Int.J.Curr.Microbiol.App.Sci (2024) *13*(06): 69-77

International Journal of Current Microbiology and Applied Sciences
ISSN: 2319-7706 **Volume 13 Number 6 (2024)**
Journal homepage: http://www.ijcmas.com

Original Research Article https://doi.org/10.20546/ijcmas.2024.1306.007

Incidence of Mucormycosis, An Invasive Fungal Infection and its Relation with Covid-19 in A Tertiary Care Centre in Jammu

Perika[1], Priyanka Sharma[2]*, Suharshi Gupta[3], Sikander Chairag[4], Shashi Sudhan Sharma[5] and Mukesh Kumar[6]

[1]Medical Officer, Department of Microbiology, GMC Jammu, India
[2]Lecturer, Medical Officer, Department of Microbiology, GMC Jammu, India
[3]Medical Officer, Co-PI, VRDL, Department of Microbiology, GMC Jammu, India
[4]Assistant Professor, Department of Microbiology, GMC Jammu, India
[5]Prof. and Head, PI. & Nodal Officer, VRDL, Department of Microbiology, GMC Jammu, India
[6]Lab.Technician, Department of Microbiology, GMC Jammu, India

**Corresponding author*

Keywords

COVID-19, Mucormycosis, Immuocompromised, Invasive Fungal Infection

Article Info

Received:
20 April 2024
Accepted:
26 May 2024
Available Online:
10 June 2024

A B S T R A C T

Mucormycosis, an invasive fungal infection has been seen to affect a large number of COVID-19 patients due to the overdosage, panic and injudicious use of corticosteroids among COVID-19 patients and presence of diabetes as a risk factor increases the chances of getting COVID-19 infection. The combination of Mucormycosis and COVID-19 infection has posed a double health threat to a collapsing healthcare system in India. Hence, the present study was conducted to study the incidence of Mucormycosis and its relation with COVID-19 so that awareness among the public can be generated and appropriate steps could be planned to combat the syndemic of COVID-19 and Mucormycosis. In our study, a total of 30 cases of Mucormycosis were reported, out of which Rhinocerebral Mucormycosis (RCOM) was the most common type 25(83.3%). Among the cases, 20 (66.6%) were male and 10 (33.33 %) were female. Maximum cases- 15 (45.8%) were in 51-60 years age group and among the cases, 18 (75%) were COVID positive. The present study was planned so that early diagnosis of such cases could be done, which would further help in providing appropriate treatment and hence subsequent reduction of morbidity and mortality.

Introduction

Mucormycosis is an acute opportunistic infection caused by several fungi belonging to phylum Glomeromycota. These saprotrophic fungi are found ubiquitously in the soil and environment. Mucormycosis is the third most common invasive fungal infection with high morbidity and mortality following Aspergillosis and Candidiasis (Ribes *et al.,* 2002). In the past these were rather treated as fungal contaminants in the diagnostic microbiology laboratory. But in today's scenario these are now emerging pathogenic organisms invariably entailing to

fatal consequences especially when an obvious underlying predisposing factor exists in a particular clinical setting. This rising trend in infectious cases may be due to increased awareness, advances in diagnostic techniques, and the increase in the prevalence of predisposing factors (Prakash *et al.,* 2019). The cases are being increasingly reported among healthy individuals also where no obvious underlying risk factor is present.

In the tissue, these fungi are seen as broad, non-septate hyphae. Several species which are included in the order Mucorales are involved in rhino cerebral, pulmonary, cutaneous, and gastrointestinal and other less frequent infections in immunocompetent and immunocompromised individuals and all have a tendency to disseminate. In India Rhino-orbital-cerebral (ROCM) is the most common form based on clinical presentation, because of its possible association with uncontrolled diabetes and diabetic Ketoacidosis. They have predilection to invade blood vessels being Angioinvasive in nature thereby leading to extensive necrosis of the surrounding area and forming embolism. Since morphology of all these organisms is indistinguishable in histopathological sections, hence culture is essential for an exact identification of the causative fungal species.

Transmission of the disease is linked to either by inhalation of the spores or by direct inoculation of the spores into disrupted skin or mucosa. The course and outcome of the disease differs according to anatomical site affected as well as nature of fungal species involved in a particular patient. Unlike other fungal diseases, even the AIDS pandemic could not significantly affect the incidence and prevalence of mucormycosis during last 3.5 decades.

The major risk factors implicated in causing mucormycosis include uncontrolled diabetes, diabetic ketoacidosis, prolonged steroid therapy, persistent neutropaenia, haematological malignancies, illicit use of intravenous drugs, autoimmune disorders, Voriconazole prophylaxis, breach of cutaneous or mucous membrane barrier due to trauma, burns and surgical wounds (Chakrabarti and Singh, 2011; Mantadakis and Samonis, 2009). Also, cases of Mucormycosis may be seen even in patients with no underlying disease (Chakrabarti and Singh, 2011; Mantadakis and Samonis, 2009). However, upsurge in the number of diabetics has really changed the entire scenario more or less like an epidemic in Southeast Asia posing a very serious health threat. There has been an alarming rise in the number of mucormycosis cases from developing countries including India and most common infection is common in patients with uncontrolled diabetes, in contrast to patients with hematological malignancies and transplant recipients of developed countries (Kontoyiannis *et al.,* 2016). There is a considerable variation in the presentation of mucormycosis between the developing and the developed nations, with differences in the prevalence, risk factors and causative agents involved (Chakrabarti *et al.,* 2009; Chakrabarti *et al.,* 2006; Chakrabarti *et al.,* 2001; Meis and Chakrabarti, 2009). Variations with respect to temperature, rainfall, humidity have also been seen in mucormycosis cases (Chakrabarti *et al.,* 2009; Chakrabarti *et al.,* 2006; Chakrabarti *et al.,* 2001; Meis and Chakrabarti, 2009).

Among the various agents causing Mucormycosis, *Rhizopus arrhizus* is the predominant agent Worldwide, whereas other etiological agents show a geographical variation. *Apophysomyces variabilis* is the second most common agent in India (Skiada *et al.,* 2011).

Even though awareness about the disease has been rising, early diagnosis of mucormycosis remains elusive due to difficulty in sample collection from deep tissues and absence of a specific biomarker. Polymerase Chain Reaction (PCR) for early diagnosis of mucormycosis has shown good results in recent years, but no standardized commercial kit is available for routine use (Prakash *et al.,* 2019).

COVID-19 Pandemic which had its origin in Dec 2019 in Wuhan City of China, has created huge havoc and devastation and India is in the midst of a grim battle with the deadly second wave of COVID-19 pandemic and is also gearing itself up to fight third COVID-19 wave as predicted by the experts. Recently, Mucormycosis cases (BLACK FUNGUS) have been detected very frequently among COVID-19 patients.

While cases are on the rise, there has been no documented outbreak of BLACK FUNGUS so far. It is possible that mucormycosis which has an overall mortality rate of 50%, may be being triggered by the use of steroids, a life-saving treatment for severe and critically ill COVID-19 patients.

Steroids reduce inflammation in the lungs for COVID-19 and appear to help stop some of the damage that can happen when the body's immune system goes into over drive to fight off Coronavirus. But they also reduce

immunity and push up blood sugar levels in both diabetics and non-diabetic COVID- 19 patients. It's thought that this drop in immunity could be triggering these cases of mucormycosis.

Hence, considering the present scenario the present study was done to see the relation between increasing mucormycosis cases and COVID-19 so that timely detection of such mucormycosis cases could be done and accordingly manage the patients and prevent the development of complications.

Materials and Methods

The present study was conducted in the MYCOLOGY section, Department of Microbiology GMC, Jammu over a span of 8 months.

Samples of suspected Mucormycosis cases admitted in various wards of GMC, Jammu were obtained in the Mycology Lab, Dept. of Microbiology, GMC Jammu.

Study Groups

Majority of patients included in the study were adults admitted in various clinical departments with a high index of clinical suspicion of Mucormycosis. Majority of the enrolled individuals were diabetic and on steroid therapy.

Defined Parameters

Case histories of the patients were analysed regarding the site of involvement, underlying disease, COVID-19 status, clinical course, mode of diagnosis, agents isolated, treatment instituted, and outcome of the disease. The diagnosis of mucormycosis was confirmed by the presence of broad aseptate/ sparsely septate, ribbon like hyphae with right angled branching. Patients with a clinical suspicion of mucormycosis but without mycology or histopathology confirmation were not included.

Sample Processing

Testing of Samples in the MYCOLOGY lab included direct KOH mount examination, fungal culture on Sabourauds's Dextrose Agar (SDA). Direct demonstration of fungal elements in the clinical sample is essential for establishing diagnosis.

Microscopic examination of KOH mount (10-20% potassium hydroxide) were done to detect characteristic broad, sparsely septate, ribbon-like hyphae with wide-angle or right –angle branching at irregular intervals.

After confirmation by KOH mount, sample was inoculated onto two tubes of SDA with antibiotics and on two tubes without antibiotics, one tube from each set incubated at 37°C and 22°C. Cultures were examined for the growth daily for the first week and twice a week for the subsequent period. Fungal isolates were finally identified by conventional techniques like Lactophenol cotton blue mount (LPCB).

Results and Discussion

A Total of 129 samples were received for the Suspected cases of Mucormycosis.

Out of 129 samples processed, Mucor was seen in 30(23.2%) cases, Aspergillus - 33(25.58%) cases, Candida- 38(29.4%), Paecilomyces -2(1.55%) while in 26(20.1%) cases no growth was seen. (FIGURE 3).

Out of 30 cases of Mucormycosis diagnosed, 17 (56.66 %) were confirmed by culture on SDA, 10 (33.33%) were diagnosed by HPE, 2 (6.6%) were clinically diagnosed and 1 case was diagnosed both by culture and HPE (TABLE 1).

The present study showed that Rhinocerebral Orbital Mucormycosis (RCOM) was the most common type -25 (83.3%), Pulmonary in 1 (3.3 %) case and in 4 (13%) cases, type was not known (FIGURE 4).

Among the cases, 20 (66.6%) were male and 10 (33.33%) were female patients (FIGURE 5). District wise distribution of the cases showed that maximum cases were from Jammu District -23 (76.6%), 2 (6.6%) cases were found from Samba and Kathua and 1 (3.33%) case was found in the Districts of Kishtwar and Udhampur (FIGURE 6).

Age wise distribution of the cases showed that 15(45.8%) cases were in the age group of 51-60 years, 7 (20.8%) in 41-50 years while 2 (8.3%) cases were in the age groups of 30-40, 61-70, 71-80 and 81-90 years (FIGURE 7).

Among the cases diagnosed, 18(75%) were COVID positive while 6 (25 %) cases were COVID negative (FIGURE 8).

Since the start of COVID-19 pandemic in December 2019, India has experienced a detrimental surge of Coronavirus disease 2019 cases during its second wave with a total of 28, 996, 949 cases and 351 344 deaths as of June 2021, which is increasing with every passing day (WHO, 2021).

The sudden rise of COVID-19 cases is attributed to an interplay of various factors, such as the appearance and arrival of variants of concern like B.1.617.2, B.1. 1.7, B.1.351 and P.1, breach of standard public health protocols such as hand washing, wearing a mask and social distancing. Along with COVID-19 India has been experiencing an outbreak of Mucormycosis, a deadly fungal infection which has affected thousands of COVID-19 patients.

Black fungus has emerged as a public health concern in India, especially among COVID-19 patients and it was also declared as a Notifiable disease in accordance with the Epidemic Diseases Act of 1897 (Over 28,200 "black fungus" cases recorded In India, 2021).

In the present study ROCM was the most common form- 21 (87.5%) of Mucormycosis found. This is consistent with the studies done by Prakash *et al.,* (2019) and Patel *et al.,* (2019) in which ROCM was found in 63.9% cases and 67.7% cases respectively. ROCM mucormycosis has a very strong association with Diabetes Mellitus and in our study all the patients diagnosed were diabetic and on steroid therapy.

Our study showed a predominance of male population among the cases detected -14 (58.3%) as compared to female population 10 (41.6%). Similar results were seen in the studies done by Bala *et al.,* (2015) and Prakash *et al.,* (2019). Also, our study showed that that maximum cases 11(45.8%) were distributed in the age group of 51-60 years while studies by Bala *et al.,* (2015) and Prakash *et al.,* (2019) showed mean age as 45.5 and 40 years respectively.

In our study culture confirmation was seen in 18 (70.8%) cases, HPE confirmation in 5 (20.8%) cases while 2 (8.3%) cases were detected on clinical grounds. Study by Bala *et al.,* (2015) showed that culture was positive in 61 % cases and HPE was positive in 34.2 % cases.

Out of patients diagnosed, 22 (91.6%) survived showing a higher survival rate which is consistent with the studies by Bala *et al.,* (2015) (70.8%) and Prakash *et al.,* (2019) (65%). This higher survival rate is attributed to the cases being diagnosed easily and treatment in the form of Amphotericin B being provided on time.

Out of the cases diagnosed in our study, maximum 18 (75%) were COVID positive thereby posing a double health threat to healthcare system in India. Mucormycosis has a tendency to infect patients with a deprived level of immunity and COVID -19 patients are predisposed to immune dysregulation in the form of steroid treatment, presence of comorbidities including diabetes, cancer, kidney or heart disease thereby posing the threat of Mucormycosis in them (Bhat *et al.,* 2021). Hence, considering the relation of COVID-19 with mucormycosis cases, the present study was conducted with the objective of timely detection of such cases so that treated and management options can be taken as early as possible and the development of complications can be prevented.

Table.1 Showing the different methods of diagnosis of Mucormycosis cases

Culture(SDA)	**17**
Histopathological Examination (HPE)	**10**
Clinical	**2**

Figure.1A Showing LPCB Preparation from growth on SDA
Figure.1B Showing hyphae in KOH mount preparation

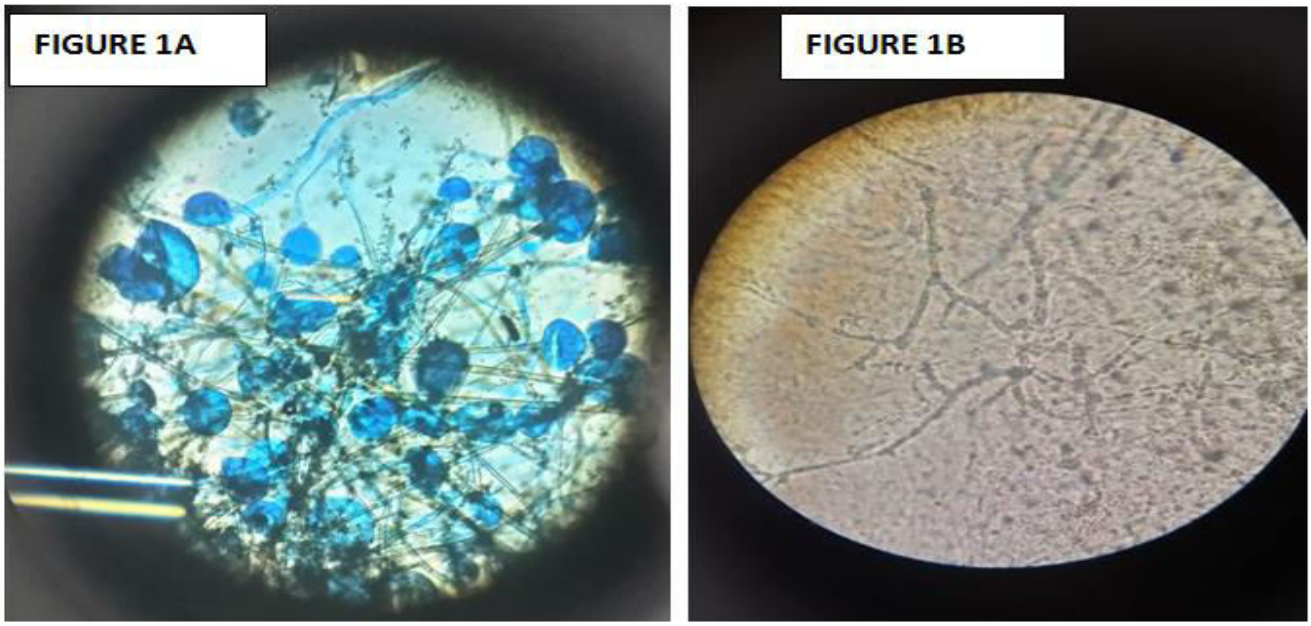


Figure.2 Showing growth of Mucor on SDA Slant

Figure.3 Showing distribution of different fungi obtained from different samples

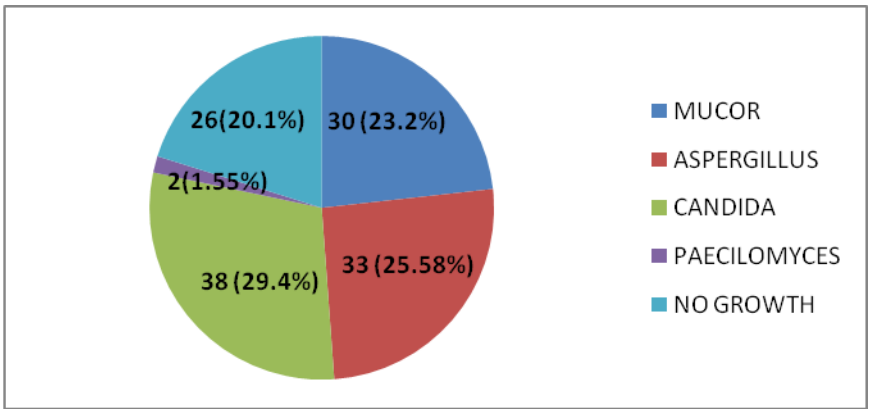


Figure.4

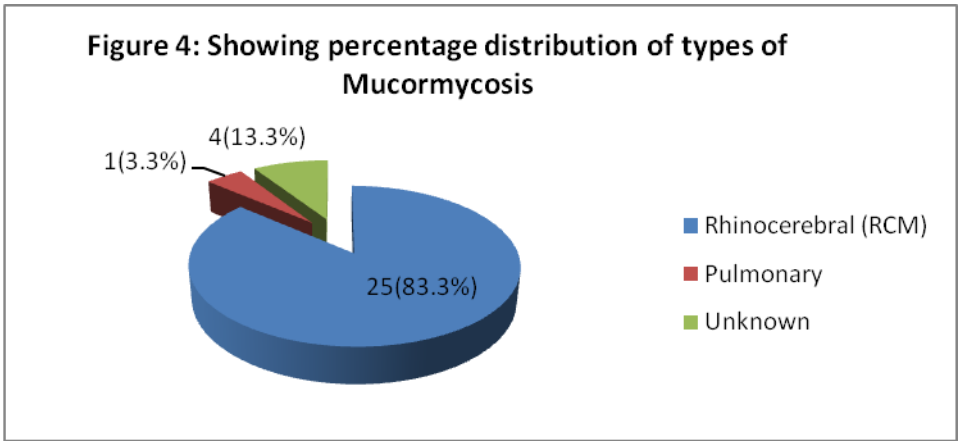


Figure.5

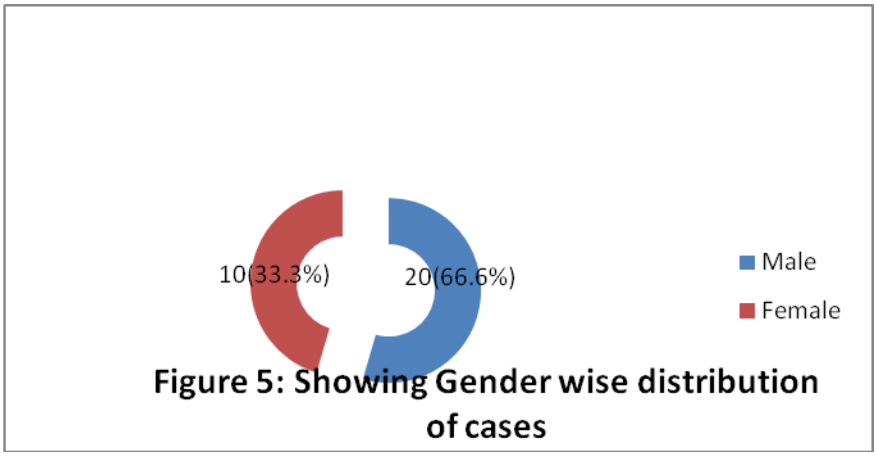


Figure.6 Showing District wise distribution of Mucormycosis cases

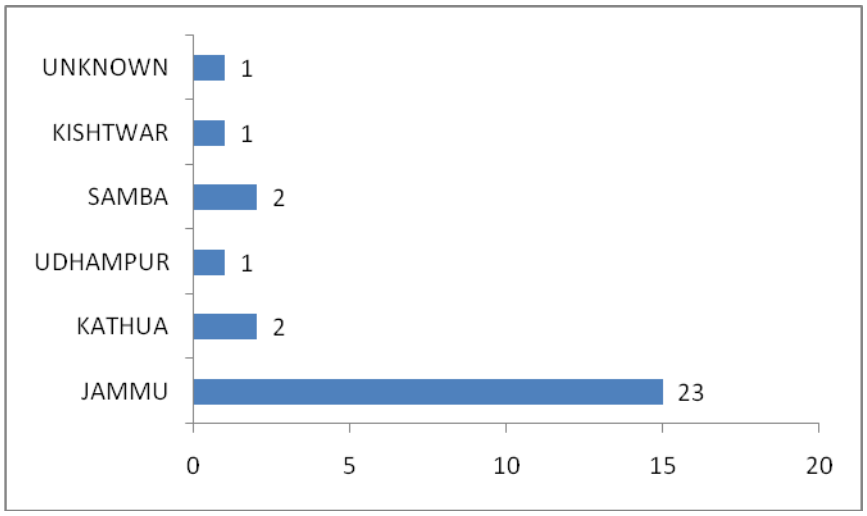


Figure.7 Showing Age distribution of the cases

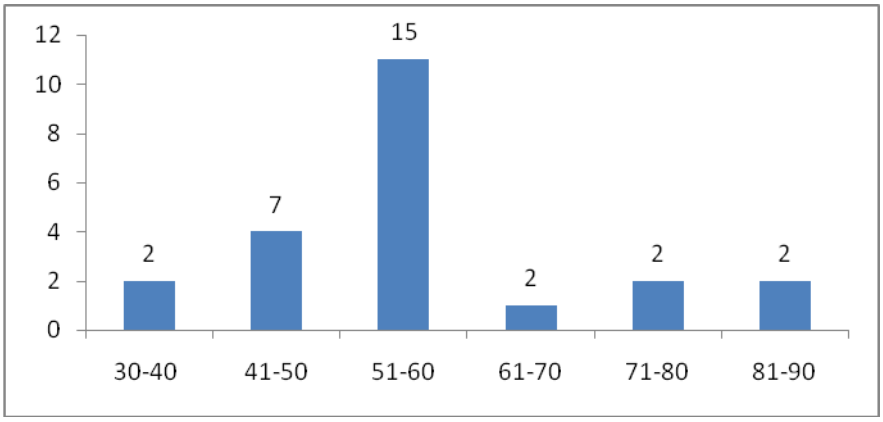
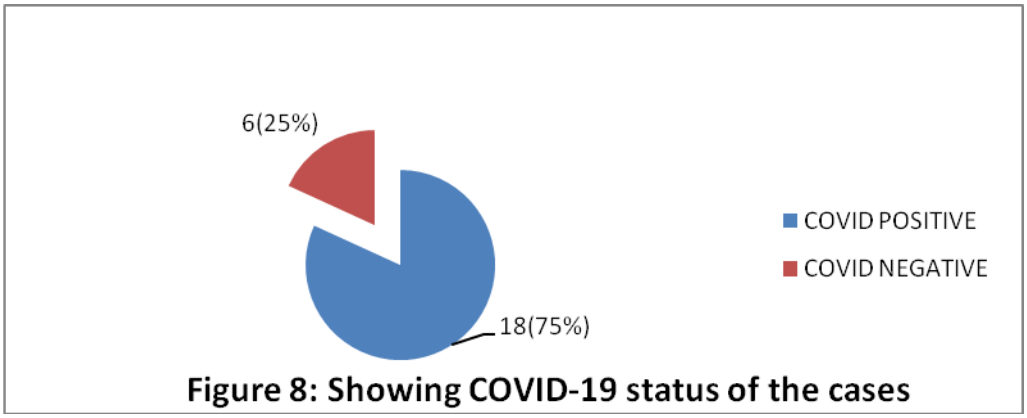


Figure.8



With the ongoing COVID-19 Pandemic cases of Mucormycosis infection with COVID-19 have been emerging, but as of now no major outbreak has been seen. This infection is most likely to occur in those on steroid therapy, diabetics and people with other comorbidities. COVID-19 infection is associated with immune dysregulation and the widespread use of steroids/monoclonal antibodies/ broad spectrum antibiotics further increases the patient's risk of getting fungal infection. It is imperative on the part of the physicians to be aware of such risk factors. Hence, the present study was planned so that early diagnosis of such cases could be done, which would further help in providing appropriate treatment and hence subsequent reduction of morbidity and mortality.

Author Contribution

Perika: Investigation, formal analysis, writing—original draft. Priyanka Sharma: Validation, methodology, writing—reviewing. Suharshi Gupta:—Formal analysis, writing—review and editing. Sikander Chairag: Investigation, writing—reviewing. Shashi Sudhan Sharma: Resources, investigation writing—reviewing. Mukesh Kumar: Validation, formal analysis, writing—reviewing.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

References

Bala K, Chander J, Handa U, Punia R S, Attri A K. A prospective study of mucormycosis in north India: Experience from a tertiary care hospital. *Int Soc Hum Anim Myc*. 2015; 53(3): 248-257. https://doi.org/10.1093/mmy/myu086

Bhat I, Beg M A, Athar F. A contemporary intimidation for COVID-19 patients coinfected with mucormycosis in India. *J Bacteriol Mycol Open Access* 2021; 9(2):69-71. https://doi.org/10.15406/jbmoa.2021.09.00298

Chakrabarti A, Chatterjee S S, Das A *et al.,* Invasive zygomycosis in India: experience in a tertiary care hospital. *Postgrad Med J* 2009; 85: 573–81. https://doi.org/10.1136/pgmj.2008.076463

Chakrabarti A, Das A, Mandal J *et al.,* The rising trend of invasive zygomycosis in patients with uncontrolled diabetes mellitus. *Med Mycol* 2006; 44: 335–42. https://doi.org/10.1080/13693780500464930

Chakrabarti A, Das A, Sharma A *et al.,* Ten years' experience in Zygomycosis at a tertiary care centre in *India. J Infect* 2001; 42: 261–6. https://doi.org/10.1053/jinf.2001.0831

Chakrabarti A, Singh R. The emerging epidemiology of mould infections in developing countries. *Curr Opin Infect Dis* 2011; 24: 521–6. https://doi.org/10.1097/QCO.0b013e32834ab21e

India: WHO Coronavirus Disease (COVID-19) Dashboard With Vaccination Data | WHO Coronavirus (COVID-19) Dashboard With Vaccination Data. (Available from: https://covid19.who.int/region/searo/country/in) [9 Jun 2021]

Kontoyiannis D P, Yang H, Song J *et al.,* Prevalence, clinical and economic burden of mucormycosis-related hospitalizations in the United States: a retrospective study. *BMC Infect Dis*. 2016; 16: 730. https://doi.org/10.1186/s12879-016-2023-z

Mantadakis E, Samonis G. Clinical presentation of zygomycosis. *Clin Microbiol Infect* 2009; 15(Suppl. 5): 15–20. https://doi.org/10.1111/j.1469-0691.2009.02974.x

Meis J F, Chakrabarti A. Changing epidemiology of an emerging Infection: zygomycosis. *Clin Microbiol Infect* 2009; 15(Suppl. 5): 10– 4. https://doi.org/10.1111/j.1469-0691.2009.02973.x

Over 28,200 "black fungus" cases recorded In India. (Available from: https://www.aa.com.tr/en/asia-pacific/over-28-200-black-fungus-cases-recorded-in-india/2266396) [9 Jun 2021]

Patel A, Kaur H, Xess I, Michael J S, Savio J, Rudramurthy S *et al.,* A multicentre observational study on the epidemiology, risk

factors, management and outcomes of mucormycosis in India. *Clin. Microbiol. Infect.* https://doi.org/10.1016/j.cmi.2019.11.021

Prakash H, Ghosh A K, Rudramurthy S M, Singh P, Xess I, Savio J *et al.,* A prospective multicenter study on mucormycosis in India: Epidemiology, diagnosis, and treatment. *Med Mycol.* 2019 Jun 1; 57(4):395-402. https://doi.org/10.1093/mmy/myy060

Ribes J A, Vanover-Sams C L, Baker D J. Zygomycetes in human disease. *Clin Microbiol Rev* 2002; 13: 236–301. https://doi.org/10.1128/CMR.13.2.236

Skiada A, Pagano L, Groll A *et al.,* Zygomycosis in Europe: analysis of 230 cases accrued by the registry of the European Confederation of Medical Mycology (ECMM) Working Group on Zygomycosis between 2005 and 2007. *Clin Microbio Infect*. 2011; 17: 1859–1867. https://doi.org/10.1111/j.1469-0691.2010.03456.x

How to cite this article:

Perika, Priyanka Sharma, Suharshi Gupta, Sikander Chairag, Shashi Sudhan Sharma and Mukesh Kumar. 2024. Incidence of Mucormycosis, An Invasive Fungal Infection and its Relation with Covid-19 in A Tertiary Care Centre in Jammu. *Int.J.Curr.Microbiol.App.Sci.* 13(6): 69-77. **doi:** https://doi.org/10.20546/ijcmas.2024.1306.007