SARS CoV-2 infection induced changes in physiological function

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ABSTRACT

Coronavirus, identified as the causative microbe for infectious disease, severe acute respiratory syndrome 2 at the end of 2019 in Wuhan, China. The virus has spread to every part of the globe and created a pandemic claiming millions of lives. The infection becomes symptomatic through a cold, sore throat, fever and other symptoms. Diffuse alveolar damage with an opacity of the lobes of the lungs in elderly with associated comorbidities leads to fatal conditions. Angiotensin-converting enzyme 2 (ACE 2), the receptor for the spike glycoprotein of SARS CoV-2 is widely expressed on different cell surfaces facilitating viral entry and pathogenesis with multi-organ damage. In children, the chances of infection are less associated with fast recovery compared to adults—inflammatory reactions with cytokine storm trigger rapid changes in severe stages of infection that require medical intervention. The repurposing of existing antiviral drugs has improved some infected patients to recover. But at large, the entire world has come to a standstill with hampered progress due to non-availability of a vaccine for treatment for SARS CoV-2. This review focuses on the infection of different organs and the diagnosed features in the case studies with implemented treatment measures.

INTRODUCTION

Coronavirus has caused three major outbreaks in the 21st century. SARS CoV in 2003, MERS CoV in 2012 and the recent COVID-19, in December 2019, renamed as SARS CoV-2. SARS CoV-2 traces back for its origin in a local seafood market in Wuhan, China, when the seafood sellers or delivers presented with symptoms of severe pneumonia. World health organisation has declared it as a pandemic. (da Costa et al., 2020) coronavirus, identified for its enriched presence in bats which serves as a tremendous reservoir of the virus, was predicted for causing future disease outbreaks due to the habits of consuming exotic animals, which would function as a time bomb. Soon the virus spread to a broader population through human transmission by respiratory droplets, and it has spread to people in 216 countries with 10,004,707 cases and 499,619 deaths around the world as on 29th June 2020. (WHO, 2020) The symptoms of the disease caused by SARS CoV-2 include fever, dry cough, cold and dyspnoea. To prevent spread from asymptomatic patients social distancing is strongly recommended and mildly infected patients presented with hyposmia as a symptom rather than fever.

Binding receptor and mode of transmission

In a study conducted with HeLa cell lines, SARS CoV-2 infected ACE2 protein-coated or expressing cells but not cells without ACE2 receptor. The mode of infection of SARS CoV-2 and the target of binding of the virus was identified to be through a recep-
tor ACE2 (Angiotensin-converting enzyme2) that is expressed on nasal epithelial cells, cilia and to a greater extent in the pneumocytes. The receptor is widely expressed in different cells which includes conjunctiva, respiratory tract, lungs, heart, liver, kidneys and gut intestinal cells. Hence, the mode of transmission also includes lachrymal secretions of eyes and faecal-oral transmissions. The presence of the virus in the viral culture of self-collected salivary samples and its decline after hospitalisation indicates the mode of transmission of the virus through saliva.

Angiotensin-converting enzyme 2 (ACE2) is an enzyme that is widely expressed in the cells of heart and lung cells. ACE2 functions as a binding receptor for the spike glycoprotein of SARS CoV-2. Expression of increased levels of the receptor in lung and heart of patients with cardiovascular disease and lung ailments increases the viral entry and multiplication in the alveolar cells. (Zheng et al., 2020)

The expression of ACE2 and TMPRSS2 was observed to a greater extent in nasal cells (goblet and ciliated cells) with co-expression in other tissues (cornnea, oesophagus, ileum, colon, gall bladder and bile duct) suggesting alternate modes of transmission (ocular or faecal-oral transmission). Hence, the study (Sungnak et al., 2020) urges the immediate need for intranasal drug or vaccine to prevent the spread. Higher levels of DPP4 have been reported in diseases like type 2 diabetes, obesity and other metabolic syndromes. A wide distribution of DPP4 might contribute to a more significant number of target organs for attack by SARS CoV-2, which are even higher than the ACE2 receptors.

According to the interpretation made in a study comparing infection by SARS CoV, SARS-CoV-2 and MERS CoV, the pathogen SARS-CoV-2 was detected for its presence in type I pneumocytes. Apart from its presence, SARS CoV-2 exhibited wide replication in bronchial cells compared to SARS CoV, suggesting it to be the cause for the severe transmission and pandemic situation. The severity of the disease is predicted for coronavirus depending on the site of infection.

If it infects the upper respiratory tract, and the epithelial cells lining the airways, chances of recovery from the disease are greater. If the virus infection occurs in the lung cells in the gaseous exchange cavity of the lungs, infection of the type II alveolar cells and damage causes rapid disruption in the function of the lung cells leading to diffuse alveolar damage and fibrosis. Recovery from infection at this stage requires strong innate and acquired immune response. (Mason, 2020)

**SARS CoV-2 and Immune response**

Cytokine storm which occurs during the moderate and severe diseased conditions of SARS CoV-2 infection has revealed that Interferon-gamma induced protein 10 (IP-10) and Monocyte chemotactic protein -3 (MCP-3) could be used as biomarkers to forecast the disease progression. Though there are other three cytokines like hepatocyte growth factor, monokine induced gamma interferon and macrophage inflammatory protein 1 alpha which elevates in disease progressing conditions. In case studies from COVID-19 infection conducted in pulmonary and skin samples, thrombotic injury of microvasculature was a generalised feature in critically ill patients.

Pathological changes observed include activation of the complement pathway with deposits of complement observed in skin and lung lesions. In a case report (Xu et al., 2020b) the lung cells presented with infiltration of inflammatory mononuclear cells in both the lungs predominated by lymphocytes. Still, viral inclusions within the cytoplasm or nucleus were not observed. Also, the liver biopsy examination revealed steatosis of microvesicles but not much damage in heart tissue except for infiltration of mononuclear cells.

Kidney transplant recipients infected with COVID-19 due to immunosuppression suffered from decreased T-cell subsets with 28% greater mortality than people infected with COVID-19 in a general population of 1-5% mortality. In a study conducted in an animal model in dogs with canine coronavirus type –IIa, hyper-virulent viral strain, the levels of CD4+ T cells decreased within a few days of infection. It returned to normal levels only after two months of infection though the levels of serum immunoglobulins G and M did not suffer any significant changes. Nevertheless, the levels of CD14+ and B lymphocytes decreased in 3 days but gradually recovered within 14 days and 5 days.

Patients affected with the severe form of infection by SARS CoV-2 suffer from decreased levels of CD4+, CD8+ T cells and IFN-γ. Due to the association with an extreme disease condition, these markers analysis gain importance in SARS CoV2 infection. The transcriptional profiling of SARS CoV-2 in various cell line models demonstrated the decreased expression of interferons and high levels of chemokines which mediates an imbalance in the response of host cells to the virus and hence future drugs for treatment must have the immune-modulating function to control the inflammatory response. (Blanco-Melo et al., 2020).
SARS CoV-2 and respiratory system

According to the case report in lung biopsy of a patient infected with SARS CoV-2, diffuse alveolar damage was identified. Similar such diffuse alveolar damage was also presented in a study with SARS-CoV in autopsy cases. In a study, in patients who were suffering from lung cancer were found to be infected with SARS-CoV-2 post-surgery, but were asymptomatic for pneumonia or other symptoms at the time of surgery. The early changes in the infection were hyperplasia of type II pneumocytes, multinucleated enlarged cells and protein exudates in alveolar spaces. Asymptomatic patients of COVID-19 infection who had a history of exposure to SARS CoV-2 exhibited CT imaging of ground-glass opacities in one or both the lobes of lungs. Since asymptomatic infections act as covert transmitters, it is crucial to monitor the asymptomatic patients with SARS CoV-2 infection. (Meng et al., 2020)

SARS CoV-2 and cardiovascular system

Though biochemical abnormalities were observed in asymptomatic patients like varying fibrinogen, C — reactive protein and myocardial enzymes, the results were not significant when compared with symptomatic patients. Despite, levels of creatine kinase-MB were elevated in the asymptomatic group. But the study emphasises that more studies related to the levels of creatine kinase-MB might be essential to demonstrate the role of this enzyme in symptomatic and asymptomatic patients. In another editorial letter, (Yao et al., 2020) it was reported that in a ready to discharge patient, who yielded to cardiovascular death, the post-mortem analysis revealed the presence of SARS CoV-2 viral DNA in the lung tissue samples by digital PCR but not in other tissues like liver, heart, intestine or skin and histopathological observations explained fibrin exudation, a proliferation of type II alveolar epithelial cells, hyaline membrane formation similar to the changes observed in SARS CoV and MERS infections. Hence, the study emphasises the detection of viral DNA by a polymerase chain reaction in lavage fluid for follow-up in discharged patients and patients with other secondary complications like diabetes or cardiovascular disorders.

Human-induced pluripotent stem cells derived cardiomyocytes was prone to be infection by SARS CoV-2 suggesting that in the absence of counteracting immune reactions, the heart is also a target for the virus infection to cause a series of altered physiological functions. The upregulation of pro-inflammatory cytokines in SARS CoV-2 infection may lead to multi-organ failure due to systemic inflammatory response, including damage to the heart.

Heart fatty acid-binding protein, a biomarker for myocardial damage increases during severe infection with SARS CoV-2 and the elevated protein in patients, is also a prognostic indicator of transition from mild to severe form of infection. In a case study, patients with COVID-19 infection along with myocardial infarction presented with inflammatory reactions mediating cytokine storm inducing plaque rupture. Coronary angiography at the right time was the primary decision. Spread of SARS CoV-2 infection in European countries has a greater incidence in old aged people with hypertension. The difference in the incidence of infection among different countries might be due to a difference in expression of Angiotensin-converting enzyme 2 (ACE2) by different races. (Ruocco et al., 2020)

SARS CoV-2 and gastrointestinal system

In a case study performed in a 78-year-old patient infected with SARS CoV-2, the viral nucleocapsid protein was detected in gastric, duodenum, rectum epithelial cells but not in the oesophageal epithelium. Similarly, ACE2 expression is more significant in the intestinal epithelium but rarely in the oesophagus. The presence of SARS CoV2 in faeces sample raises the demand for routine diagnosis in faecal samples as the virus is capable of gastrointestinal infection and transmission of infection via faecal-oral mode even after the clearance of the virus from the respiratory tract. The broader expression of ACE2 in cholangiocytes (~60%) than liver cells (~3%) suggests a greater probability of damage to biliary ducts within the liver cells than the hepatic cells. Altered levels of transaminases, increased prothrombin time and decreased protein levels reports mild to moderate damage to liver cells in SARS CoV-2 infection.

Gastrointestinal manifestations in COVID-19 infection include elevation in the liver enzymes. Medications used for the management of SARS CoV-2 infection might serve as a basis for gastrointestinal or liver injury. The greater expression of ACE2 in the ileum predisposes the viral infection in the gastrointestinal tract. Infection of SARS CoV-2 on liver ductal organoids induces cell death of cholangiocytes after two days. It disrupts the barrier function of epithelial cells of the bile duct by modulating the expression of genes. (Zhao et al., 2020)

In patients infected with SARS CoV-2 with liver abnormalities exhibit wide variation in levels of aminotransferases and gamma-glutamyl transferases in severe conditions. The presence of the virus in the cytosol of liver inducing cytopathic effect has been observed using an electron microscope in case studies. The hepatic viral clearance
needs to be monitored in patients for a better outcome. In a retrospective study, patients with abnormal liver function increased after admission who had received lopinavir or ritonavir medications suffered from elevated bilirubin and liver enzymes and the hospital stay prolonged. Hence, precautionary measures are needed in the administration of the drugs for COVID-19 infected patients. (Fan et al., 2020)

In a study conducted in 93 patients with COVID-19 infection, the levels of aspartate aminotransferase, other enzymes of the liver, bilirubin increased markedly. The risk of the need for intensive unit treatment and the increased mortality rate was associated with an increase in levels of AST and bilirubin based on the statistical analysis. In a liver allograft recipient, hepatitis was observed, and later the mother donor was detected positive for COVID-19.

The infant recipient exhibited five-fold variations in the levels of liver enzymes with liver biopsy depicting hepatitis with clusters of apoptotic cells. Patients infected with COVID-19 and suffering from the non-alcoholic fatty liver disease had more significant risks of abnormal liver function, longer viral shedding time and progress to severe stages. Impaired immune response by the macrophages in the liver cells might contribute to worsening conditions.

The patients had to be re-admitted due to gastrointestinal disturbances after initial discharge based on the absence of SARS CoV-2 in the respiratory tract. The infection lasted for more than 30 days in 3 cases studied, and hence clinicians must also focus on proper management of the dysfunction of digestive symptoms in COVID-19 infected patients. Hence, the criteria followed during discharge based on the infection must consider the absence of SARS CoV-2 in respiratory and faecal samples. (Wang, 2020).

SARS CoV-2 infects the intestinal cells in an organoid model. The rate of infection appeared equal for the precursors of enterocytes and enteroctyes. The expression of ACE2 increases 1000 fold upon differentiation at the mRNA. The transcriptomic analysis revealed upregulation of a wide range of cytokines and interferon genes. Bat enteric organoid culture supported the strong growth of SARS CoV-2, which demonstrated the intestinal cells of bat promote SARS CoV-2 infection.

Similarly, human intestinal organoids have exhibited complete replication of the virus and cytopathic effect in colonoids than enteroids with up-regulation of type III interferons. But the mode of infection of intestinal tract occurs secondary to respiratory tract infection, or it may be through faecal-oral transmission requires further investigation. (Zhou et al., 2020)

Expression of transmembrane serine proteases in the intestinal cells (TMPPRSS2 and TMPPRSS4) along with excess ACE2 activates the viral entry and membrane fusion. Simulated large intestinal fluid inactivates the virus than simulated small intestinal fluid. Thus, the infectious virus decreases in the stool samples, and the chances of faecal-oral transmission are less. But suitable precautionary measures are to be taken to prevent transmission of viral infection from hospital admitted SARS CoV-2 patients as long as faecal samples indicate the presence of viral RNA.

SARS CoV-2 and renal system

Detection of viral particles of SARS CoV-2 in the tubular epithelium of the kidney confirms the direct infection of the virus in acute kidney injury. The virus with its envelope and crown-like projections and double-membrane vesicles detected in the ultrastructural evidence from an autopsy of the infected patient suggest it as a useful histologic marker for SARS CoV-2 infection. Acute kidney injury in COVID-19 infected patients occurs in severe cases with respiratory failure requiring mechanical ventilation. The cytokine storm that occurs during respiratory failure and other circulating substances might be responsible for acute kidney injury within a day of intubation. (Hirsch et al., 2020)

SARS CoV-2 and nervous system

Patients infected with SARS CoV-2 also present symptoms of anosmia, encephalitis and encephalopathy and delirium in older patients. Based on the number of positive COVID-19 cases presenting delirium as a symptom, it has been suggested to include mental status changes in the list of testing criteria for SARS CoV-2 infection.

Patients with COVID-19 also had a higher risk of cryptogenic stroke due to hypercoagulability compared with their contemporary controls. Most of them were younger men with elevated troponin, erythrocyte sedimentation rate and D-dimers. In patients with COVID-19 infection, neurologic manifestations like cerebrovascular disease, consciousness impairment and skeletal muscle dysfunction present in severely infected older individuals with other complications like hypertension. In a 54-year-old patient infected with SARS CoV-2, anosmia and interstitial pneumonia and seizures were diagnosed. Demyelinating lesions were observed in the MRI. Dexamethasone treatment for ten days showed improvement in lung function and neuro-
logical symptoms. (Zanin et al., 2020)

**SARS CoV-2 and sensory organs**

In a case study from Italy, a patient was identified positive for the presence of SARS CoV-2 in ocular fluids. Due to the conjunctivitis symptom, ocular swabs were diagnosed for the presence of virus from 3rd day until 21st day. Though the virus declined and conjunctivitis improved, even on day 27, the ocular swab analysis implicated the presence of virus suggesting the replication in conjunctiva for a longer duration. Hence, ophthalmologists have been advised to be precautious during an examination of patients for avoiding cross-infection. Future studies on patients with conjunctivitis and SARS CoV-2 are required to provide further insights onto the mode of infection through eyes. In another study, 12 of 38 patients presented with symptoms of infection in eyes and 11 of them had confirmed the presence of a virus in nasopharyngeal swabs, and 2 of them reported for positive viral presence in both ocular and nasopharyngeal swabs. The expression of ACE2 receptor mRNA and protein is very low in the conjunctival samples suggesting the chances of viral entry and infection through conjunctiva to be an unlikely event. In patients infected with COVID-19, oral blisters appeared as symptoms in 3 cases. The virus induces exanthematic lesions that resemble other viral processes. Therefore, intra-oral examination of SARS CoV-2 patients has been recommended. (Carreras-Presas et al., 2020)

**SARS CoV2 in infants**

Reports on children infected with SARS CoV-2 were less compared with adults. In a case study report on five children infected with SARS CoV-2, as a difference from the conventional symptoms of respiratory tract infections in COVID-19, these children initially presented with gastrointestinal symptoms and some required immediate surgical intervention though others suffered from gastroenteritis. Increase in levels of cytokines IL-6, IL-10 with decreased levels of T-lymphocytes reports varying immune response due to infection. Thus, cytokine storm during infection had been the primary cause for multi-organ dysfunction in some cases. Multi-organ dysfunction in major organs like liver, kidney, heart and lung has been observed. Infants less than three months of age presenting with fever should be screened for SARS CoV-2 and associated seizures.

The incidence of COVID-19 in cystic fibrosis patients in Italy was reported for one adult and one child during the pandemic outbreak. The symptoms were asymptomatic in the child based on the nasopharyngeal swab analysis, and the infection did not advance further with any symptoms. The plasticity of the immune system with the lesser expression of ACE 2 receptors might report a low incidence in children. Children are less affected by SARS CoV-2, as the alveolar epithelium regeneration capacity is tremendous that decreases the susceptibility to infection. The comorbidities like obesity, smoking and other diseases are less in children that decrease the number of positive COVID-19 cases in children. The presence of SARS CoV-2 in faecal specimens was observed in an electron microscope. Also, the percentage of paediatric patients exhibiting positive SARS CoV-2 in faecal samples is more significant than in adults. The differences in the microenvironment in gastrointestinal tracts in adults and children might cause a difference, or the intestinal flora might protect the virus from the immune response in the host. (Mao et al., 2020).

In an infant five-month-old with COVID-19 with existing comorbidity of mucopolysaccharidosis’s type I Hurler syndrome and heart failure, multisystem damage with cardiac arrest resulted in a fatality. Infants with associated disorders in infants, especially cardiovascular damage, are of particular concern in SARS CoV-2 infection. Infants with COVID-19 infection below one year of age are suffering from severe symptoms than older children. IL-6 levels in the premature born eight-week-old infant were higher than the threshold levels reported in adults for respiratory failure. Increased inflammatory response associated with multiple organ damage and its prognosis in affected children is crucial for treatment. In the case of children infected with COVID-19, they presented fever, mild respiratory symptoms when compared to adults. Abnormalities of liver, heart or kidney enzymes were not reported.

Lymphocyte counts, blood glucose, were normal. But the presence of the virus in stool samples was prominent until 21 days of infection. Hence, virus diagnosis in throat swabs and stool samples are required to avoid faecal-oral transmission and practice hand hygiene in children. The chances of infection are less in children, and recovery is quick. (Pin Tan et al., 2020)

**SARS CoV2 in pregnancy**

Admission to intensive care units was greater in case of COVID-19 infected pregnant women with associated comorbidities and for women with age beyond 35 years. Higher mortality was associated with increased utilisation of antiviral drugs in cohorts that requires an explanation from residual confounder analysis. In pregnant women who were mild symptomatic of COVID-19 with cough, fever, sore throat and other symptoms, screening for infection was recommended. In patients with declin-
ing respiratory function, in 2 cases, the emergency caesarean section was performed. One child was positive for SARS CoV-2 and developed pyrexia and pneumonia that settled after antibiotics supplementation.

To prevent infection of the foetus during vaginal birth when the mother is symptomatic with less than 14 days of infection with SARS CoV-2, Caesarean section is recommended for the birth due to the absence of maternal Immunoglobulin G in their serum and persistent diarrhoea in mother. In a particular case, a pregnant woman with 34 weeks of gestation, presented with symptoms of fever, dry cough. An ultrasound scan revealed amniotic fluid with a depth of less than 13 mm and amniotic fluid index less than 48 mm indicating oligohydramnios. Due to the suffering of a foetus with a forced posture, caesarean section was performed with a premature birth weight of 2.15Kg. Pregnant women should be monitored for oligohydramnios in COVID-19 infection.

Pregnant women with COVID-19 infection reported increased IL-6 levels compared to non–pregnant women. From earlier studies, maternal systemic inflammation influences the brain of the foetus due to placental foetal interactions and greater risk of neuropsychiatric disorders by 12 -24 months of age. The cytokine storm and hyperinflammatory response in COVID-19 infection in pregnant women are to be assessed for brain development and its function in the new-borns. In a study conducted in Washington in pregnant patients, 15% of pregnant women had an infection with SARS CoV-2 due to associated obesity or overweight conditions. Chances of a preterm birth increase due to obesity in COVID-19 infection to improve the maternal pulmonary function. In a case study report, 7 out of 9 pregnant women infected with SARS CoV-2 ended with a fatal outcome due to pulmonary or cardiovascular complications. None of them suffered from other comorbidities like gestational diabetes mellitus, hypertension. The age of the patients was above 35 years though two still survived. A decrease in levels of lymphocytes and eosinophil counts were a common observation in pregnant women infected with SARS CoV-2, which might facilitate early diagnosis of COVID-19 infection. (Xu et al., 2020a)

**SARS CoV2 and other complications**

Administration of GLP-1 before surgery reduces the incidences of increased blood glucose post-surgery in cardiac or other surgeries. Since the rate of consumption of GLP-1 analogues by SARS CoV-2 infected people is high, the effect of GLP-1 analogues in reducing hyperglycaemia and inflammatory response in SARS CoV-2 infection could be studied.

Metformin elevates the expression of ACE2 and phosphorylation of a serine residue at a specific position. The stability of ACE2 enhances by ubiquitination that prevents its degradation. Hence, metformin might also increase the levels of ACE2 facilitating SARS Cov-2 infection. Further analysis in diabetic patients infected with the virus might help better understanding. According to the reports from Centre for disease control and prevention (CDC), people with BMI more than 40 are at more significant threat for infection by SARS CoV-2 apart from those suffering from hypertension, diabetes or cardiovascular disease. The lack of co-expression of TMPRSS2 and ACE2 in testicular cells and ovarian cells excludes the possibility of long term effects due to SARS CoV-2 infection in reproductive function. (Stanley et al., 2020)

Elevation of protein, albumin in urinary excretions, increased blood urea nitrogen and serum creatinine was the common changes in biochemical profile in the hospitalised COVID-19 infected patients. ACE2 receptors expressed on skin cells may facilitate viral binding, entry and replication through injured sites on the skin from respiratory droplets or contaminated surfaces. Screening of skin lesions along with respiratory swabs for SARS CoV-2 might facilitate in correct diagnosis in patients with accompanying skin injury.

**SARS CoV2 and treatment**

Human recombinant soluble ACE2 (HrsACE2) decreases the recovery of SARS CoV-2 from Vero cells, demonstrating inhibiting action of hrsACE2 against SARS CoV-2 to the Vero cells. Also, human recombinant soluble ACE2 inhibits the binding of SARS CoV-2 to blood vessels and kidney organoids. Hence, the potential of hrsACE2 to block initial stages of infection by SARS-CoV2 has been suggested. SARS CoV-2 was capable of infecting human capillary organoids and kidney organoids due to the expression of ACE2.

HrsACE2 inclusion to the organoids reduced the viral load in the blood capillary and kidney organoids in a dose-dependent manner in the early stages of infection. Ribonucleoside analogue, β-3-N- hydroxycytidine decreases the viral load of SARS CoV-2 in Vero cells and Calu -3 cells and human airway epithelial cells in a dose-dependent manner. According to the recommendations of the World health organisation, corticosteroids administration in COVID-19 infected patients is not recommended as it delays the clearance of the virus from the respiratory tract. (World Health Organization,
In a case report of an 80-year-old woman with ulcerative colitis, corticosteroid administration was marked by an improvement in condition in initial stages which worsened later, and the patient died after 14 days due to COVID-19 infection. Hence, the diagnosis of viral infection before treatment with corticosteroids has been suggested in the pandemic situation. Long term use of corticosteroids is a cause for gastric ulcer, and high doses lead to perforation and peritonitis. Due to the COVID-19 infection of the patient, minimally invasive surgical method and rapid enteral route initiation in post-operative conditions hastened recovery with a better outcome in 14 days after surgery.

In a 66-year-old patient with SARS-CoV-2 infection, presented with abdominal discomfort followed by typical symptoms of COVID-19, treatment with lopinavir or ritonavir and ribavirin for three days produced discomforts like diarrhoea or vomiting that led to discontinuation of drug administration but that followed improvement of the lung function and COVID-19 symptoms. Due to the short time therapy, a possible positive effect of the antiviral drugs requires further support from additional case reports.

In a randomised, double-blind, placebo-controlled multi-centre trial with remdesivir, it was not associated with significant clinical benefits. Although not significant, patients receiving remdesivir less than ten days of infection exhibited reduced time for clinical improvement than placebo, which requires support from large sample studies. In a cohort study consisting of 61 patients infected with COVID-19, 68% of infected had improvement in symptoms on treatment with remdesivir. More evidence on the efficacy and safety of remdesivir is expected from randomised placebo-controlled trials. Infection with SARS-CoV-2 and associated inflammation increases the oxidative stress and associated cell damage.

Early treatment with N-acetyl cysteine has been suggested as a cost-effective protective measure to prevent damage to lung cells due to reactive oxygen species and also to balance the drug-induced oxidative species in viral infection. In a 55-year-old case study report of a patient with two episodes of infection with COVID-19, symptoms presented include erythematous — oedematous plaques on the skin in 1st episode and urticarial lesions on the shoulder in 2nd episode. Treatment with cortisone and rapid improvement might have prevented examination of COVID-19 if systemic symptoms had not been presented and zinc administration for ten days aided the incomplete recovery of systemic symptoms. (Medeiros and Silva, 2020)

In another case study in a 57-year-old woman, though the typical symptoms of COVID-19 infection were not presented, lung examination revealed opacity. Nasal swab examination confirmed SARS-CoV-2 infection. The patient presented with a complaint of swelling and a pain in the left leg suggestive of deep vein thrombosis that subsided on treatment with heparin. In a case study of a 46-year-old woman infected with SARS-CoV-2, the RT-PCR reported positive for infection after two negative results prior. For those in convalescence, the respiratory tract sampled might provide persistent positive results in the course of the disease. The patient recovered with antimicrobial treatment consisting of oseltamivir, arbidol, lopinavir/ritonavir and moxifloxacin.

Increased mortality due to COVID-19 infections in Spain, Italy, in older people beyond 70 years has been correlated with Vitamin D deficiency (<0.25ng/L). Elimination of Vitamin D deficiency decreases the risk of elevated C-reactive protein during cytokine storm in severe infection due to SARS-CoV-2. Several studies in support of Azithromycin in treatment of SARS-CoV-2 have been reviewed based on its immune modulation and antiviral properties which suggests for single-drug therapy in a clinical investigation against SARS-CoV-2. (Bleyzac et al., 2020)

Colchicine was suggested for the treatment of SARS-CoV-2 due to its capability to inhibit the production of Interleukin-1, which requires support from the clinical trials. Hydroxychloroquine, an antimalarial drug that had reported antiviral effect in other viral infections, had been used for treatment worldwide to reduce the COVID-19 symptoms. The ability of the drug to bind to porphyrins prevents the viral binding to the host cell. The harmful effects of hydroxychloroquine include the rise in vasoconstrictor with a reduction in vasodilator with the increase in risks for heart strokes in patients predisposed with hypertension or cardiovascular diseases. Tocilizumab, anti-IL-6 receptor antibody, had been recommended for reducing cytokine storm in patients infected with SARS-CoV-2 despite drawbacks of liver toxicity and elevated triglyceride levels due to the drug.

Methylprednisolone administration was recommended in severe cases of COVID-19 infection to reduce lethal effects of cytokine storm though it has not been recommended by WHO due to lack of positive support. Zinc was found to be effective in inhibition of RNA dependent RNA polymerase.
activity, template binding or elongation of SARS CoV-2. In a cancer patient admitted in a hospital for treatment, developed fever and diagnosis of throat swab confirmed positive for SARS CoV-2. Treatment with Kaletra (lopinavir/ritonavir) improved pneumonia and other symptoms. Inclusion of statin before the infection by influenza virus on kidney cells reduced the new viral cell production by 95%, suggesting the possibility of exploring statin in protecting COVID-19 infection.

In a case report, a 35-year patient presented with adult otitis media and SARS CoV-2 infection confirmed by RT-PCR without any symptoms of COVID-19 infection. The other clinical manifestation diagnosed includes hearing loss and lung involvement. Treatment with oseltamivir and quarantine improved the conditions. Hence, a complete examination of the patients is a requirement for the diagnosis of COVID-19 infection when typical symptoms are not presented. In a case study, for a patient infected with SARS CoV-2 and other viruses in the respiratory tract, the patient developed fever and gastrointestinal complications (bloody diarrhoea, haemorrhagic colitis) and respiratory complications (breathing difficulty).

With hydroxychloroquine and other medications, though the situation improved after 20 days, at the time of discharge, the patient was re-admitted due to changes in mental status. In a study comparing the autopsy lungs samples of patients infected with COVID-19 and H1N1 infection, micro-thrombi in alveolar capillaries were nine times higher in COVID-19 infection along with 2.7 times increased new vessel growth than in influenza. (Ackermann et al., 2020)

CONCLUSIONS

Hence, infection by SARS CoV-2 causes disturbances in the function of various organs in the body due to overwhelming inflammatory response which causes multi-organ damage in severe conditions. Therapeutic interventions in the form of a vaccine to prevent infection by SARS CoV-2 causing coronavirus is the immediate need of the hour. With the pharmacists and researchers around the globe widely working on clinical trials for the vaccine, the hope is that the day for complete cure of the disease is not far beyond.

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