Review Article

MUCORMYCOSIS AND IT'S ~~PREVELANCE~~ PREVALENCE IN THE PATIENTS OF COVID-19

ABSTRACT

The world today is going through a series of uncalled events, that has hindered the balance of livelihood in the current population. This is due to the emergence of the COVID-19 but along with that, the COVID-19 has accompanied several other rare and extremely fatal fungal infections under its shadows, such as the Mucormycosis. Mucormycosis is caused particularly in the immunocompromised hosts by the saprophytic fungi of Mucorales species. This infection leads to several clinical conditions, under the influence of the COVID-19 Associated Mucormycosis, commonly being the conditions such as the rhino-cerebral disease. This condition occurs mainly in ~~the~~ patients with diabetes mellitus. Several other respiratory, gastrointestinal, and cutaneous contaminations also occur during this condition. COVID-9 accompanied with diabetes mellitus can be extremely life threatening. Now, there are several predisposing factors to the Mucormycosis which could accompany the severity of the conditions such as ~~the~~ Ketoacidosis in the patients with diabetes mellitus, patients on ~~the~~ immunosuppressive therapies, previous pulmonary infections, and other nosocomial contaminations. There are no specific biomarkers available to diagnose Mucormycosis; Histopathological examination of the biopsied tissue and imaging of the involved area are most important in diagnosis. Mucormycosis being an angioinvasive fungus, usually is present in the surroundings with wet surfaces and dead and decaying vegetable matter. The term black fungus is used ~~as in~~ for the dematiaceous fungi, which are an entirely different group. Since the COVID-19 pandemic is on it~~'~~s massive widespread in the country, the new variant being more infectious, people are more tend to some other complications of the COVID-19 contamination such as that of the secondary fungal infections causing high mortality rates.

KEYWORDS: COVID-19, Mucormycosis, fungal infections, black fungus, histopathology, biomarkers, clinicopathological findings.

INTRODUCTION:

The cases of both Mucormycosis and the cases of Aspergillosis are scarce in the population, even though they are capturing and lethal infections. The specific agents that cause this infection mainly ~~being~~ are the Aspergillus fumigatus and the Rhizopus arrhizus species. Henceforth, the rate of lethality ~~being~~ is over 40%. [1]

The Rhizopus arrhizus infections, if noted, chiefly include the syndromes of the respiratory tract, the cutaneous, and the gastrointestinal tract. The rhino-orbital-cerebral is also included in this, Rhizopus arrhizus infections. In ~~the~~ severely immunocompromised patients, these extreme angio-invasive infections may spread and this then leads to ~~the~~ high fatality rates in the population.[2]

The sars-CoV-2 infection, so drastically changing itself, has several complications occurring in itself. A few of these complications that are ~~recognised~~ recognized and accepted are ~~the~~ Invasive Aspergillosis and Mucormycosis infections. The patients that are under the category of the severely affected by the Covid-19 are under the treatment for the same in the Intensive Care Units (ICU), the infections are mostly seen in these extremely ill patients.

The patients of invasive pulmonary aspergillosis, an infection caused during the same extreme conditions, ~~has~~ have been seen to have decreased in number in the cases of these COVID -19 patients that have been admitted in the ICUs, the stats being close to around 35% when noted. Turns out these cases of pulmonary aspergillosis have been kept on ~~a~~ closely linked with the corticosteroid therapy that has been provided ~~prior to~~before the infection.[3]

BLACK FUNGUS "a crisis in the pandemic".

The current crisis of COVID-19 has already affected the world to a far extent but under all of this current pandemic, there is a recent cataclysm evolving all over. This has been noted to be spreading at vast degrees throughout the country and causing unprecedented deaths, where~~-~~as the rapidly evolving and changing strains of the corona~~-~~virus ~~has~~ have already made the situation out of grasp. [4]

The Indian population ~~being~~ is unique in its socio-economic, healthcare and genetic status~~,~~ develops a certain high level~~l~~led incubator for the sustaining of the "black fungus" infection to achieve a powerful grasp. According to the health minister, there are around 2000 outlet cases of Mucormycosis in the state of Maharashtra itself. A term defined ~~to~~ as the "Perfect storm", basically the classic combination of Diabetes mellitus, the COVID-19, and immunosuppression, has shown an enormous upward ~~manoeuvre~~ maneuver in the country all over. Hence it can be noticeably said that within the global pandemic exists an underlying epidemic~~-~~, that is the "black fungus" (Mucormycosis)~~-~~.[5]

The results so far.

In an overall estimation, ~~till~~ to date, all around the world for Mucormycosis in patients with Corona infestation, out of the 101 cases registered, around 82 cases and 19 cases were from India and the rest of the world, respectively. Apparently in males, the Mucormycosis cases are more prevalent as compared to the females. In the males, in people who were currently infected with COVID-19 and the ones who had recovered the cases shown were 60% and 40% respectively. Around 76.3% of the cases were recorded that were formulated for the treatment of COVID-19 through ~~the~~ corticosteroid therapy.[6]

A case study of the Mucormycosis coinfection.

A study was made to do a further investigation for the COVID-19 and the Mucormycosis infestations during the same. Here, nine proclamations were made, apart from a certain case, rest all the other cases were found to have occurred in men in the age range 23-85 years of age. If we consider the different clinical forms of the Mucormycosis, the uppermost type was the rhino-orbital. Another clinical form considered after the rhino-orbital type is the pulmonary type, which is then noted as a chief clinical form for the Mucormycosis coinfection.[7]

Every year, the number of cases is reported ~~are~~ in just one of the either gastrointestinal or ~~the~~ rhino-orbital conditions. Included in the main subject ~~to~~ risk factors were ketoacidosis, use of the broad-stretch antibiotics and the glucocorticoids, diabetes mellitus. In addition to this, further main factors susceptible to high risks for the Mucormycosis infection in the respiratory tract were reported namely the ischemic cardiac myopathy, high blood pressure and ~~end~~ end-stage kidney diseases, and other renal disorders.[8]

The diagnosis for the mycosis was built mainly ~~on the basis of~~based on ~~the~~ histopathological investigations and culture analysis. Different methods were used for determining the clinical picture, in one of the cases, PCR and sequencing were used for detection whereas, in the other two cases, the methods of magnetic resonance imaging (MRI) were appraised for the detection and the finding out of the pathogen. Several pathogens were detected, the~~ir~~ etiological order in which they have been noted are in the following descending orders: Mucor spp., Rhizopus microspores, Rhizopus spp., and Lichteimia spp. In not less than 35 percent of the cases, the fungal species ~~was~~ were not identified. Nevertheless provided with so many options of several antifungal curative methods, such as amphotericin B and Isavuconazole~~.~~, just ~~the~~ half of the patients showed an~~y~~ improvement in ~~there~~ their clinical statistics. Hence the rate of lethality was considered to be around 50%.[9]

Culture is an essential technique for diagnosing mucormycosis since it may help identify the genus and species that caused the infection as well as evaluate antifungal susceptibility. Culture has ~~a~~ poor sensitivity~~,~~ since it might be mistakenly negative 50% of the time. When incubated at 25–55°C, Mucorales grows fast on most fungal culture medium, such as Sabouraud agar and potato dextrose agar, and this may be used to differentiate it from the closely related Aspergillus~~.~~. The hyphae are fibrous, resembling cotton candy. Light colo~~u~~r, generally yellow on the back of the plate, and colo~~u~~rful sporulating colonies ranging from white to black are further distinguishing characteristics. The presence of rhizoids, stolons, and columella on lactophenol cotton blue mounts can be used to distinguish between fungus species.[10]

A biopsy of the lesion can be collected and submitted for histological investigation, which will reveal Mucorales-like fungal hyphae. Fungal infiltration of blood vessels, vasculitis, thrombosis, tissue infarction, bleeding, perineural invasion, and a large neutrophilic infiltrate are all seen on histology Hematoxylin and eosin staining can sometimes reveal merely the cell wall, with no internal structures, or highly degenerate hyphae. The fungus can then be seen using special stains as Grocott-methenamine silver and periodic acid-~~schiff~~ Schiff stain.[11]

The fungus may be identified with high sensitivity using molecular approaches such as PCR-based techniques. The fungus can be detected early in the infection using a quantitative multiplex polymerase chain reaction-based 18S rRNA test. Internal transcribed spacer sequencing for molecular identification is strongly suggested as a future method.[12]

Nasal endoscopy and noncontrast CT of the paranasal sinuses are the first-line investigations for rhino-orbito-cerebral mucor, although gadolinium-enhanced MRI is preferable for identifying intra-orbital or intracranial extension. Mucormycosis is strongly indicated by sinus opacification, ~~localised~~ localized bone erosions, ~~extrasinus~~ extra sinks spread, the black turbinate sign (cavernous sinus involvement), and intracranial extension.[13]

Nodules or masses, halo sign, inverted halo sign (region of ground-glass opacity encircled by a ring of consolidation), consolidation, central necrosis, air-crescent sign, and blockage of pulmonary arteries on CT angiography are all signs of pulmonary mucormycosis.[14]

Early suspicion, quick diagnosis, and elimination of the predisposing conditions are essential for effective care of mucormycosis. The combination of surgical debridement of the lesion and early antifungal medication improves the clinical result. The rhino-oculo-cerebral type necessitates extensive surgical debridement of necrotic regions and surrounding tiny normal portions, with several procedures necessary in most instances. In a large majority of situations, this can result in an improvement.[15]

The treatment arsenal available includes amphotericin B, posaconazole, and isavuconazole, with amphotericin B being the most effective. Amphotericin B polyene liposomal is recommended over amphotericin B deoxycholate because it has less nephrotoxicity and intolerance. Amphotericin works against fungi by attaching to sterols, particularly ergosterol, which gives fungal cells structure and stiffness. It's best to give 5–10 mg/kg/day for at least 3 weeks and then titrate with PCR.[16]

However, the time can be adjusted based on the individual's reaction, and triazole maintenance can also be explored. 10 mg/kg dosages and prolonged treatments are required for CNS and disseminated types. The total cumulative dosage for the whole therapy should be 2.5–3 g in the ideal case. Amphotericin B deoxycholate is a feasible alternative since it is less expensive and more readily available. During treatment, serum potassium and kidney parameters must be constantly monitored.[17]

For individuals who are intolerant to amphotericin B, the triazoles posaconazole and isavuconazole are considered second-line and salvage treatment. Posaconazole has just been accessible in IV and oral forms, which may impact therapy in the future given that it is now only used in syrup form. It might also be used as a preventative measure. Posaconazole is usually taken in doses of 200 mg every 6 hours or 400 mg every 12 hours.[18]

Isavuconazole is still in its early phases of development and is thus not routinely prescribed, however its high bioavailability, linear pharmacokinetics, and broad-spectrum properties may make it more popular in the future. The current protocol is a loading dosage of 200 mg every 8 hours for two days, followed by 200 mg once a day.[19]

Mucormycosis has not been shown to be treatable with itraconazole, terbinafine, voriconazole, or caspofungin. Other therapeutic possibilities include hyperbaric oxygen, iron chelation with non-desferrioxamine chelators, and granulocyte-macrophage colony-stimulating factor.[20]

Incidences of Mucormycosis.

There had been recent reports of spreading out of the incidence of Mucormycosis from India that indicate these~~s~~ incidences occurring. The cases of Mucormycosis occur~~ring~~ more prominently in the COVID-19 patients. Mucormycosis can be fatal~~,~~ if the fungus species that causing the same penetrates ~~into~~ the central nervous system. These fungal species are ~~basically~~ filamentous fungi or, belong to the order Mucorales. The COVID-19 associated Mucormycosis (CAM) has been ~~on~~ at its maximum height ever since its invasion into the

country. Currently, Rhizopus arrhizus has proven to be the determiner and common etiological agent for the same. In India, a few cases had also shown the prevalence of etiological agents such as the Mucor irregularis, Rhizopus ~~microscopus~~microscopes, Saksenaea erythrospora, and the Rhizopus homothallic~~us~~. ~~Patients~~ For patients that are undergoing ~~an~~ immunosuppressive therapy and the patients with diabetes or the immunocompromised convalescents, the Mucormycosis infections are more customary. There had been many surveys regarding the prevalence of the cases of Mucormycosis in India. [21]

Among all these surveys the use of corticosteroids and ~~its~~ their significance in the covid patients along with the fatality of the Covid Associated Mucormycosis (CAM) were of main concern, each being 76.3% and 30.7% respectively. It is still uncertain whether the cases of Mucormycosis are worldwide or just ~~localised~~ localized to certain areas. A clear record has to be created of all such cases reported till now ~~in order~~ to carry forward the research regarding this matter. Although, when we consider India, there has been a certain conclusion that, the risk factors and the extreme lengths of the widespread presence of CAM in India ~~is~~ are mainly due to the faultily managed diabetes patients and the very long use of ~~the~~ steroids for the treatment of the COVID-19 patients. [22]

As if now, in several patients, all over the country and the world, suffering from COVID-19 associated pneumonia, the use of steroids for the effective treatment of the same has been very common. Now due to this prominent use of certain steroids, the secondary fungal contaminations are being observed on an elevated scale of high risks. This can further lead to fatality and a substantial increase in ~~the~~ death rates. Talking about death rates, the fact that India has been beholding a steep rise to the COVID-19 incidences and has maintained its position of the increasing fatality rates is a matter of concern. It has been very difficult to manage the COVID-19 pandemic chiefly because of the different critical aspects and the risk factors, mainly, the aspects of pneumonia and pulmonary thrombosis. The reason why there is an augmented or expanding increase in the COVID-19 cases is because of a lack of awareness in the population for ~~the~~ corona prevention. [23-27]

COVID 19 has been a particularly challenging pandemic to contain, because ~~to~~ of the high rates of pneumonia and thrombosis. Since the beginning of the COVID pandemic in December 2019, secondary infections of both bacterial and fungal types have been detected. Following natural catastrophes such as the tsunami in India in 2004 or the tornado in Missouri in 2011, mucormycosis has been reported to rise in prevalence. Fungal infection was the leading cause of mortality in individuals with severe acute respiratory syndrome during the SARS-CoV pandemic in 2003, accounting for 25%–73.7 percent of deaths.[28-29]

The exponential surge during the coronavirus epidemic, on the other hand, was unprecedented. Patients were mostly treated with home isolation and, in a few cases, steroids during the initial wave. However, many patients in the second wave required greater doses of steroids for longer periods ~~of time~~, as well as high-flow oxygen for extended periods ~~of time~~ owing to hypoxia. Mechanical ventilation was necessary for a far larger number of patients.[30]

Diabetes ~~as~~ is a common comorbidity, pre-existing ~~alveolo~~alveolar-interstitial lung disease, increased use of steroids and other immunosuppressives, covid pneumonia, increased chances of nosocomial infection, prolonged ICU stays, ~~hospitalisation~~hospitalization, mechanical ventilation, and immune alterations caused by Covid-19 infection have all contributed to the rise in mucormycosis cases. The main risk is certainly diabetes, which is a predisposing factor for not just fungal infections but also more serious covid infections. ~~Diabetes that is~~

~~uncontrolled~~Uncontrolled diabetes raises the risk by a factor of ten. Another issue with diabetes is renal involvement.[31-37]

CONCLUSION:

In conclusion, we believe that ~~analysing~~ analyzing and ~~reanalysing~~ reanalyzing the data collected from the patients of COVID-19, the type of infection, the risk factors involved, and the methods of treating these fungal infections come in handy during the COVID-19 treatment. The prevalence of Covid Associated Mucormycosis is expectedly high in India. In an overall survey conducted, it has been that the mortality rate of the cases outlined from India ~~were~~ was no less than 36.5% which when noted, was comparatively less than the cases extensively reported at the global level which is around 70%. This might be probably due to the preponderance of the rhino-cerebellar Mucormycosis. There had been several surveys conducted so far, out of these the most multiresolution scrutiny or examination, it has been that pulmonary or the promulgated Mucormycosis cases and the registered cases to the Intensive Care Units are interrelated with an elevated ~~the~~ level~~s~~ of fatality, whereas the intermixed medical therapy into a combination has boosted up the rate as well as the chances of survival. It has been noticed that the reason why there is a rarity in the cases of pulmonary or propagated Mucormycosis cases from India is ~~because~~ that there are not any registered cases of a lot many COVID-19 Associated Cases either because they were not diagnosed or because they were not reported sooner. Further, with help of a lot, many researched articles ~~coming~~ conclude~~to a conclusion~~ that there is an elevated and ~~an~~ extremely sizeable and meaningfully significant rise in the cases of the COVID-19 Associated Mucormycosis. Hence, Mucormycosis solely has been an effective cause of high risks in the patients of the COVID -19. Since it has been known that the Mucormycosis is a very probable threat to the life ~~for~~ of the people who are already suffering from the COVID-19, hence, it must require ensured care and proper facilities for the management of such patients belonging in the Intensive Care Unit facilities. The management of these patients also requires large-scale surgical processes and also at the very most a dragged out and ~~a~~ very protracted medical therapy with the amphotericin-B. Now, even though we know that there is a certain correlation between the COVID-19 and Mucormycosis being a risk factor for the same, still we do not have a lot many research studies and records proving the same and showing this existing correlation in the patients. ~~In order t~~To have a proper record regarding this fungal infestation, Mucormycosis, during the COVID-19 the government needs to maintain the proper records for the patients that are registered in ICU facilities and all the samples collected needs to be arranged sequentially, followed by a histopathological laboratory diagnosis for the identification of the fungus associated and a CT scan. Apart from that, this routine has to be followed by providing the patients with proper antifungal medications and the competence of a surgical expert alongside the operative facilities. A managed and equitable distribution of the resources for the COVID-19 support has to be managed ~~in order~~ to decrease the fatality rates of the patients.

Comment [BK1]: Is it conclusion? How? Please just add you results and conclude as finalize your paper

REFERENCES:

1. Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: a systematic review of cases reported worldwide and in India. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2021 May 21.
2. Mishra N, Mutya VS, Thomas A, Rai G, Reddy B, Mohanan AA, Ray S, Thiruvengadem AV, Siddini V, Hegde R. A case series of invasive mucormycosis in

patients with COVID-19 infection. Int J Otorhinolaryngol Head Neck Surg. 2021 May;7(5):867-70.
3. Patel A, Agarwal R, Rudramurthy SM, Shevkani M, Xess I, Sharma R, Savio J, Sethuraman N, Madan S, Shastri P, Thangaraju D. Multicenter epidemiologic study of coronavirus disease–associated mucormycosis, India. Emerging infectious diseases. 2021 Sep;27(9):2349.
4. do Monte Junior ES, Dos Santos ME, Ribeiro IB, de Oliveira Luz G, Baba ER, Hirsch BS, Funari MP, De Moura EG. Rare and fatal gastrointestinal mucormycosis (Zygomycosis) in a COVID-19 patient: a case report. Clinical endoscopy. 2020 Nov;53(6):746.
5. Al-Tawfiq JA, Alhumaid S, Alshukairi AN, Temsah MH, Barry M, Al Mutair A, Rabaan AA, Al-Omari A, Tirupathi R, AlQahtani M, AlBahrani S. COVID-19 and mucormycosis superinfection: the perfect storm. Infection. 2021 Jul 24:1-21.
6. Selarka L, Sharma S, Saini D, Sharma S, Batra A, Waghmare VT, Dileep P, Patel S, Shah M, Parikh T, Darji P. Mucormycosis and COVID- 19: An epidemic within a pandemic in India. Mycoses. 2021 Oct;64(10):1253-60.
7. Kumar M, Sarma DK, Shubham S, Kumawat M, Verma V, Singh B, Nagpal R, Tiwari RR. Mucormycosis in COVID-19 pandemic: Risk factors and linkages. Current Research in Microbial Sciences. 2021 Dec 1;2:100057.
8. Maini A, Tomar G, Khanna D, Kini Y, Mehta H, Bhagyasree V. Sino-orbital mucormycosis in a COVID-19 patient: A case report. International Journal of Surgery Case Reports. 2021 May 1;82:105957.
9. Pal P, Singh B, Singla S, Kaur R. Mucormycosis in COVID-19 pandemic and its neurovascular spread. European Archives of Oto-Rhino-Laryngology. 2021 Oct 12:1-8.
10. Mahalaxmi I, Jayaramayya K, Venkatesan D, Subramaniam MD, Renu K, Vijayakumar P, Narayanasamy A, Gopalakrishnan AV, Kumar NS, Sivaprakash P, Rao KR. Mucormycosis: An opportunistic pathogen during COVID-19. Environmental Research. 2021 Jul 6:111643.
11. Ravani SA, Agrawal GA, Leuva PA, Modi PH, Amin KD. Rise of the phoenix: Mucormycosis in COVID-19 times. Indian journal of ophthalmology. 2021 Jun 1;69(6):1563-8.
12. Bhogireddy R, Krishnamurthy V, Pullaiah CP, Manohar S. Is Mucormycosis an inevitable complication of Covid-19 in India?. Brazilian Journal of Infectious Diseases. 2021 Oct 1;25.
13. Ghazi BK, Rackimuthu S, Wara UU, Mohan A, Khawaja UA, Ahmad S, Ahmad S, Hasan MM, dos Santos Costa AC, Ahmad S, Essar MY. Rampant increase in cases of mucormycosis in India and Pakistan: a serious cause for concern during the ongoing COVID-19 pandemic. The American Journal of Tropical Medicine and Hygiene. 2021 Aug 30;1(aop).
14. Mekonnen ZK, Ashraf DC, Jankowski T, Grob SR, Vagefi MR, Kersten RC, Simko JP, Winn BJ. Acute invasive rhino-orbital mucormycosis in a patient with COVID-19-associated acute respiratory distress syndrome. Ophthalmic plastic and reconstructive surgery. 2021 Mar;37(2):e40.
15. Banerjee I, Robinson J, Asim M, Sathian B, Banerjee I. Mucormycosis and COVID-19 an epidemic in a pandemic?. Nepal journal of epidemiology. 2021 Jun;11(2):1034.
16. Avatef Fazeli M, Rezaei L, Javadirad E, Iranfar K, Khosravi A, Amini Saman J, Poursabbagh P, Ghadami MR, Parandin MM, Dehghani A, Ahmadi Jouybari T. Increased incidence of rhino- orbital mucormycosis in an educational therapeutic hospital during the COVID- 19 pandemic in western Iran: An observational study. Mycoses. 2021 Jul 31.

17. Pakdel F, Ahmadikia K, Salehi M, Tabari A, Jafari R, Mehrparvar G, Rezaie Y, Rajaeih S, Alijani N, Barac A, Abdollahi A. Mucormycosis in patients with COVID- 19: A cross- sectional descriptive multicentre study from Iran. Mycoses. 2021 Oct;64(10):1238-52.
18. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. Cureus. 2020 Sep;12(9).
19. John TM, Jacob CN, Kontoyiannis DP. When uncontrolled diabetes mellitus and severe COVID-19 converge: the perfect storm for mucormycosis. Journal of Fungi. 2021 Apr;7(4):298.
20. Buil JB, van Zanten AR, Bentvelsen RG, Rijpstra TA, Goorhuis B, van der Voort S, Wammes LJ, Janson JA, Melchers M, Heusinkveld M, Melchers WJ. Case series of four secondary mucormycosis infections in COVID-19 patients, the Netherlands, December 2020 to May 2021. Eurosurveillance. 2021 Jun 10;26(23):2100510.
21. Szarpak L, Chirico F, Pruc M, Szarpak L, Dzieciatkowski T, Rafique Z. Mucormycosis—A serious threat in the COVID-19 pandemic?. Journal of Infection. 2021 May 21.
22. Joshi AR, Muthe MM, Patankar SH, Athawale A, Achhapalia Y. CT and MRI findings of invasive mucormycosis in the setting of COVID-19: experience from a single center in India. American Journal of Roentgenology. 2021 Jun 23:1-2.
23. Muthu V, Rudramurthy SM, Chakrabarti A, Agarwal R. Epidemiology and pathophysiology of COVID-19-associated mucormycosis: India versus the rest of the world. Mycopathologia. 2021 Aug 19:1-6.
24. Khan AU, Proma AA, Akter M, Rahaman MM, Das S. A Review on Coronavirus Disease (COVID-19) Epidemic Threat for Global Health in 2020. American Journal of Microbiological Research. 2020;8(2):57-62.
25. Khan AU, Khan FU, Khanom S, Khan AU. Novel Coronavirus Disease (COVID-19): Pandemic Situation in Bangladesh. Nujs Journal of Regulatory Studies. 2020 5(2): 1-10.
26. Khan AU, Ema IJ, Afsana AS, Khan AU, Zannaty A, Faruk MF, Rahman S. Effects of Coronavirus Disease (COVID-19) on Agricultural Sectors in Bangladesh: A Review. International Journal for Asian Contemporary Research. 2021; 1(1): 89-97, 2021.
27. Khan AU, Akter R, Khan FU, Khanom S, Khan AU, Afsana AS. Second wave and pandemic situation of COVID-(2020-2021) in Bangladesh. Qubahan Academic Journal. 2021; 1(4): 25–31.
28. Honavar SG. Code mucor: guidelines for the diagnosis, staging and management of rhino-orbito-cerebral mucormycosis in the setting of COVID-19.
29. Khan AU, Talucder MSA, Das M, Noreen S, Pane YS. Prospect of The Black Pepper (*Piper nigrum* L.) as Natural Product Used to an Herbal Medicine. Open Access Macedonian Journal of Medical Sciences. 2021;9(F):563-573. Doi: 10.3889/oamjms.2021.7113
30. Bhattacharyya A, Sarma P, Sharma DJ, Das KK, Kaur H, Prajapat M, Kumar S, Bansal S, Prakash A, Avti P, Thota P. Rhino-orbital-cerebral-mucormycosis in COVID-19: A systematic review. Indian Journal of Pharmacology. 2021 Jul;53(4):317.
31. Werthman-Ehrenreich A. Mucormycosis with orbital compartment syndrome in a patient with COVID-19. The American journal of emergency medicine. 2021 Apr 1;42:264-e5.
32. Nambiar M, Varma SR, Damdoum M. Post-Covid alliance-mucormycosis, a fatal sequel to the pandemic in India. Saudi Journal of Biological Sciences. 2021 Jul 10.

33. Shah D, Talwar D, Kumar S, Acharya S, Dubey A. Mucormycosis as a complication of LOIN G COVID: A case series. MEDICAL SCIENCE. 2021 Jun;25(112):1331–7.
34. Hepat S, Wadekar A, Goyal A, Shukla S, Acharya S, Kumar S. Garcin syndrome: A rare complication of rhinocerebral mucormycosis in post covid patient. MEDICAL SCIENCE. 2021 Jul;25(113):1788–94.
35. Khanna S, Talwar D, Kumar S, Acharya S, Hulkoti V, Madan S. Facial colliculus syndrome with inflammatory cranial neuritis in a patient with covid 19 with mucormycosis superinfection. MEDICAL SCIENCE. 2021 Jul;25(113):1517–21.
36. Patel M, Talwar D, Kumar S, Acharya S, Dubey A, Hulkoti V, et al. Cutaneous mucormycosis with maxillary sinus fistula as a presenting feature of COVID-19: A rare case report. MEDICAL SCIENCE. 2021 Jul;25(113):1507–12.
37. Dronamraju S, Nimkar S, Damke S, Agrawal S, Kumar S. Angioinvasion of anterior cerebral artery by rhinocerebral mucormycosis leading to intraparenchymal hemorrhage: A rare case report. MEDICAL SCIENCE. 2021 May;25(111):1088–91.