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Review Article

The Impact of COVID-19 on Healthy Related Issues, A structured Review

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ABSTRACT

Coronavirus: (COVID-19) is a recently discovered viral disease caused by a new strain of coronavirus.

The majority of patients with corona-virus infections will have a mild-moderate respiratory disease that recovers without special care. Most often, the elderly, and others with chronic medical conditions such as asthma, coronary disease, respiratory illness, and malignancy are seriously ill.

COVID-19 is spread mostly by salivary droplets or nasal secretions when an infected person coughs or sneezes.

COVID-19 causes severe acute respiratory illness (SARS-COV-2). The first incidence was recorded in Wuhan, China, in 2019. Since then it spreads leading to a pandemic.

The typical incubation time for COVID-19 infection is 2-14 days (normally 5). The common features include fever, cough, tiredness, difficulty in breathing, loss of smell or taste. Occasionally, signs are absent. COVID-19 complications include renal failure, syndrome of cytokine release, pneumonia, respiratory failure, lung fibrosis.

Introduction

Coronaviruses are a virus family that causes diseases including common cold, Middle East respiratory syndrome, and acute respiratory syndrome. In 2019, a novel coronavirus was reported as a source of an epidemic that emerged in China. The virus is related to the RNA virus family, which infects numerous animal species (1).

The 30000 nucleotides of the coronavirus genome are included. The encoding process encompasses 4 structural proteins, nucleocapsid (N), membrane (M), and envelope (E), and other non-structural protein molecules (nsp). The capsid is a protein capsule. A nuclear capsid (N-protein) is anchored to positive-single-stranded virus RNA, allowing viruses to infect cells and transform them into viral manufacturing. N protein covers the RNA genome of a virus that has a vital role in reproduction/transcription. In MHV (murine coronavirus) and IBV (infectious bronchitis virus) strains, N protein binds to sub-genomic and genomic RNAs processing viral replication and transcription. This is critical in the development of a drug that prevents viral replication and transcription by preventing interactions between the N-terminus of the N-protein and RNA strand (2)

M-protein, which is a viral surface protein, is a core controller for coronavirus production. S-protein is viral surface protein and is responsible for virus attachment to host cells receptors, in addition to membrane fusion between the virus and the host cell membrane, which allows the virus to enter the host cell (3).

E-protein is an essential protein in viral assembly, host cell membrane permeability, and virus-host cell contact (4). A lipid membrane surrounds the genetic material. On the surface of the virus, the hemagglutinin-esterase-dimer (HE) has been identified. The HE protein is required for viral entrance but not replication. Apparently, It is necessary for normal host-cell invasion (5).

COVID-19 Transmission

The infection spreads from one person to another by droplets. It is possible to occur via a fecal-oral pathway. Sputum, pharyngeal

swabs, and feces will also contain the virus. COVID-19 has a 5.2-day incubation period, with most patients experiencing symptoms after 11.5-15.5 days (6).

Pathogenesis mechanisms

The SARS-COV2 virus reaches host cells by binding to ACE2 (Angiotensin-converting enzyme2) via S-spike protein. The virus's strong infectivity is due to novel mutations at the receptor-binding domain and the S-spike protein's acquirement of the furan cleavage site. In predisposed patients, the virus's association with ACE2 would lower anti-inflammatory activity and boost angiotensin2 effects (7) During the therapy of COVID-19 in hypertensive patients, Some people have advocated for the use (or discontinuation) of AT1 receptor blockers and ACE inhibitors (8).

When the virus infects alveolar cells, myocytes, and endothelial cells in the vasculature, pro-inflammatory cytokines such as TNF-alpha, IL-6, IL-10, granulocyte colony-stimulating factor (GCSF), macrophage-inflammatory protein1 alpha, induced release of programmed-cell-death 1, and T cell immunoglobulin and mucin domain-containing protein 3 (Tim-3). All of these factors contribute to lung injury, myocyte injury from hypoxia, the body's immune response, enhanced myocardial cell disruption, and intestinal and cardiopulmonary alterations (9).

Body organs affected by COVID-19

The respiratory system is the first system to be impacted by COVID-19. For diagnosis, a real-time PCR for SARS-COV2 virus RNA from a nasopharyngeal swab or sputum is needed. In the early stages of the illness, the result could be negative. Other studies should be performed, such as IgM, IgG antibodies for SARS-COV2, CD4, CD8. SARS-COV2 causes a decrease in CD4 and CD8 cells. Lungs would develop microscopic alveolar trauma, cellular fibro-myxoid infiltrates, and mononuclear cells infiltrate with lymphocytic dominance in the interstitial space (10).

COVID-19 infection normally affects the cardiovascular system; elevated IL-6, troponin-T, natriuretic-peptides are prominent, and their gradual increase is linked to a negative prognosis. Diffuse micro-thrombi, myocarditis, arrhythmias, heart failure, and angina/infarction are possible complications, which have the potential to result in death (11).

In the gastrointestinal system, COVID-19 produces nausea, vomiting, diarrhea, and stomach discomfort. RNA from SARS-COV-2 has been found in feces samples and anus/rectum swabs (12). ACE2 has been detected in gastrointestinal cells, indicating that the virus enters by ACE2 receptors. SARS-COV2 will cause liver damage, and serum alanine-aminotransferase and aspartate-aminotransferase levels may be raised (13).

COVID-19 patients have a similar level of kidney involvement. COVID-19 individuals with acute renal failure ranged from 0.5 percent to 29 percent. COVID-19 severity was influenced by acute renal failure, which included proteinuria and hematuria (14).

The most common neurological signs of COVID-19 are olfactory and/or gustatory dysfunction (15) It is thought that covid 19 binds to the ACE2 receptor, triggering a sequence of signaling cascades that result in a variety of negative neurological outcomes, such as olfactory malfunction, after entering CNS through systemic circulation or nose (16). Stroke, encephalitis/encephalopathy, and other rare conditions can often occur (17). Stroke is a poor prognostic factor, and COVID-19 patients who develop stroke have a threefold increased risk of death (18).

COVID-19 affects the dermatological system directly through virus attack on basal cells of the epidermis, via keratinocytes ACE2 expression as a potential target, and indirectly via inflammatory action against virions (19). Erythematous rash, including maculopapular, and erythema-multiforme like eruptions, are common dermatological manifestations (20).

The next most common symptoms were pseudo-chilblain and urticarial lesions, as well as cases of mouth ulcers, blistering, and herpetiform rash (21). COVID-19 has the potential to infect the brain or cause an immune response that with a negative impact on brain processes and mentality (22). Mental illnesses may be affected by brain injury and can be exacerbated specifically by hypoxia (which is caused by virus infection (23) or indirectly through the immune system or immunotherapy-induced side effects (24).

Clinical features of COVID-19

COVID-19 symptoms include fever, coughing, respiratory difficulties, nausea, and loss of smell and/or taste. Symptoms generally develop one to fourteen days after the virus has been exposed. The majority of patients experience minor side effects, but some develop acute-respiratory-distress-syndrome (ARDS), which is caused by a cytokine storm, which is a cascade of auto-amplifying cytokine development caused by an unchecked host immune response to various causes such as viruses, cancer, rheumatic disorders, and so on (25).

According to others, a cytokine storm is a systemic inflammatory reaction to pathogens and drugs that results in excessive immune cell activation and production of inflammatory cytokines. Organ trauma, such as septic shock, multiorgan loss, and blood clots, is a longer-term hazard (especially the lungs and heart). For months following, certain people experience memory loss, extreme exhaustion, muscle stiffness, breathlessness, and low-grade fever as a result of COVID.

When an infected individual comes into direct contact with another, the virus spreads. During breathing, coughing, sneezing or speaking, tiny droplets containing viruses spread from the nose and mouth. If people come into touch with contaminated surfaces, they will be infected for ten days in moderate instances and two weeks in severe cases (26).

Problems with mood and fatigue

COVID-19 patients with serious symptoms are often treated in a hospital intensive care unit, where they can need artificial breathing support such as ventilators. This will increase the risk of developing post-traumatic stress disorder (PSTD), anxiety, and depression.

Many patients who recovered from SARS COV-2 developed chronic fatigue syndrome, a complicated condition marked by acute fatigue that worsens with physical or emotional exercise but does not improve with rest. Since recovering from COVID-19, several major medical centers are opening specialist facilities to treat patients who have chronic symptoms or illnesses (27).

COVID-19 can cause the following long-term signs and symptoms:
1-loss of olfactory and gustatory senses. 2-Hair loss or rashes.
3-Headache or muscle pain. 4-A beating or quick heartbeat.
5-Problems with memory, concentration, or sleep.

Risk factors in COVID-19

COVID-19 is correlated with many clinical risk factors, including old age, male gender, diabetes, chronic kidney disorder, elevated

BMI, and immunosuppression. Hypertension, lung disease, liver disease, cardiovascular disease, or asthma are all conditions that increase mortality risk (28).

Age increases risk for hospitalization

If COVID-19 is confirmed, Adults over the age of 65 are more likely to need hospitalization or die. The odds of getting admitted to the hospital increase as you become older. For example, people in their 50s have a greater chance of major disease than those in their 40s. People in their 60s and 70s are also more vulnerable to major illnesses than those in their 50s.COVID-19 causes severe illness in people aged 85 and over.

An individual with COVID-19 who has a severe illness may need to be hospitalized, receive intensive care, or use a ventilator (29). Since the generation of native T & B cells declines with age, and the activity of the innate immune system diminishes. Innate immune cells have a lower chance of being triggered. These changes decrease viral clearance efficiency and increase the risk of triggering a dysregulated immune response in which activated immune cells release cytokines, culminating in a cytokine storm. Because of the chronic ailments they suffer from, elderly people in long-term care institutions are at the greatest danger (31)

COVID-19 and Diabetes Mellitus

Diabetes mellitus seems to be consistent with COVID-19 prevalence and increased mortality (32). COVID-19 mortality is also increased by the occurrence of typical diabetes complications (cardiovascular disease, cardiac failure, and chronic kidney disease (33).

Hyperglycemia may impair immune function, and a dysregulated immune system has been related to diabetes mellitus macrovascular complications. Type 2 diabetes mellitus is linked to immunological dysregulation, which is similar to accelerated aging, which can clarify why patients with diabetes and COVID-19 have a weak prognosis (34). Diabetes mellitus is linked to a pro-inflammatory condition as well as a weakened innate immune response. (35). Diabetes has been related to an increased susceptibility to and negative consequences from infections such as pneumonia and influenza (36). Metabolic diseases can affect lymphocyte and macrophage functions, lowering immune function and increasing the risk of disease consequences. Diabetes patients are more likely to suffer hypertension, ischemic heart disease, and heart failure. They propose an angiotensin-converting enzyme inhibitor (ACE1) or an angiotensin receptor blocker (ARB) for the management of hypertension in diabetic patients (37) (38).

There's a chance that ACE1/ARB will upregulate ACE2 and enhance SARS-COV-2 entrance into cells, putting people at risk of infection or making COVID-19 worse (39) Also many antidiabetic agents may affect the expression and activity of ACE2.
(40)

Diabetes is known to cause both microvascular and macrovascular problems. Hyperglycemia, insulin resistance, and metabolic abnormalities in type 2 diabetes cause oxidative stress, endothelial dysfunction, platelet hyperactivity, and low-grade inflammation, all of which damage the vascular wall. All of these factors contribute to vasoconstriction and thrombus development, raising the risk of morbidity and death in diabetes patients. When diabetic individuals contract SARS-COV-2, their vascular dysfunction and prothrombotic condition enhance their risk of thrombotic complications and mortality (41-42)

COVID-19 and BMI

Obesity (BMI>30 kg/m2) was shown to be associated with a 2.35-fold higher incidence of COVID-19. Individuals with excess fat, particularly visceral adipose tissue, obesity, and significant cardiometabolic issues such as hypertension, cardiovascular disease, type 2 diabetes, and a variety of malignancies have a strong link with important COVID-19 (43). Obese people's underlying metabolic and inflammatory variables have a role in the development of serious lung illnesses. Susceptibility to acute respiratory distress syndrome, the major cause of COVID-19 death, is higher in obese people, as is innate and adaptive immune response impairment (44).

COVID-19 and chronic kidney disease

Chronic kidney disease (CKD) raises the risk of death during covid 19 disease outbreaks, and several studies have highlighted the high prevalence and seriousness of this infection for dialysis patients. Owing to compromised immunity, pathological inflammation, higher oxidative stress, uremia, and endothelial malfunction, CKD patients have a higher chance of symptomatic infection. Kidney damage in terms of proteinuria, hematuria, and elevated blood urea and creatinine levels are frequent in COVID-19 (45).

SARS-COV-2 may have a direct effect on the kidney due to viral tropism. By attaching its spike protein to ACE2, which is found in renal tubular epithelial cells and podocytes, the virus infects cells. Renal damage in COVID-19 infection is caused by endothelial failure, coagulopathy, and complement activation. Microangiopathy and complement activation are the two main causes of kidney damage. COVID-19-related coagulopathy is linked to high D-dimer levels, microvascular damage, and endothelial dysfunction. The SARS-COV-2 infection has been related to the onset of a cytokine storm, an overactive inflammatory response that can harm the kidneys and other organs (46).

Sepsis may be the cause of acute renal injury in those who have COVID-19. Systemic hypotension, renal vasoconstriction, endothelial dysfunction, tubular cell death, inflammatory cell infiltration into the renal parenchyma, and capillary thromboembolism are all variables that lead to acute kidney injury. The innate immune system's reaction to sepsis can result in a cytokine storm (47)

COVID-19 and cardiovascular disease

Cardiovascular disease (CVS) is a risk factor exacerbated by COVID-19 infection, which causes or aggravates myocardial damage, but when combined with myocardial injury, patients die. COVID-19 appears to be related to poorer outcomes and a higher risk of death in patients with pre-existing cardiovascular disease. COVID-19 can cause myocardial damage, arrhythmia, acute coronary syndrome, and venous thromboembolism (48). SARS-COV-2 infections cause ACE2 to be downregulated, which can lead to cardiac dysfunction. The immunological response to SARS-COV-2 may have an indirect effect on the heart and blood arteries. In individuals infected with SARS-COV-2, there is also fatty acid metabolism disruption. When compared to individuals who did not have SARS-COV-2, blood levels of lysophosphatidylcholine, free fatty acids, phosphatidylglycerol, and lysophosphatidylethanolamine were higher in these patients (49).

As a result, heart diseases and diabetes double the chance of mortality compared to other risk factors. A substantial majority of COVID-19 fatalities are caused by people who have cardiovascular disease. (50) Also, because cardiovascular illness is more common as people get older, a compromised immune system might raise the chance of severe COVID-19 (51)

Patients on immunosuppressive drugs

A study conducted by researchers at the Johns Hopkins School of Public Health has shown that people on immunosuppressive medications do not fare worse than other patients when admitted to hospitals with COVID-19. (52). Immunosuppressive medications might be used to treat and prevent COVID-19's hyperinflammatory phase, however, they impede the host's immunological response to the virus and could be detrimental in the early stages of the virus (53).

According to several studies, immunocompromised people are at a greater risk of infection and more severe illness with COVID-19, whether owing to a natural immune deficiency or attributable to the use of immunosuppressive medications. Infection with SARS-COV-2 causes local inflammatory and immunological responses in the respiratory tract, resulting in the production of cytokines and priming of adaptive T and B-cell immune responses. It mostly aids in the resolution of infection; but, in rare circumstances, a defective immune response may develop, resulting in systemic harm (54)

The advantage of low-dose dexamethasone (glucocorticoids) on survival in severe COVID-19 has just been described. Immunosuppression is beneficial in such diseases because of its anti-inflammatory properties, which may reduce the clinical manifestations of the disease, including an increased immunological response to viral infection. (55)

COVID-19 and hypertension

The connection between high blood pressure and serious coronavirus infection is still unclear. Uncontrolled blood pressure, according to others, causes chronic inflammation in the body, that affects blood vessels and causes immune system dysregulation. This makes it difficult to combat the virus or causes a risky immune system overreaction to COVID-19.

The viral structural spike(S) protein binds to the angiotensin-converting enzyme 2 (ACE2) receptor to enter cells. Angiotensin-converting-enzyme inhibitors (ACE inhibitors) and angiotensin-receptor-blockers (ARBs) were once considered to worsen inflammation, however, this theory has now been debunked (56). The mechanism by which hypertension increases the likelihood of COVID-19 infection is unclear; nevertheless, when COVID-19 infection is exacerbated by myocardial damage and in the presence of cardiovascular disease, the prognosis for individuals with hypertension is poorer (57). Cardiovascular events and end-organ damage are associated with poor control of high blood pressure (58)

The correlations between age, hypertension and the severity of COVID-19 infection are explained by older age, poor blood pressure management, and cardiovascular disease (59).

COVID-19 and asthma

Asthmatic patients, especially infants, are less vulnerable to coronavirus, have a low risk of asthmatic exacerbations, and have a good prognosis (60). During influenza epidemics, asthma is present in more severe situations, and some patients, including children, need artificial ventilation. Different levels of ACE2 expression, innate immune memory, and a higher lymphocyte count in children could all play a role (61).

Some studies show that individuals with COVID-19 have a reduced prevalence of asthma. Many people with acute are under careful medical supervision owing to the chronic nature of the condition, and these patients are warier of viral infections. Anti-inflammatory drugs, such as corticosteroids, may also protect asthmatic patients. Variations in susceptibility to severe COVID-19 might be due to genetic differences (62)

Asthma is a chronic illness that needs long-term medical care, and asthmatic patients are particularly sensitive to the effects of COVID-19. (63) COVID-19 rendered patients with severe asthma and those on high-dose inhaled corticosteroids at a higher risk of serious illness and death (64).

Most individuals diagnosed with COVID-19 have vague signs and symptoms, such as dyspnea, cough, wheezing, fatigue, and fever, which can be difficult to distinguish from those of other infections and asthma. Because the symptoms of COVID-19 are similar to those of other viral infections and asthma exacerbations, patients with asthma and COVID-19 patients may be confused about the need for COVID-19 testing, isolation requirements, and illness management. (65)

Conclusion

Due to the rapid spread of COVID-19 infection, a lack of screening equipment, and a global shortage of intensive care units, we rely on other considerations, such as COVID-19 clinical features, to provide early notice and prompt effective measures to reduce the number of COVID-19 deaths. As a result, the major symptoms of COVID -19, such as fever, cough, dyspnea, and weakness, should be considered for early disease diagnosis.

Many studies have shown that even after healing from COVID-19, some patients will have at least one symptom, most often nausea and dyspnea. Male ethnicity, older age, and patients with comorbidities such as asthma, diabetes, cardiovascular disease, and others were all linked to a higher risk of death among COVID-19 patients admitted to hospitals. These results will aid healthcare professionals and doctors in recognizing the risk of high mortality among COVID-19-infected patients and developing appropriate intervention plans in the healthcare field to reduce this high mortality rate and fight the COVID-19 pandemic to save human lives.

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