



FUNGAL INFECTIONS DUE TO COVID-19: A REVIEW

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Abstract: With the outbreak of the corona virus disease (COVID-19) pandemic, patients have developed a good range of life-threatening fungal co-infections. Some fungal infections have symptoms that are similar to COVID-19, such as fever, cough, and shortness of breath. To identify if an individual features a mycosis or COVID-19, laboratory testing is required. COVID-19 and a mycosis might occur within the same patient. People with severe COVID-19, like those within the medical care unit (ICU), are more vulnerable to bacterial and fungal infections. Aspergillosis and invasive candidacies are the most frequent fungal diseases in COVID-19 patients. These fungal co-infections are becoming more common, and they're linked to serious sickness and death from these infections. Here in the review we have considered history of COVID-19 & the overall confections associated with COVID-19, focusing especially on the immunology, risk factors, diagnosis, treatment and current challenges.

Keywords : Covid-19, mycosis, fungal diseases, aspergillosis , invasive candidacies.

I. INTRODUCTION

COVID-19's worldwide popularity and the potential of fungal co-infection.

Coronavirus disease 2019 (COVID-19), a human-to-human transmitted disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2), has been a global public health disaster. COVID-19 has spread to 212 nations, resulting in approximately 5 million laboratory-confirmed illnesses and over 310,000 deaths worldwide as of May 18th, 2020. SARS-CoV-2, like SARS-CoV and the Middle East respiratory syndrome coronavirus (MERS-CoV), causes lower respiratory infections and can lead to acute respiratory distress syndromes (ARDS). COVID-19 patients always had immunosuppression with a decrease in CD4+T and CD8+T cells critically ill patients who were brought to the intensive care unit (ICU) and required mechanical ventilation, in addition to the diffuse alveolar injury with severe inflammatory exudation. or possessed, or had a longer duration of hospital stays ,even as long as 50 days, were more likely to notice that COVID- 19 patients can develop further fungal infections during the center and latter stages of this disease, especially severely ill ones.[2]

It has been proven that activating antiviral immunity in infected patients' host tissue (the lungs are the foremost afflicted organs in COVID-19-positive patients) can produce a beneficial outcome

environment for the establishment, growth & development of various classes of micro-organisms. as an example , a considerable increase of fungal infections (e.g. candidiasis, aspergillosis, cryptococcosis, pneumocytosis, and histoplasmosis) has been detected in individuals with active infection caused by the human immunodeficiency virus (HIV), severe flu and COVID-19.[3]

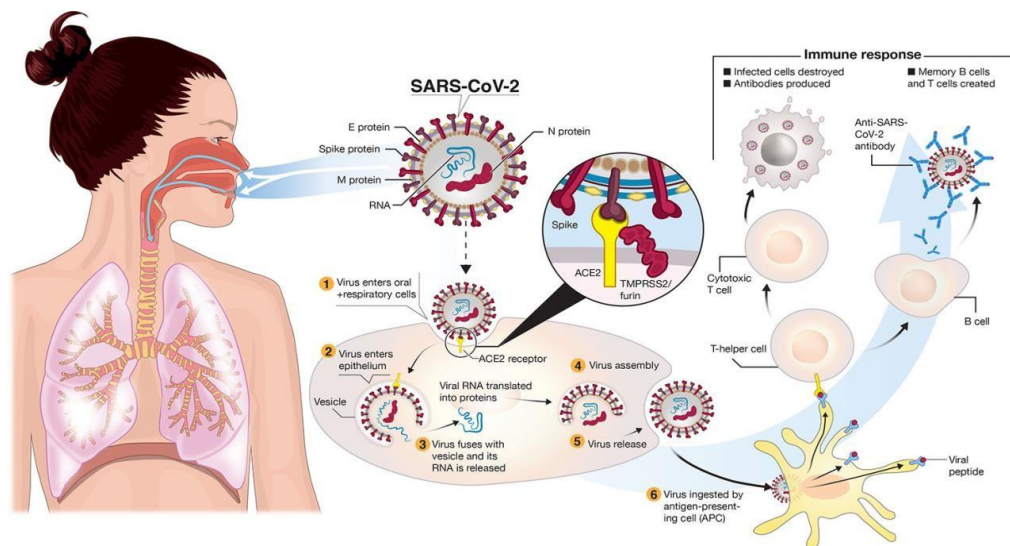


Figure 1 :History of covid-19 & fungal infections due to covid-19

Coronavirus disease 2019 (COVID-19) is a coronavirus 2 virus that causes severe acute respiratory sickness. (SARS-CoV-2). In December 2019, the first known case was detected in Wuhan, China. The disease has since spread over the globe, resulting in an epidemic.

Fever, cough, headache, weariness, breathing issues, and a loss of smell and taste are all signs of COVID-19. Symptoms might appear one to 14 days after being exposed to the virus. At least one-third of people affected show no signs or symptoms. The majority of those with symptoms severe enough to be classed as patients (81%) had mild to moderate symptoms (up to mild pneumonia), whereas 14 percent have severe symptoms (dyspnea, hypoxia, or really severe pneumonia). and 5% suffer critical symptoms (respiratory failure, shock, or multiorgan dysfunction). Older people are at a better risk of developing severe symptoms. Some people still experience a selection of effects (long COVID) for months after recovery, and damage to organs has been observed. Multi-year studies are underway to further investigate the long-term effects of the disease.

COVID-19 transmits when people inhale air contaminated by droplets and little airborne particles containing the virus. The risk of breathing these in is highest when people are in close proximity, but they will be inhaled over longer distances, particularly indoors. Transmission can also occur if splashed or sprayed with contaminated fluids within the eyes, nose or mouth, and, rarely, via contaminated surfaces. People remain contagious for up to twenty days, and may spread the virus albeit they are doing not develop symptoms. The condition is diagnosed via a variety of testing methods. The virus' macromolecule is detected by real-time reverse transcription polymerase chain reaction (rRT-PCR), transcription-mediated amplification (TMA), or reverse transcription loop-mediated isothermal amplification (RT-LAMP) from a nasopharyngeal swab as the standard diagnostic procedure.

Several COVID-19 vaccines have been licenced and are being delivered in a number of countries that have begun mass vaccination efforts. Physical and social interventions are examples of other preventive approaches. Hands should not be near the face if they haven't been cleansed. To reduce the risk of transmissions, the use of face masks or coverings has been advocated in public places. While research on antiviral drugs is ongoing, the first line of defence is symptomatic treatment. Symptom management, supportive care, isolation, and experimental approaches are all part of the management process.[4]

Etymology

During the initial outbreak in Wuhan, the virus and illness were termed "coronavirus" and "Wuhan coronavirus," and the condition was dubbed "Wuhan pneumonia." Many diseases have been named after geographical places in the past, including the Spanish flu, Middle East respiratory syndrome, and Zika virus. In January 2020, the WHO proposed 2019-nCoV and 2019-nCoV acute respiratory sickness as interim names for the virus and disease, based on 2015 recommendations and global norms against using geographical regions or groups of individuals in illness and viral names to minimise social stigma. The official names of COVID-19 and SARS-CoV-2 were released by the WHO on February 11, 2020. CO stands for corona, VI for virus, D for disease, and 19 for number, according to Tedros Adhanom. The WHO additionally uses "the COVID-19 virus" and "the virus responsible for COVID-19" in public communications.[6]

Symptoms of COVID-19

The intensity of Covid-19 symptoms varies, from mild to severe illness. Symptoms include headache, loss of smell and taste, nasal congestion and runny nose, cough, muscle aches, sore throat, fever, diarrhoea, and breathing difficulties. People infected with the same virus may have a wide range of symptoms that fluctuate over time. A respiratory symptom cluster with cough, sputum, shortness of breath, and fever has been detected, as well as a musculoskeletal symptom cluster with muscle and joint pain, headache, and weariness, and a digestive symptom cluster with abdominal discomfort, vomiting, and diarrhoea. COVID-19 has been related to a loss of taste and smell in individuals without a history of ear, nose, or throat problems, and it has been seen in up to 88 percent of cases. Of people who show symptoms, 81% develop only mild to moderate symptoms (up to mild pneumonia), while 14% develop severe symptoms (dyspnea, hypoxia, or more than 50% lung involvement on imaging) and 5% of patients suffer critical symptoms (respiratory failure, shock, or multiorgan dysfunction). At least one-third of those infected with the virus never show any symptoms. Asymptomatic carriers are less likely to be tested, allowing the disease to spread. Other infected persons will develop symptoms later, or have very weak symptoms, and can spread the virus. There is a lag between when a person becomes sick and when the first symptoms occur, as is common with infections. COVID-19 features a four to 5 day median delay. Symptoms appear within the majority of sick people two to seven days after exposure, and almost everyone has a minimum of one symptom within 12 days.

The majority of patients get over the disease's acute phase. However, some patients — more than half of a group of home-isolated young adults — continue to have symptoms such as weariness months after recovery, a condition known as persistent COVID, and organ damage has been reported. Long-term studies are being carried out in order to learn more about the disease's long-term consequences. [8]

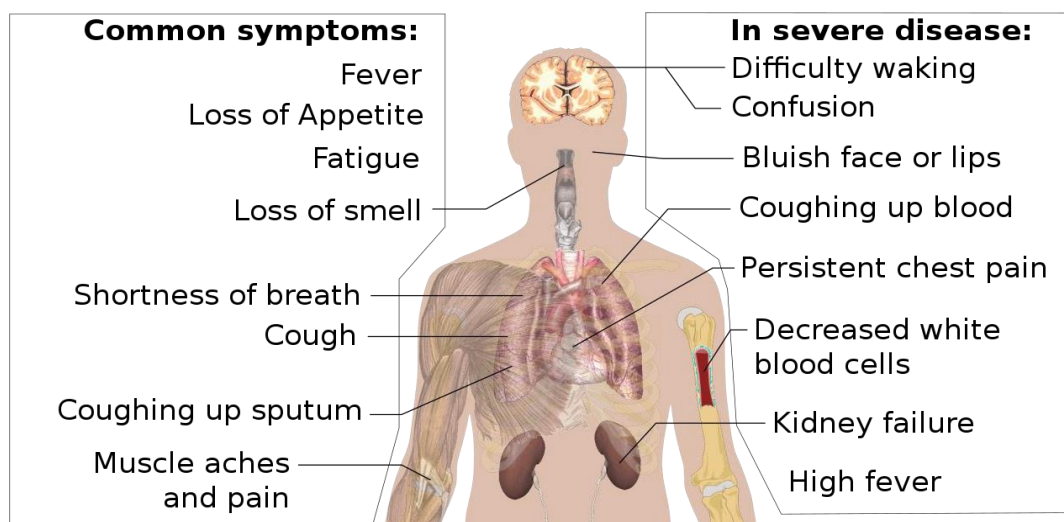


Figure 2 : Symptoms of covid-19

CAUSE

COVID-19 is caused by infection with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus strain.[5]

TRANSMISSION

The disease is typically transmitted by the respiratory route when people inhale droplets and small airborne particles (that form an aerosol) that infected people exhale while breathing, talking, coughing, sneezing, or singing. COVID-19 is more likely to spread when infected people are physically close. COVID-19 is caused by infection with the coronavirus 2 that causes severe acute respiratory syndrome (SARS-CoV-2). Infection, on the other hand, can spread across longer distances, especially indoors. Infectivity can appear 1-3 days prior to the onset of symptoms. Infected people can spread the disease even if they are asymptomatic or pre-symptomatic. In upper respiratory tract samples, the highest viral load usually occurs near the time of infection. In most cases, the peak viral load in upper respiratory tract samples comes close to the onset of symptoms and then diminishes after the first week. According to current research, viral shedding and infectiousness can last up to 10 days after symptom start in people with mild to moderate COVID-19, and up to 20 days in people with severe COVID-19, including immunocompromised people. Infectious particles range in size from small aerosols that float in the air for a long time to bigger droplets that float or fall to the ground. Furthermore, COVID-19 research has reshaped our knowledge of how respiratory viruses are transmitted. The largest droplets of respiratory fluid do not go far and can infect mucous membranes of the eyes, nose, and mouth if breathed or landed on them. Aerosol concentrations are highest when humans are physically near together, making viral transmission simpler. However, airborne transmission can occur over greater distances, particularly in poorly ventilated areas, where small particles can remain suspended in the air for minutes to hours.

Only 10 to 20% of persons are responsible for the disease's propagation, therefore the number of people infected by one infected person fluctuates. It spreads in clusters, with infections linked to an patient or a selected geographic place. In many of these cases, super spreading episodes occur, in which a single individual infects a large number of people.[9]

VIROLOGY

The coronavirus that causes severe acute respiratory syndrome 2 (SARS-CoV-2) is a new coronavirus that causes severe acute respiratory syndrome. It was discovered in three persons who had pneumonia and were linked to a Wuhan cluster of acute respiratory disease cases. In nature, similar coronaviruses have all of the structural properties of the novel SARS-CoV-2 virus particle.

Household soap, which breaches the virus's protective bubble outside of the human body, kills it.

SARS-CoV-2 is related to SARS-CoV. It's assumed to be a zoonotic (animal-borne) disease. The coronavirus genetically clusters with two bat-derived strains in the subgenus Sarbecovirus (lineage B) of the genus Betacoronavirus, according to genetic study. At the moment, it's 96 percent the same.[10]

PATHOPHYSIOLOGY

SARS-CoV-2 can infect a wide range of body cells and systems. The effects of COVID-19 on the upper respiratory system (sinuses, nose, and throat) and the lower respiratory tract (bronchitis, pneumonia, and bronchitis) are the most well-known (windpipe and lungs). Because the virus enters host cells through the receptor for the enzyme angiotensin-converting enzyme 2 (ACE2), which is widespread on the surface of type II alveolar cells in the lungs, the lungs are the organs most affected

by COVID-19. To bind to the ACE2 receptor and enter the host cell, the virus uses a "spike," a unique surface glycoprotein.[22]

Respiratory tract

COVID-19 infects the ciliated epithelium of the nasopharynx and upper airways after viral introduction.[22]

Nervous system

Loss of smell is a typical symptom caused by infection of the olfactory epithelium's support cells, which leads to damage to the olfactory neurons. Many medical journals have reported on COVID-19's involvement of both the central and peripheral nervous systems. Many persons with COVID-19 have obvious neurological or mental health problems. In the majority of COVID-19 individuals with neurological disorders, the virus is not found in the CNS. However, SARS-CoV-2 has been found in the brains of COVID-19 victims at low levels, but these findings need to be validated. While the virus has been found in autopsy cerebrospinal fluid, the particular process by which it enters the CNS is unknown. Given the low levels of ACE2 in the brain, it may first attack peripheral neurons. The virus could also enter the bloodstream through the lungs and then cross the blood-brain barrier to reach the CNS, possibly through an infected white blood cell.

Gastrointestinal tract

The virus also affects gastrointestinal organs as ACE2 is abundantly expressed within the glandular cells of gastric, duodenal and rectal epithelium also as endothelial cells and enterocytes of the tiny intestine.[22]

Cardiovascular system

The virus has the potential to cause both acute myocardial infarction and long-term cardiovascular harm. Acute cardiac injury was discovered in 12% of infected persons admitted to a hospital in Wuhan, China, and is more common in people with severe disease. Because of the systemic inflammatory response and immune system problems that occur as disease progresses, rates of cardiovascular symptoms are high, but acute myocardial damage may also be linked to ACE2 receptors in the heart. ACE2 receptors are found in abundance in the heart and play a role in cardiac function. People admitted to intensive care units (ICU) with COVID-19 infections have a high rate of thrombosis and venous thromboembolism, which may be linked to a poor prognosis. In people infected with SARS-CoV-2, blood vessel dysfunction and clot formation (as suggested by high D-dimer levels caused by blood clots) are thought to play a significant role in mortality. Incidences of clots leading to pulmonary embolisms, as well as ischemic events within the brain, have been noted as complications leading to death. Infection appears to trigger a cascade of vasoconstrictive responses in the body; constriction of blood vessels in the pulmonary circulation has also been proposed as a mechanism by which oxygenation declines as viral pneumonia develops. Furthermore, microvascular (arterioles and capillaries) vessel damage has been documented during a small number of brain tissue samples – without SARS-CoV-2 – and neural structure samples from COVID-19 victims. COVID-19 was also discovered to produce significant morphological and mechanical changes in blood cells, such as enlarged sizes, which could last for months after hospital discharge.[22]

Other organs

Complications of the kidneys are another significant cause of mortality. Early estimates indicate that up to 30% of hospitalised patients in China and New York, including some who had no prior renal problems, have suffered some form of kidney impairment. People who died with COVID-19 had diffuse alveolar injury and lymphocyte-containing inflammatory infiltrates in their lungs, according to autopsies.[22]

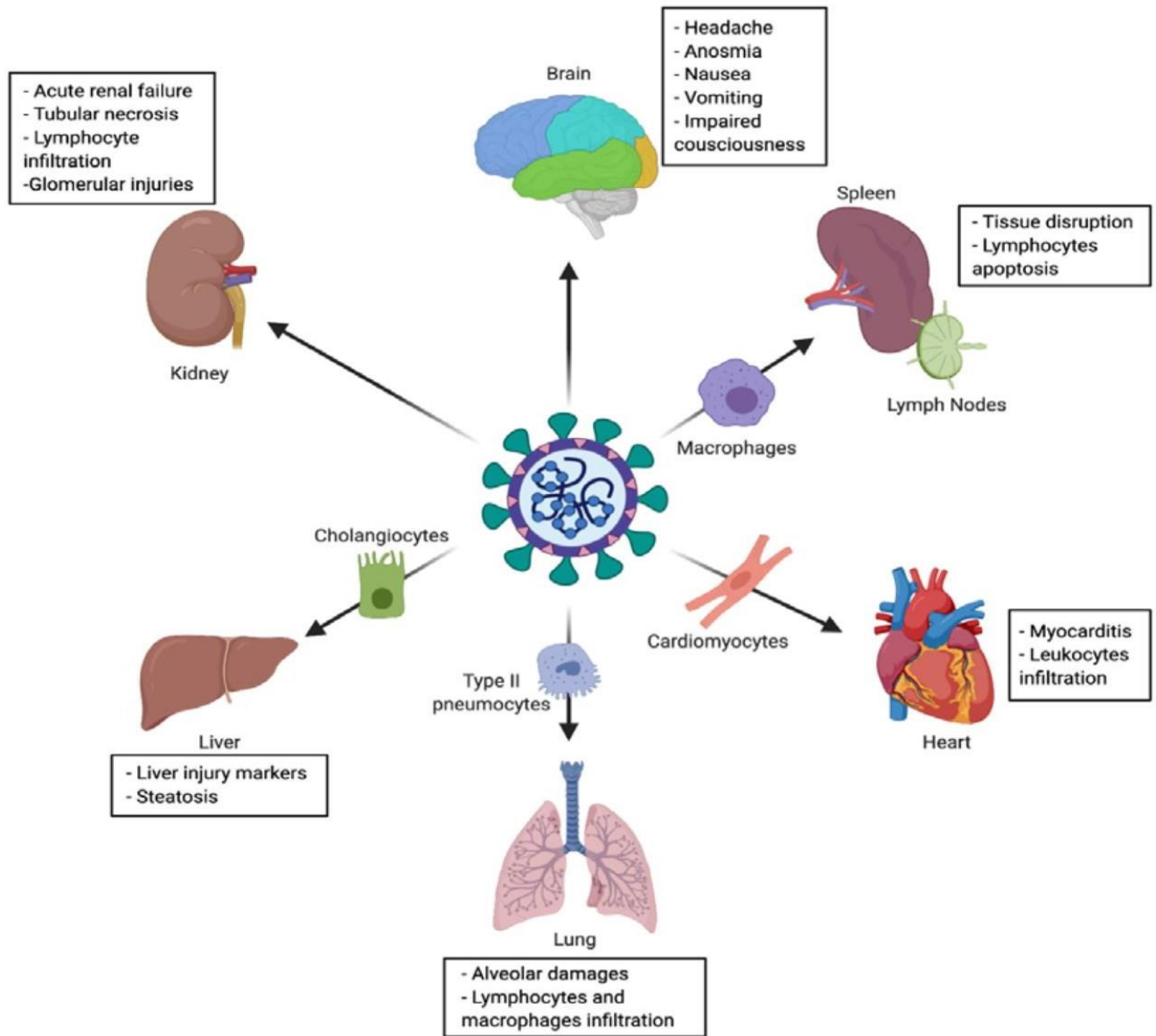


Figure 3 : Tropism and multiple organ injuries in SARS-CoV-2 infection. SARS-CoV-2 infection has been associated with multiple organ injuries due to viral tropism. Among injured organs (and targeted cell) we can find: lung (type II pneumocyte), heart (cardiomyocyte), liver (cholangiocyte), spleen and lymph nodes (macrophage), kidney and brain.[11]

LONGER -TERM EFFECTS

According to preliminary research, 10-20% of COVID-19 patients will have symptoms that last more than a month. Long-term difficulties, such as weariness and shortness of breath, are reported by the majority of people brought to hospital with severe disease. Approximately 5–10% of hospitalised patients develop severe or critical illness, such as pneumonia or abrupt respiratory failure.

The lungs are the most impacted organs in COVID-19 due to a multitude of reasons. Even if the patient's condition has improved clinically, up to 98 percent of CT scans performed in persons who require hospitalisation reveal lung abnormalities after 28 days.

Long-term problems, such as lung fibrosis, are more common in those who are older, have a serious condition, stay in the ICU for a long time, or smoke. Even in asymptomatic persons, about one-third of those tested after four weeks will have signs of pulmonary fibrosis or impaired lung function as measured by DLCO, with the possibility of further improvement with time.[12]

PREVENTION

Vaccination, staying at home, wearing a mask in public, avoiding crowded places, keeping a safe distance from others, ventilating indoor spaces, managing potential exposure durations, washing hands with soap and water frequently and for at least twenty seconds, practising good respiratory hygiene, and avoiding touching the eyes, nose, or mouth with unwashed hands are all ways to reduce the risk of infection. Those who have been diagnosed with COVID-19 or suspect they may be infected are advised to stay at home except for medical care, call ahead before visiting a healthcare provider, wear a face mask before entering the healthcare provider's office and when in any room or vehicle with another person, cover coughs and sneezes with tissues, wash hands frequently with soap and water, and avoid sharing personal home items.

1. FACE MASKS & RESPIRATORY HYGINE.
2. INDOOR VENTILATION & AVOIDING CROWDED INDOOR SPACES.
3. HAND WASHING & HYGINE.
4. SOCIAL DISTANCING.
5. SURFACE CLEANING.
6. SELF-ISOLATION.
7. HEALTHY DIET & LIFESTYLE.
8. TRAVELLING RELATED MEASURES.

COVID-19 × FUNGAL INFECTIONS

interkingdom interactions

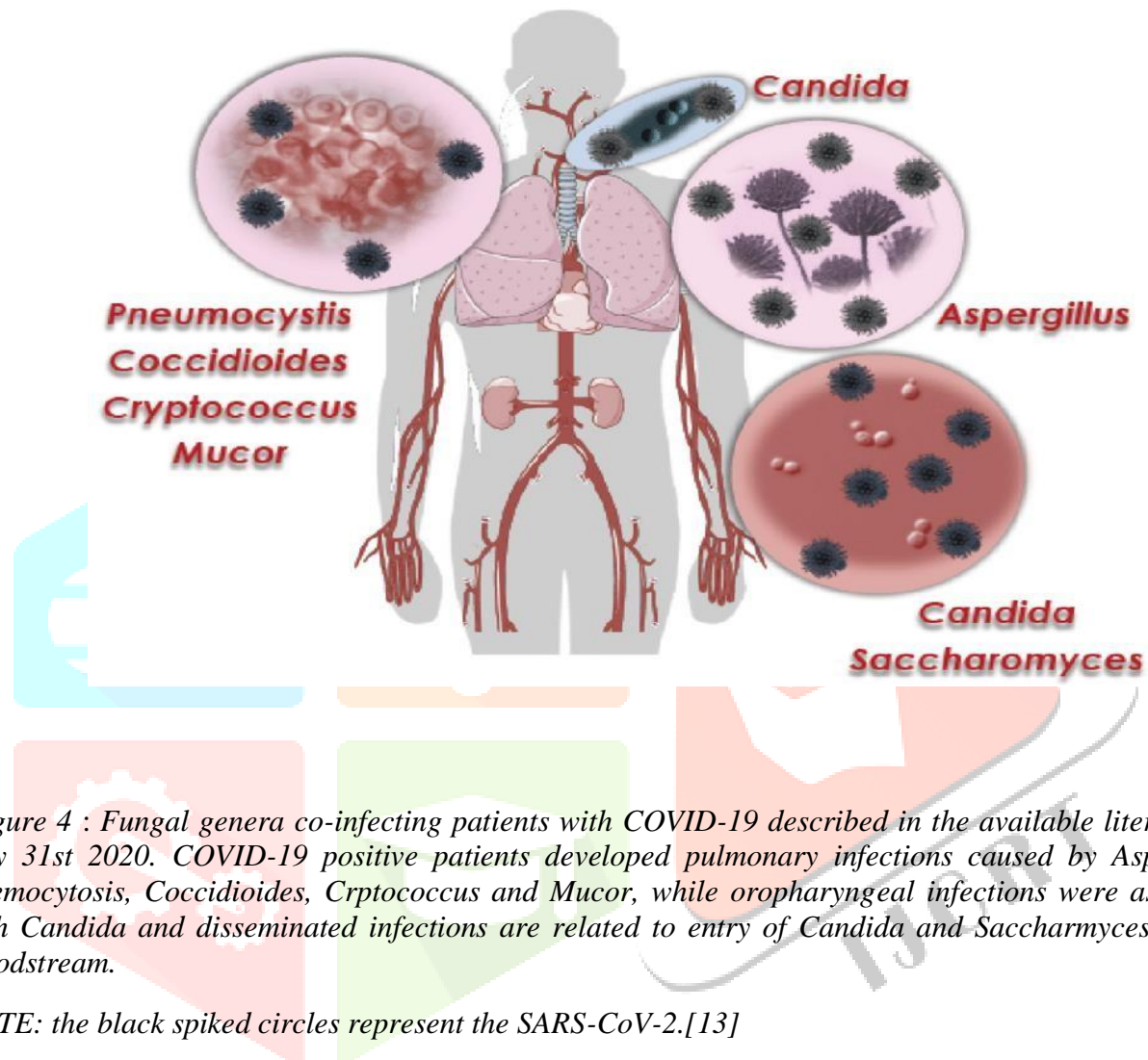


Figure 4 : Fungal genera co-infecting patients with COVID-19 described in the available literature on July 31st 2020. COVID-19 positive patients developed pulmonary infections caused by *Aspergillus*, *Pneumocystis*, *Coccidioides*, *Cryptococcus* and *Mucor*, while oropharyngeal infections were associated with *Candida* and disseminated infections are related to entry of *Candida* and *Saccharomyces* into the bloodstream.

NOTE: the black spiked circles represent the SARS-CoV-2.[13]

COVID-19 X ASPERGILLUS

Many research have revealed bacterial or virus co-infections with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but awareness of *Aspergillus* co-infection among patients with coronavirus disease 2019 (COVID-19) was limited. It was discovered that *Aspergillus* spp. can cause co-infections in COVID-19 patients, particularly in those with severe/critical disease. In COVID-19, the prevalence of IPA ranged from 19.6 percent to 33.3 percent. The most prevalent complication was acute respiratory distress syndrome, which necessitated mechanical ventilation. Overall mortality was significant, with up to 64.7 percent (n = 22) in the Pooled analysis of 34 reported cases. The traditional invasive aspergillosis risk factors were not present in these groups. Fungus culture and galactomannan assays, especially from respiratory specimens, can help with early diagnosis. *Aspergillus fumigatus*, followed by *Aspergillus flavus*, was the most prevalent species causing co-infection in COVID-19 individuals. Although voriconazole is the most often used antifungal and recommended anti-*Aspergillus* medicine, azole-resistant *Aspergillus* can induce aspergillosis. When used in conjunction with anti-SARS-CoV-2 medications, voriconazole should be used with caution due to the likelihood of complicated drug–drug interactions and increased cardiovascular damage. Finally, doctors should be aware of the likelihood of pulmonary aspergillosis in severe/critical COVID-19

patients, and comprehensive microbiologic testing should be indicated in addition to SARS-CoV-2 testing via respiratory specimens.

Severe immunosuppression, particularly that associated with hematologic malignancies and transplantation, is a common cause of invasive aspergillosis. It is distinguished by hyphal invasion of bronchial or lower airway tissues, as well as the possibility of vascular invasion and radiographic abnormalities that imply haemorrhage and necrosis. However, *Aspergillus* species generate a broader spectrum of pulmonary illness, characterised pathologically by airway inflammation and acute and chronic invasion, which is mostly dependent on host risk. Much recent research has focused on the incidence and importance of aspergillosis that occurs after severe viral infections, including influenza and coronavirus illness (COVID-19).

In this scenario, the most commonly used drugs are the new triazoles voriconazole and isavuconazole, followed by less common cases treated with liposomal amphotericin B and caspofungin. European countries such as France, Germany, Belgium, and the Netherlands have recently reported high rates of chronic pulmonary aspergillosis among COVID-19-positive patients.[3]

The table summarizes studies describing antifungal failure in the treatment of COVID-19 patients co-infected with *Aspergillus* species.

Table: Antifungal therapy used to treat aspergillus infection in COVID-19 patients.[3]

Country	Number of patients	Fungal species	Anti-fungal therapy	Outcome
Germany	5	<i>A.FUMIGATUS</i>	Two patients received voriconazole, one patient used isavuconazole and two patients received caspofungin followed by voriconazole	4 deaths 1 alive
France	2	<i>A.FUMIGATUS</i>	one patients received voriconazole and the other one caspofungin	2 deaths
Belgium	6	<i>A.FUMIGATUS</i>	Four patients received voriconazole and two others received voriconazole plus isavuconazole	3 deaths 3 alive
France	1	<i>A.FUMIGATUS</i>	Voriconazole	death
France	1	<i>A.FLAVUS</i>	Voriconazole switched to isavuconazole	death

Netherlands	6	<i>A.FUMIGATUS</i>	Five patients received voriconazole plus anidulafungin and one patient was treated with liposomal amphotericin B	4 deaths 2 alive
Italy	1	<i>A.FUMIGATUS</i>	Liposomal amphotericin B	death
Germany	2	<i>A.FUMIGATUS</i>	Liposomal amphotericin B	2 death

COVID-19 X PNEUMOCYTOSIS

With the rising number of cases of coronavirus disease 2019 (COVID-19) around the world, fungal coinfection has become more prevalent, complicating COVID-19 treatment. Although aspergillus spp. appears to be the foremost common fungal pathogen in COVID-19 pneumonia patients, reports of pneumocystis jirovecii pneumonia (PCP) co-occurring with or following COVID-19 are getting more common. Co-infections in patients with corona virus disease-2019 (COVID-19) and feel that fungal co-infections are under-estimated, based on findings from a few research. Although the severe acute respiratory syndrome coronavirus-2 (SARS-CoV2) is still circulating, roughly 5-10% of COVID-19 patients may require intensive care unit (ICU) therapy, and 30% may develop secondary pneumonia with no known cause. Superinfections acquired in the hospital, such as those documented in severely ill patients with influenza virus, can be suspected. Since pneumocystis is usually reported in patients with T-cell immunodepression, less attention has been paid to pneumocystis jirovecii in non-immunocompromised ICU patients although it accounts for 7% of the co-infections reported in those admitted with influenza. Interestingly, COVID-19 patients may develop lymphocytopenia and acute respiratory distress syndrome (ARDS) requiring adjunctive steroids and/or immunomodulatory therapies, well known susceptibility factors for developing pneumocystis is was studied to investigate the prevalence of P.jirovecii acid nucleic detection in respiratory specimens sampled to identify co-infections in COVID-19 patients in the ICU.[14]

COVID-19 X COCCIDIOIDOMYCOSIS

Coronavirus disease (COVID-19) interacts with coccidioidomycosis, a respiratory ailment produced by inhaling coccidioides fungus spores in dust. We looked at the risk of co-infection in construction and agricultural workers, incapacitated people, Black and Latino people, and people who live in high-dust areas. We also looked at age, diabetes, immunosuppression, racial or ethnic minority status, and smoking as potential co-infection risk factors. Because both infections have similar symptoms, the COVID-19 pandemic could worsen coccidioidomycosis diagnosis delays, thereby preventing timely antifungal therapy administration. Finally, the clinical implications of co-infection were investigated, including severe COVID-19 infection and reactivation of latent coccidioidomycosis. A underlying respiratory infection is a significant risk factor for developing severe asthma. COVID-19 the Centers for Illness Control and Prevention revealed that 9.2 percent of COVID-19 patients in the United States had a chronic lung disease, such as chronic obstructive pulmonary disease, asthma, or emphysema; chronic lung disease was the most prevalent concurrent condition after diabetes.

The frequency of chronic lung disease is higher (15%) among hospitalised patients, and it is highest among critical care unit patients (21 percent). Several investigations of COVID-19 patients in China have found that individuals with underlying chronic respiratory diseases have a higher risk of mortality and severe disease. Although acute coccidioidomycosis is usually self-limiting, 3-5 percent of

individuals develop a persistent lung infection. Patients with chronic pulmonary coccidioidomycosis may be prone to severe COVID-19, based on findings indicating chronic lung illness increases the likelihood of severe COVID-19.[15]

.Coccidioidomycosis Reactivation

In a coccidioidomycosis patient whose sickness has progressed to a chronic but quiescent stage, infection with COVID-19 could trigger disease. After an initial coccidioides infection has cleared, the fungus can remain dormant in the lungs and reawaken under certain circumstances.

Reactivation of coccidioidomycosis has been recorded in pregnant women, particularly in those who had previously had disseminated coccidioidomycosis.

Coccidioidomycosis reactivation is more common in patients who have had organ transplants, which frequently necessitate immunosuppressive medicines.

Immune dysregulation, particularly lymphopenia, has been linked to SARS-CoV-2 infection, which may reduce the host's ability to control coccidioides infection. Coccidioidomycosis reactivation in COVID-19 patients has not been reported in any study.[15]

COVID-19 X CANDIDA

Candida auris is a new fungus that has the potential to cause severe infections in hospitals. It has spread most widely in long-term care institutions in the United States, where patients with serious medical issues are cared for. C. auris outbreaks have been documented in COVID-19 units of acute care hospitals since the beginning of the COVID-19 pandemic. During the COVID-19 pandemic, modifications in normal infection control methods, such as reduced availability of gloves and gowns or reuse of these items, as well as changes in cleaning and disinfection practises, may have contributed to these outbreaks. Multiple states have lately reported new C. auris infections with no known connections to previous cases or healthcare abroad, implying an increase in undetected transmission. Because healthcare facilities and health departments' resources have been redirected to respond to COVID-19, screening for C. auris colonisation, a key aspect of containment efforts, has become increasingly limited.[19]

Invasive candidiasis in COVID-19 patients

Patients with COVID-19 who are admitted to the hospital are at risk of developing healthcare-associated infections (HAIs), such as candidaemia or Candida-related bloodstream infections. In patients with severe COVID-19, fungal infections resistant to antifungal therapy have also been reported. In patients with severe COVID-19 fungal co-infections, early detection and surveillance for Candida infections and antifungal resistant infections (e.g., C. auris, azole resistant Aspergillus) are critical to minimising death from COVID-19.[19]

COVID-19 X SACCHAROMYCES

Due to the quick rate of transmissibility and mortality, the coronavirus disease 2019 (COVID-19) pandemic has had a significant impact on public health. In critically ill patients, it also has a negative influence on care-related infections (CRIs). Intensive care patients are vulnerable to fungal infections such as central venous catheter-related candidemia and pulmonary aspergillosis, both of which have been reported in COVID-19 patients.[16]

COVID-19 X CRYPTOCOCCUS

Cryptococcus neoformans is a saprophytic fungus that infects immunocompromised people and produces deadly disseminated infections. Multiple cases of secondary viral, bacterial, and fungal infections have been recorded in individuals with SARS-CoV-2 infection since the start of the COVID-19 pandemic. Many observational and retrospective studies have been published during the present COVID-19 pandemic that show a link between COVID-19 infection and various bacterial, viral, and rare fungal illnesses like streptococcus pneumonia, mycoplasma, rhinovirus, influenza, and aspergillosis. So far, two cases of cryptococemia have been reported, with blood cultures developing the fungus in COVID-19 patients, one in a transplant recipient, and the other in a patient treated with tocilizumab for COVID-19-induced cytokine storm. Blood cultures for *Cryptococcus* were positive in both of these instances, although meningoencephalitis was not mentioned. In one of them, there was an underlying immunosuppressive condition. We present a case of cryptococcal meningoencephalitis in an otherwise healthy elderly patient who had SARS-CoV-2 infection and was treated with dexamethasone.[17]

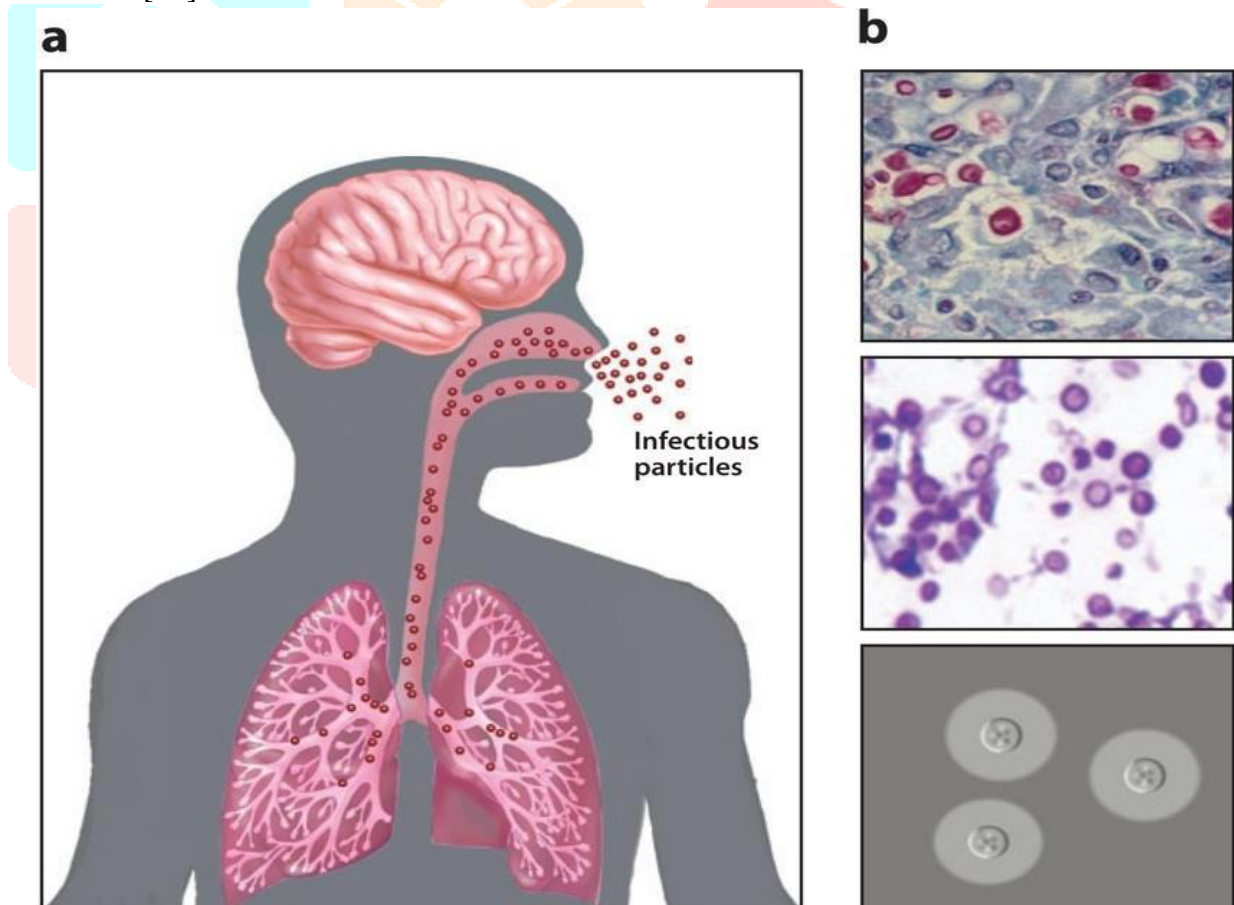


Figure :

a) Cryptococcosis is contracted by inhalation of the infectious particle, which initiates a pulmonary infection. The most common site of dissemination is the central nervous system.

b) Images (top to bottom): infected lung tissue, infected brain tissue, and an India ink stain of cryptococcal cells showing the characteristic halo appearance where capsule material excludes the ink particles. Lung histology image.[20]

COVID-19 X MUCOR

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been related to a good range of opportunistic bacterial and fungal infections. Both *Aspergillus* and *Candida* are reported because the main fungal pathogens for co-infection in people with COVID-19. Several cases of mucormycosis in patients with COVID-19 have recently been documented all over the world, particularly in India. Mucorales spores appear to germinate in people with COVID-19 because of a perfect environment of low oxygen (hypoxia), high glucose (diabetes, new-onset hyperglycemia, steroid-induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritins), and decreased phagocytic activity of white blood cells. Mucormycosis is a rare but deadly mycosis that can affect patients with weakened immune systems. Mold fungus of the genus *Rhizopus*, *Mucor*, *Rhizomucor*, *Cunninghamella*, and *Absidia* of the Order Mucorales, Class Zygomycetes, produce mucormycosis, which is an angioinvasive illness caused by mould fungi of the genus *Rhizopus*, *Mucor*, *Rhizomucor*, *Cunninghamella*, and *Absidia*. The *Rhizopus Oryzae* is commonest type and liable for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhino-orbital-cerebral (ROCM) form. The inhalation of fungus spores is the mode of contamination. According to a recent projection for the years 2019–2020, mucormycosis prevalence worldwide ranged from 0.005 to 1.7 per million persons, with the prevalence in India being nearly 80 times higher (0.14 per 1000) than in industrialised countries. To put it another way, India has the highest rate of mucormycosis in the world. [18]

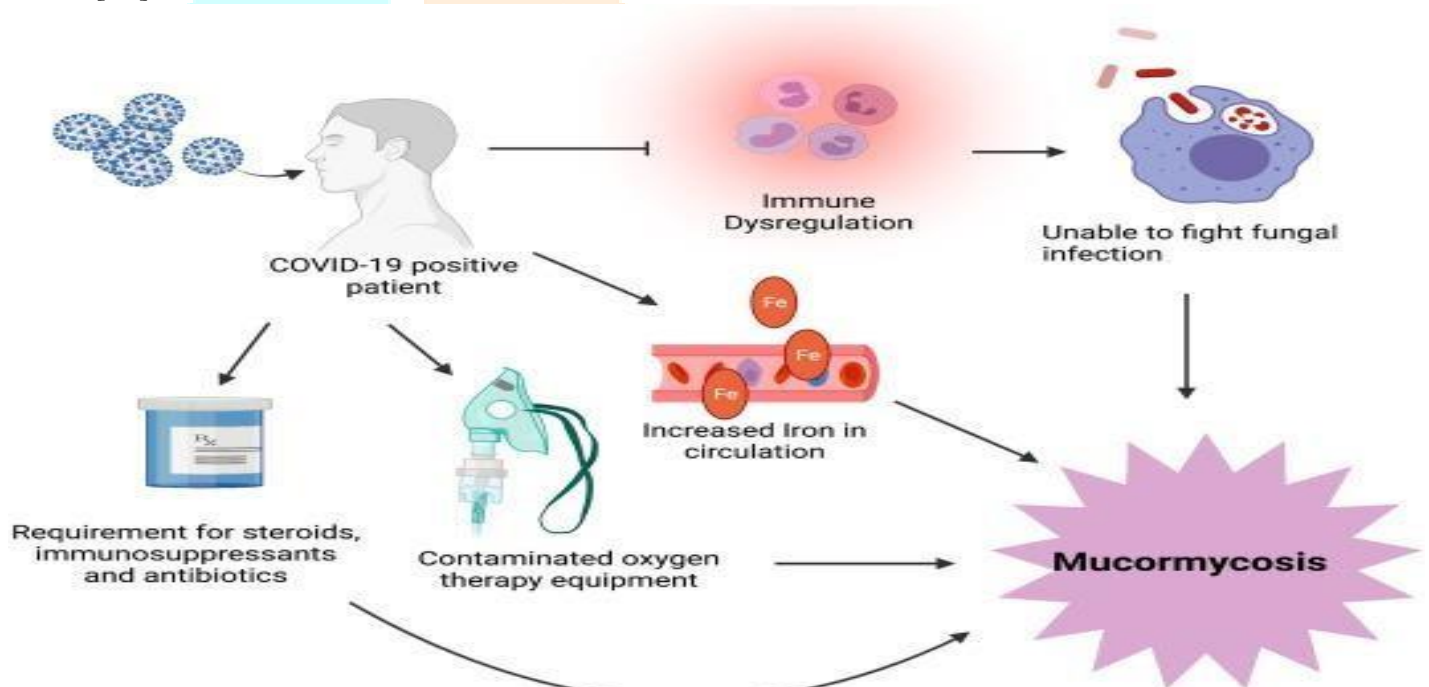


Figure 6 : Covid-19 & Mucormycosis

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