wjpmr, 2020,6(7), 208-214

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

SARS CoV 2: THE NEW DISEASE WITHOUT PROPHYLAXIS & TREATMENT

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Article Received on 21/05/2020 **Article Revised on 11/06/2020** **Article Accepted on 01/07/2020**

ABSTRACT

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] It was first identified in December 2019 in Wuhan, China, and since spread globally, resulting in an ongoing pandemic.[2,3] The first case may be traced back to 17 November 2019.[4] Common symptoms include fever, cough, fatigue, shortness of breath, and loss of smell and taste.[5,6,7] While the majority of cases result in mild symptoms, some progress to acute respiratory distress syndrome (ARDS) likely precipitated by a cytokine storm, multi-organ failure, septic shock, and blood clots.[8,9,10] The time from exposure to onset of symptoms is typically around five days but may range from two to fourteen days.[511] The virus is primarily spread between people during close contact,most often via small droplets produced by coughing, sneezing, and talking.[5,12,15] The droplets usually fall to the ground or onto surfaces rather than travelling through air over long distances.[6] Less commonly, people may become infected by touching a contaminated surface and then touching their face.[6,12] It is most contagious during the first three days after the onset of symptoms, although spread is possible before symptoms appear, and from people who do not show symptoms.[512] The standard method of diagnosis is by real-time reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab.[16] Chest CT imaging may also be helpful for diagnosis in individuals where there is a high suspicion of infection based on symptoms and risk factors; however, guidelines do not recommend using CT imaging for routine screening.[17,18]

KEYWORDS: SARS CoV 2, Covid 19, Pathogencity of Covid.

INTRODUCTION

Fever is the most common symptom, but it is highly variable in severity and presentation, with some older, immunocompromised, or critically ill people not having fever at all.[19,20] In one study, only 44% of people had fever when they presented to the hospital, while 89% went on to develop fever at some point during their hospitalization. A lack of fever does not verify someone is disease free.

Other common symptoms include cough, loss of appetite, fatigue, shortness of breath, sputum production, and muscle and joint pains.[1,5,11] Symptoms such as nausea, vomiting, and diarrhoea have been observed in varying percentages.[22,23,24] Less common symptoms include sneezing, runny nose, sore throat, and skin lesions.[25] Some cases in China initially presented with only chest tightness and palpitations.[26] A decreased sense of smell or disturbances in taste may occur.[27,28] Loss of smell was a presenting symptom in 30% of confirmed cases in South Korea.[29]

As is common with infections, there is a delay between the moment a person is first infected and the time he or she develops symptoms. This is called the incubation period. The typical incubation period for COVID-19 is five or six days, but it can range from one to fourteen days.[30] with approximately ten percent of cases taking longer.[31,32,33]

A minority of cases do not develop noticeable symptoms at any point in time.[34] These asymptomatic carriers tend not to get tested, and their role in transmission is not yet fully known.[35,36] However, preliminary evidence suggests they may contribute to the spread of the disease.[37]

DISCUSSION

The lungs are the organs most affected by COVID-19 because the virus accesses host cells via the enzyme angiotensin-converting enzyme 2 (ACE2), which is most abundant in type II alveolar cells of the lungs.[38] The virus uses a special surface glycoprotein called a "spike" (peplomer) to connect to ACE2 and enter the host cell.[39] The density of ACE2 in each tissue correlates with the severity of the disease in that tissue and some have suggested decreasing ACE2 activity might be protective,[40,41] though another view is that increasing ACE2 using angiotensin II receptor blocker medications could be protective.[42] As the alveolar disease progresses, respiratory failure might develop and death may follow.[41]

SARS-CoV-2 may also cause respiratory failure through affecting the brainstem as other coronaviruses have been found to invade the central nervous system (CNS). While virus has been detected in cerebrospinal fluid of autopsies, the exact mechanism by which it invades the CNS remains unclear and may first involve invasion of peripheral nerves given the low levels of ACE2 in the brain.[43,44]

The virus also affects gastrointestinal organs as ACE2 is abundantly expressed in the glandular cells of gastric, duodenal and rectal epithelium as well as endothelial cells and enterocytes of the small intestine.[46]

The virus can cause acute myocardial injury and chronic damage to the cardiovascular system.[47] An acute cardiac injury was found in 12% of infected people admitted to the hospital in Wuhan, China, a is more frequent in severe disease.[48] Rates of cardiovascular symptoms are high, owing to the systemic inflammatory response and immune system disorders during disease progression, but acute myocardial injuries may also be related to ACE2 receptors in the heart.[47] ACE2 receptors are highly expressed in the heart and are involved in heart function.[47,49] A high incidence of thrombosis (31%) and venous thromboembolism (25%) have been found in ICU patients with COVID-19 infections and may be related to poor prognosis.[50, 51] Blood vessel dysfunction and clot formation (as suggested by high D-dimer levels) are thought to play a significant role in mortality, incidences of clots leading to pulmonary embolisms, and ischaemic events within the brain have been noted as complications leading to death in patients infected with SARS-CoV-2. Infection appears to set off a chain of vasoconstrictive responses within the body, constriction of blood vessels within the pulmonary circulation has also been posited as a mechanism in which oxygenation decreases alongside the presentation of viral pneumonia.[52]

Another common cause of death is complications related to the kidneys.[52] Early reports show that up to 30% of hospitalized patients in both China and New York have experienced some injury to their kidneys, including some persons with no previous kidney problems.[53]

Autopsies of people who died of COVID-19 have found diffuse alveolar damage (DAD), and lymphocyte-containing inflammatory infiltrates within the lung.[54]

Although SARS-COV-2 has a tropism for ACE2-expressing epithelial cells of the respiratory tract, patients with severe COVID-19 have symptoms of systemic hyperinflammation. Clinical laboratory findings of elevated IL-2, IL-7, IL-6, granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon-γ inducible protein 10 (IP-10), monocyte chemoattractant protein 1 (MCP-1), macrophage inflammatory protein 1-α (MIP-1α), and tumour necrosis factor-α (TNF-α) indicative of cytokine release syndrome (CRS) suggest an underlying immunopathology.[38]

Additionally, people with COVID-19 and acute respiratory distress syndrome (ARDS) have classical serum biomarkers of CRS, including elevated C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer, and ferritin.[55]

Systemic inflammation results in vasodilation, allowing inflammatory lymphocytic and monocytic infiltration of the lung and the heart. In particular, pathogenic GM-CSF-secreting T-cells were shown to correlate with the recruitment of inflammatory IL-6-secreting monocytes and severe lung pathology in COVID-19 patients.] Lymphocytic infiltrates have also been reported at autopsy.[51]

The novel coronavirus, also known as SARS-CoV-2, targets type II lung cells. These cells produce soap-like substance that helps air flow deep into the lungs. But the virus causes significant damage to the lungs when it triggers the immune system to increase its activity to defend the body. To fight the corona virus, the system sends millions of cells to the infected lung tissue, which if out of control could damage the lungs.

"SARS-CoV-2 is more severe than seasonal influenza in part because it has many more ways to stop cells from calling out to the immune system for help," Neuman said in an article posted on The Conversation. "SARS-CoV-2 blocks this by a combination of camouflage, snipping off protein markers from the cell that serve as distress beacons and finally shredding any antiviral instructions that the cell makes before they can be used."

Another reason that makes COVID-19 deadly is its effects on a protein that plays an important role in blood pressure. The coronavirus disrupts the ACE2 protein and prevents it from doing its job to regulate blood pressure.

Researchers have found that the coronavirus could easily move from an infected person to another through exposure to droplets. In one case in South Korea, one or

two people reportedly sat very close to uninfected people at a church for only a few minutes. Within two weeks, local health authorities recorded thousands of people contracted COVID-19. More than half of the cases at the time were linked to the church.

It can be a gastrointestinal disease causing only diarrhea and abdominal pain. It can cause symptoms that may be confused with a cold or the flu. It can cause pinkeye, a runny nose, loss of taste and smell, muscle aches, fatigue, diarrhea, loss of appetite, nausea and vomiting, whole-body rashes, and areas of swelling and redness in just a few spots.

In a more severe disease, doctors have also reported people having heart rhythm problems, heart failure, kidney damage, confusion, headaches, seizures, Guillain-Barre syndrome, and fainting spells, along with new sugar control problems.

It's not just a fever and coughing, leading to shortness of breath, like everyone thought at first.

This makes it incredibly difficult to diagnose and even harder to treat.

"This is a disease progression we have never seen for any infection that I can think of, and I've been doing this for a couple of decades," says Joseph Vinetz, MD, an infectious disease specialist at Yale School of Medicine.

When viral particles land in our eyes, nose, or mouth, "spike proteins" on the virus connect with a specific receptor, known as ACE2, on the surface of our cells, allowing entry. ACE2 receptors.

make a great target because they are found in organs throughout our bodies. Once the virus enters, it turns the cell into a factory, making millions and millions of copies of itself -- which can then be breathed or coughed out to infect others.

In order to evade early detection, the coronavirus uses multiple tools to prevent the infected cells from calling out for help. The virus snips off distress signal proteins that cells make when they are under attack. It also destroys antiviral commands inside the infected cell. This gives the virus much more time to make copies of itself and infect surrounding areas before it is identified as an invader. This is part of the reason why the virus spreads before immune responses, like fever, begin.

Many with mild or no symptoms are able to fend off the virus before it gets worse. These people may have symptoms only in the upper airway, at the site where they were first infected. But when someone's body can't destroy the virus at its entry point, viral particles march deeper into the body. The virus seems to take a few paths from there, either setting up camp in the lungs, fighting its way into the digestive tract, or doing some combination of both.

"There's clearly a respiratory syndrome, and that's why people end up in the hospital. Some people get a gastrointestinal illness with diarrhea, maybe some abdominal pain, which may or may not be associated with a respiratory illness," says Vinetz.

Once the virus is deeply embedded in the body, it begins to cause more severe disease. This is where direct attack on other organs that have ACE2 receptors can occur, including heart muscle, kidneys, blood vessels, the liver, and potentially the central nervous system. This may be one reason for the vast array of symptoms COVID-19 can cause.

"It's highly unlikely that any other organs can be affected through direct invasion without severe disease," Vinetz adds.

The brain and nerves may also fall prey to direct attack. Kenneth Tyler, MD, chair of the Department of Neurology at the University of Colorado School of Medicine, cautions that direct central nervous system (CNS) attack is still being worked out at this time. There are many routes a virus could take to invade the CNS. One somewhat disputed view is that the loss of smell could indicate that the nerve responsible for smell is infected and can carry the virus into the CNS, including the brain. "This can be shown to occur in experimental models with non-human coronaviruses and is a potential route of invasion for some other viruses. However, there is no evidence to date establishing that this actually occurs with SARS-CoV-2," the official name of the virus that causes COVID-19.

Early findings, including those from autopsy and biopsy reports, show that viral particles can be found not only in the nasal passages and throat, but also in tears, stool, the kidneys, liver, pancreas, and heart. One case report found evidence of viral particles in the fluid around the brain in a patient with meningitis.

Severe damage to the lungs may be one trigger that activates and overstimulates the immune system through a barrage of signaling chemicals, known as cytokines.

The flood of these chemicals can set off what is referred to as a "cytokine storm." This is a complex interplay of chemicals that can cause blood pressure to drop, attract more killer immune and inflammatory cells, and lead to even more injury within the lungs, heart, kidneys, and brain. Some researchers say cytokine storms may be the cause of sudden decompensation, leading to critical illness in COVID-19 patients.

A new finding suggests there may be another deadly culprit. Many doctors are discovering that abnormal clotting, known as thrombosis, may also play a major

role in lethal COVID-19. Doctors are seeing clots everywhere: large-vessel clots, including deep vein thrombosis (DVT) in the legs and pulmonary emboli (PE) in the lungs; clots in arteries, causing strokes; and small clots in tiny blood vessels in organs throughout the body. Early autopsy results are also showing widely scattered clots in multiple organs.

Adam Cuker, MD, a hematologist at the Hospital of the University of Pennsylvania who specializes in clotting disorders, says these clots are happening at high rates even when patients are on blood thinners for clot prevention. In one study from the Netherlands, 31% of patients hospitalized with COVID-19 got clots while on blood thinners.

Cuker says that "new studies validate what we have all been seeing with our eyes, which is that 'boy, it seems that these patients are clotting a lot.' … And it could be that the rate of thrombotic events are even higher than we truly recognize." Though the reason for the clotting is still not clear, it seems to be playing a much larger role in death than previously understood.

Beyond the collateral damage from cytokine storms and clotting, other things like low blood pressure that comes from a severe illness, low oxygen levels, ventilator use, and drug treatments themselves can all harm organs throughout the body, including the heart, kidneys, liver, brain, and other organs.

Even though researchers are learning more each day about the virus and how and where it attacks the body, treatment geared toward these targets also pose significant problems. Many drugscome with a risk of destroying the delicate balance that allows the body to help fight the disease or to manage inflammation.

The ACE2 receptor that the virus uses to enter cells is a key player in lowering inflammation and reducing blood pressure. Targeting or blocking this receptor as a treatment strategy to prevent viral entry into cells may actually worsen blood pressure, increase the risk of heart failure and kidney injury, and increase inflammation that may worsen lung injury.

Drugs that target the immune response to lower the risk of a cytokine storm may also tamp down the immune response, making it hard to kill off the virus over the long run.

Using medicines to prevent clotting may end up causing severe bleeding. Cuker points out that "we don't have a good read on bleeding … we have limited evidence about the clotting risk … we have zero evidence on bleeding risk in these patients, and it's a real priority to understand this risk, especially because one of our strategies to treat the clotting is stepping up intensity the of anti-coagulation."

Timing is likely to be key in treatment strategies. For example, patients may need a drug to boost the immune system early on in the disease, and then one to tamp it down if the disease progresses and cytokine markers begin to rise.

Cuker says that what we know about clotting and almost everything else when it comes to COVID-19 "is just the tip of the iceberg."

Sanober Amin, MD, PhD, a dermatologist in Texas, agrees. She's been tracking the wide variety of skin findings that dermatologists across the world have been noting on social media.

She recently posted images on social media that show the wide variety of skin findings she has been seeing and hearing about. Her post received a massive response. Amin says that "dermatologists from around the world, from Turkey to France to Canada to the U.S., are sharing information about rashes that they've observed in people with COVID-19."

Some rashes seem to be consistent with what's called a viral exanthema, which is a term for a general rash that can happen with almost any virus. But, Amin says, "some skin findings are more consistent with superficial clotting in blood vessels close to the skin."

This is what some have started to call "COVID toes," also called pernio. Dermatologists are seeing more cases of these small clots in toes and fingers, especially in children.

It's hard to know which skin conditions are related to COVID-19 because a lot of people without "typical" symptoms are not being tested, Amin says. Researchers will still need to work out which symptoms may be caused by the virus and which may just be unrelated early findings.

For now, much of the information we have about the symptoms of COVID-19 come from hospitalized patients who are very sick by the time they seek care and may not be able to share information about the early signs and symptoms they may have had.

Because of the lag in testing in the U.S., we still don't know the full extent of what mild and moderate versions of the disease look like, or what effects the disease has on people who have many symptoms but aren't quite sick enough to be hospitalized.

One open question is what the long-term effects may be for survivors. What does life look like after being on a ventilator or suddenly needing dialysis? Will we see decreases in heart, lung, and kidney function that is long-lasting and permanent, or will patients eventually recover?

We also don't know how people will clear infections. If the new corona virus ends up being an acute infection, like other corona viruses, most recovered people should develop at least a short-term immunity. It's also possible that the virus may persist as a latent infection, like chickenpox, lying dormant in the body, only to re-emerge periodically as shingles does, or become a chronic infection, like hepatitis B, living within the body for a sustained period of time, causing long-term damage.

CONCLUSION

The lungs are the organs most affected by COVID-19 because the virus accesses host cells via the enzyme angiotensin-converting enzyme 2 (ACE2), which is most abundant in type II alveolar cells of the lungs.[38] The virus uses a special surface glycoprotein called a "spike" (peplomer) to connect to ACE2 and enter the host cell.[39,36] The density of ACE2 in each tissue correlates with the severity of the disease in that tissue and some have suggested decreasing ACE2 activity might be protective,[40[,41,] though another view is that increasing ACE2 using angiotensin II receptor blocker medications could be protective.[4240] As the alveolar disease progresses, respiratory failure might develop and death may follow.[41]

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The common cold and flu causing normal corona virus when develop spike envelop protein S which can bind to ACE 2 (Angiotensin Converting Enzyme 2) receptors on some kind of human cells, it becomes deadly as ACE2 receptors are present numerously in lung causing pneumonia, these ACE 2 receptors are even present on kidney, heart and even brain cells. So now this modified virus due to mutation can attack and invades all most all vital organ of body.

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