis illness. The result is similar to the other studies from India, showing that 42 % of the individuals in India with diabetes remain undiagnosed and almost 76 % of patients have poor glycemic control.[23,24]With the second-highest number of diabetics in the world, India should focus on public awareness for early diagnosis and strict control of diabetes to prevent the resurgence of mucormycosis cases in the future.

A total of 169 (79.23 %) enrolled patients had symptoms of COVID-19 before the onset of mucormycosis symptoms, but 26 % (n = 54) did not get themselves tested. This suggests that asymptomatic COVID-19 infections could also predispose to mucormycosis and there was under-testing among patients during the second wave of COVID-19 in India. The government of India started the second phase of COVID-19 vaccination on 1st March, 2021 in which, people above 60 years of age and those above 45 with comorbidities were eligible for vaccination, making almost all our patients eligible.[25] Despite this, 84.13 % (n = 175) of our patients did not receive any vaccine dose which point towards vaccine hesitancy in this cohort.

Studies have reported the susceptibility of SARS-CoV-2 infection with the ABO blood group.[26] They have reported that the people with blood group A have a high risk for infection compared to reduced risk in blood group O.[26]The frequency of blood group A, B, O and AB in our CAM patients was 29.5 %, 18.9 %, 38.9 % &12.6 % respectively. On comparing our data with that of a recent systematic review showing the blood group distribution in India, it was observed that blood group A (p value 0.039) and AB (p value <0.001)was significantly high and blood group B (p value 0.001) was significantly less in our CAM cases as compared to general population.[27] The low frequency of B blood group in our patients needs to be evaluated further in a larger study to explore

Fig. 1. Growth of *Rhizopus arrhizus* on SDA.

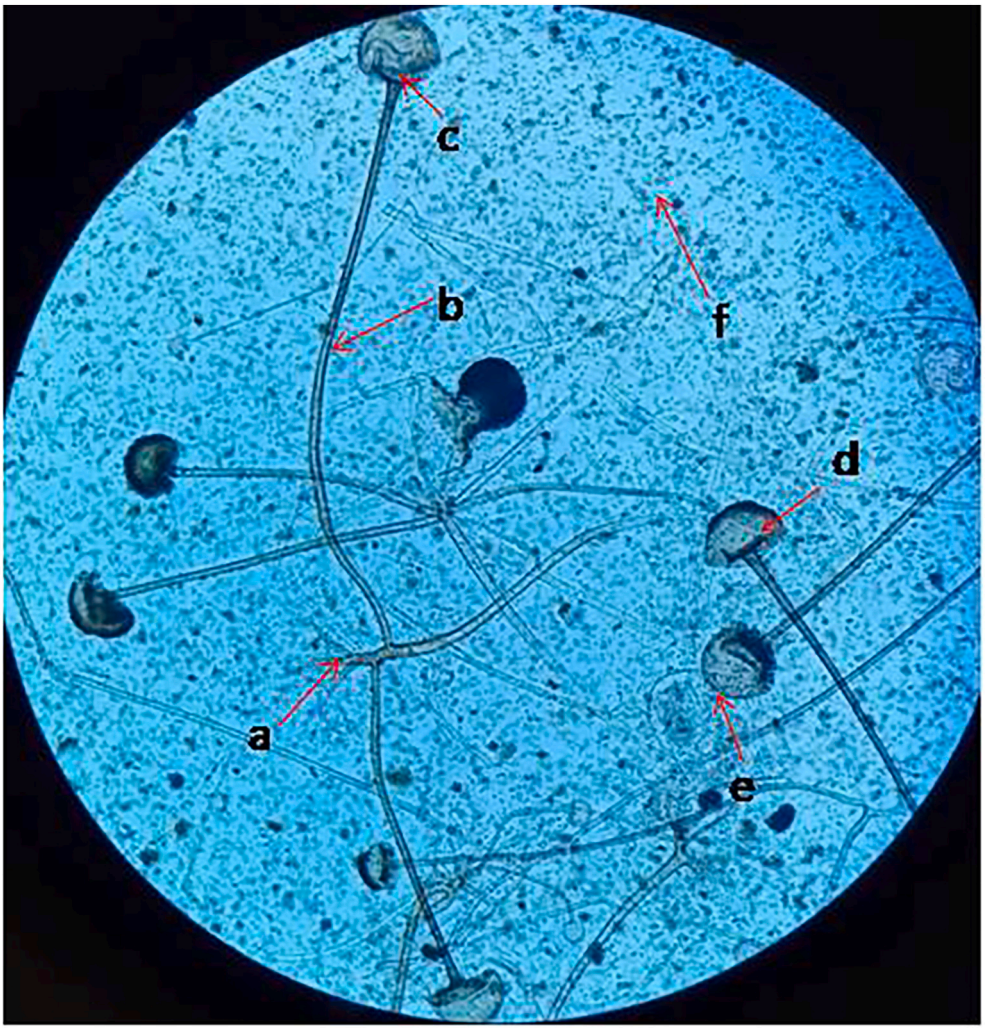

Fig. 2. *Rhizopus arrhizus* on LCB wet mount showing Rhizoid (a), Sporangiophore (b), Apophysis (c), columella (d), sporangium (e), multiple small sporangiospores (f).

any association between blood group and CAM.

During their COVID-19 illness, 39.5 % of patients required oxygen inhalation however, 64.9 % received steroids suggesting widespread misuse of steroids during the second wave of COVID-19. Similar results were seen in a systematic review of CAM cases where it was observed that inappropriate use of steroids was much higher in India than the rest of the world.[19] Even the National guidelines of May 2021 recommended that low dose steroids could be given in mild cases if there was persistent fever or cough, even in patients without hypoxia.[28] Corticosteroids are known to increase the risk of mucormycosis both by increasing hyperglycemia and impairing the phagocytosis of fungi.[29]

86.5 % of the patients were treated with antibiotics for COVID19 symptoms. Inappropriate antibiotic use had been rampant during COVID-19.[30] Antibiotics like azithromycin was also recommended by the Indian National guidelines in the first wave of COVID-19 pandemic.[31] The nasal microbiome inhibits the adhesion and invasion of *Rhizopus*, thus antibiotics by altering the microbiome, promotes fungal growth and its subsequent invasion.[32,33]

Almost 84.6 % of our patients took zinc supplementations during their COVID-19 illness. Although it was not recommended in treatment guidelines, its use was common practice during that period as studies suggested direct and indirect antiviral properties of zinc.[34,35] Zinc deficiency induces stress in fungal cells and hampers fungal development; zinc chelation is being explored as a treatment strategy for Mucorales.[36] On the other hand, zinc supplementation could potentially propagate the growth of Mucorales, which needs to be further explored. Ivermectin was another drug prescribed and recommended by guidelines for COVID-19,[28] 76.4 % of our patients had taken it.

Only 23.53 % of the patients had disease limited to the nose and sinuses, suggesting that most of our patients reported late. This delay could be due to a lack of awareness among health care workers about the disease or a delay in health-seeking behavior among patients.

The overall mortality at 6 months in our patients was 32.7 %, similar to that of the recent systematic review from India and much lower than 61.9 % of globally reported CAM cases.[18]Almost 55 % of patients died within the first 15 days of admission and 88.23 % within three months. Only eight patients died after three months and most of the deaths between 3 and 6 months were due to chronic kidney disease and in those who had stopped treatment. Our patients did not have any underlying immunosuppression but had diabetes, antibiotics, zinc as a risk factors leading to rhino-orbital-cerebral form of the disease. Thus, discontinuation of unnecessary drugs, correction of hyperglycemia, and radical debridement of infected tissue along with the availability of free treatment facilities in the hospital could have led to lesser mortality.

At three months mortality was significantly associated with higher age, and SARS-CoV-2 RT-PCR positive, suggesting active viral infection. It was also high in those with raised serum creatinine levels and raised alkaline phosphatase during treatment, which could be explained by an inability to give adequate doses of conventional amphotericin B and posaconazole. The patients who presented with facial pain and blindness

Table 2
Comparison of patients who survived with those who expired at three months.

	Expired (n = 60)	Survived (n = 148)	p-value
Age (years)			0.048
>50	41 (68.3 %)	79 (53.4)	
<50	19 (31.7 %)	69 (46.6)	
Mean ± SD	56.28 ± 13.34	51.45 ± 11.26	0.009
SARS-CoV-2 RT-PCR positivity at admission	22 (36.7)	14 (9.5)	<0.001
Duration of follow-up in days	21.11 ± 21.95	54.41 ± 20.35	<0.001
IgG Ab against SARS-CoV-2	997.80 ± 1411.83	3264.79 ± 10,413.28	0.749
Duration of diabetes	7.51 ± 5.27	6.60 ± 4.81	0.341
CD4 + T cell count	525.44 ± 215.949	543.22 ± 240.195	0.664
Number of patients receiving Inhalational O2	29 (50.0 %)	50 (35.2 %)	0.052
Patients presenting as facial pain	56 (93.3 %)	142 (95.9)	0.425
Patients presenting as blindness	4 (6.7 %)	38 (25.7 %)	0.002
Patients having serum creatinine (mg/dl)	9 (15.0 %)	10 (6.9 %)	0.071
>1.5	51 (85.0 %)	134 (93.1 %)	
<1.5			
Mean serum creatinine (mg/dl)	1.285 ± 1.0932	1.036 ± 0.80	0.072
Mean Serum Ferritin (ng/ml)	189.02 ± 212.43	110.71 ± 142.69	0.011
Mean Alkaline phosphatase (IU/L)	777.75 ± 409.30	399.80 ± 357.62	0.047

were more likely to survive as it may have led to early health-seeking behavior leading to diagnosis and treatment.

To conclude misuse of steroids, antibiotics, and zinc supplementation during SARS-CoV-2 infection in the background of uncontrolled hyperglycemia could have precipitated this epidemic within the COVID19 pandemic. Early diagnosis of diabetes with adequate control of hyperglycemia would go a long way in decreasing the future incidence of mucormycosis. Despite the massive surge of cases leading to overburdening of the health system, six months mortality in our cohort was low.

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CRediT authorship contribution statement

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Role:Conceptualisation, Data collection, managing patients
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Role: Formal analysis, Methodology, Diagnosis, Software, Writing – original draft
14. Tuhina Banerjee
Role: Formal analysis, Methodology, Software, Writing – original draft
15. Neeraj Kumar Agrawal
Role:Conceptualisation, Data collection, managing patients
16. Ravi Shankar Prasad
Role: Conceptualisation, Data collection, managing patients

Ethical statement

The Institute Ethics Committee (ECR/526/Inst/UP/2014/RR-20 dt 19.5.20) approved the study protocol.

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