**Angiotensin Converting Enzyme 2 in COVID-19 infections and the implications of COVID-19 on major body systems**

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**Abstract**

COVID-19, caused by the severe acute respiratory syndrome coronavirus (SARS-CoV-2), was first identified in China in late 2019 and since then, this disease has become a pandemic affecting many countries across the globe. Due to this outbreak, many researchers have been diligently investigating this disease for the establishment of better methods of its treatment and control. Evidence from research has led to a plethora of valuable but uncertain information on the modes of transmission of COVID-19 and the mechanisms by which SARS-CoV-2 establishes infections in targeted tissues. It is now better understood that in this disease, SARS-CoV-2 gains entrance into cells by specifically binding ACE-2 (angiotensin-converting enzyme 2); ACE-2 serves as a potential receptor for the virus. The lungs, in addition to many other organs and tissues, express ACE-2 in varying degrees. Therefore, this review will examine the role of ACE-2 in COVID-19 and the secondary effects that COVID-19 has on organs that express ACE-2. To this end, it will assist in establishing the relationship between the ACE-2 receptor and SARS-CoV-2, bringing to the forefront the correlation between the symptomatology presentation, as well as the severity of infections experienced with COVID-19. Given this, it may even provide an avenue for the generation of treatment, or create a platform for the enhanced knowledge of this novel virus, and therefore, control, and maybe unravel the mystery for long term complications.

In addition to the lungs, it has been demonstrated that ACE-2 is expressed in other parts of the body including the heart, brain, kidneys and blood vessels. Despite the fact that SARS-CoV-2 mainly affects the lung, producing respiratory symptoms, since other tissues of the body also express ACE-2 they are too susceptible, and serve potential targets for SARS-CoV-2. Therefore, this review aims at exploring ACE-2 and SARS-CoV-2 in addition to examining the effects that SARS-CoV-2 may have on major body systems.

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Renin-Angiotensin System and Angiotensin Converting Enzyme 2

A major regulator of homeostasis and fluid balance in the body is the renin-angiotensin system (RAS). Ang II, the primary hormone resulting from the activation of this system, is generated by the initial cleavage of angiotensinogen (Agt) and the eventual production of Ang II. Through the binding of specific receptors, Ang II exhibits its effect on various organs in the body including the kidneys, brain, heart and blood vessels.

Ang II is described as an alpha2- globin which is mainly produced by the liver. Renin, a prolyteolytic enzyme, cleaves Agt subsequently producing angiotensin (Ang) I. Ang I, described as a decapetide, is subsequently converted to Ang II (an octapeptide) primarily by angiotensin-converting enzyme (ACE). Ang II exhibits its effects through two G protein- coupled receptors: 1) angiotensin type 1 (AT1) receptors and 2) angiotensin type 2 (AT2) receptors. In the kidneys, vasconstriction of the afferent and efferent arterioles and the reabsorption of sodium and fluids are primarily mediated by Ang II activation of AT1 receptors. In addition, the release of aldosterone from the zona glomerulosa of the adrenal cortex is also achieved through Ang II stimulation of AT1 receptors.

Ang II is cleaved by ACE-2 to produce Ang (1-7). Ang (1-7) promotes vasodilation, limits inflammation and exhibits anti-fibrotic effects through its interactions with MAS, a G-protein coupled receptor. Furthermore, ACE-2 converts Ang I into Ang-(1-9) and ACE then converts Ang (1-9) into Ang-(1-7). The activation of the RAS depends highly on the ratio of ACE/ACE-2 found in tissues as the effects of ACE are counteracted by ACE-2. The ratio of ACE/ACE-2 determines the balance between pathways that promote or suppress inflammation and fibrosis.

Renin is considered the rate-limiting enzymatic step in the production of Ang II. In the kidneys, renin is synthesized by specialized cells found in the afferent arterioles called juxtaglomerular (JG) cells. It is then released into the vascular spaces and connective tissue within the kidneys. There are different factors that regulate the synthesis and release of renin. Its secretion is positively controlled by cyclic adenosine monophosphate (cAMP). Renin release is also influenced by factors that affect blood volume, extracellular fluid (ECF) volume and pressures within arterioles. Renin release may be regulated by: 1) baroreceptors found within the afferent arterioles of the kidneys, 2) changes in sodium chloride concentrations of the fluid delivered to cells of the macula densa and 3) influences of sympathetic innervations of arterioles of the JG apparatus.

Tissue Distribution of ACE-2

ACE-2 is expressed in the lung, small intestines and blood vessels. This protein can also be found in the kidneys, skin, oral and nasal cavities. Since ACE-2 is expressed in regions within the body that are commonly exposed to the external environment (respiratory and digestive tracts), potential routes are thus provided for the easy transmission of SARS-CoV-2 in exposed and susceptible individuals.

COVID-19 and Angiotensin Converting Enzyme 2

As stated earlier SARS-CoV-2 is the virus responsible for the development of the disease, COVID-19. This virus binds to tissue ACE-2, subsequently establishing an infection as evidence has already identify ACE-2 as a functional receptor for SARS-CoV-2. As compared to SARS-CoV-1, SARS-CoV-2 exhibits a higher binding affinity (10-20 folds higher) for ACE-2 thus potentially increasing the transmission of and susceptibility to SARS-CoV-2 in the presence of an increased expression of ACE-2. In order for the corona virus to invade and infect target cells, it utilizes a spike glycoprotein which is contained in its viral envelop. This spike glycoprotein structure contains a receptor binding domain which interacts with subdomain I of ACE-2. Cell entry of the virus is then facilitated by priming of the serine protease TMPRSS2.

ACE-2 can be identified in different organs of the body. It is established that in the lungs, ACE-2 is mainly found on type II alveolar epithelial cells and even though it is also found in the mucosal layer of the oral cavity, nasal cavity and nasopharynx, it is only weakly expressed in these areas of the body. Although evidence suggests that the lung is the main target site for SARS-CoV-2 infections, it is also possible for other organs of the body, such as the heart, kidneys and gastrointestinal (Gl) tract, to be affected by this virus as they also express ACE-2 in varying degrees.

COVID-19 and the body systems

As is previously established SARS-CoV-2 utilizes ACE-2 as a potential receptor to gain access into cells, subsequently establishing an infection. Although ACE-2 is present in the lungs, it is evident that other tissues of the body, including tissues of the small intestine, central nervous system and cardiovascular system, also express ACE-2. Therefore, in addition to exploring the effects of this disease on the lungs, it is also interesting and important to investigate the effects of COVID-19 on other systems of the body as this may give some insight into symptom presentation.

Effects of COVID-19 on the respiratory system

In the respiratory system, ACE-2 is found in the nose, bronchus and on the surface of type II pneumocytes. Respiratory symptoms are described as some of the earliest symptoms of COVID-19. COVID-19 infections may be associated with acute respiratory distress syndrome. The presence of an infection with SARS-CoV-2, induces a series of changes within the lungs and as the disease advances, pathological changes such as thickening of the alveolar septa may be observed. Inflammatory changes may also occur with the presence of mononuclear cells within the interstitium, and multi-nucleated giant cells within alveoli.

The RAS functions in the lung to control vascular tone in addition to maintaining the integrity of the alveolar capillaries and regulating inflammatory responses. Both the ACE/Ang II and ACE-2/Ang-(1-7) pathways are present in different cells of the lung; however, the ACE/Ang II pathway predominates. Insults and injuries to the lung result in the up-regulation and stimulation ACE/Ang II and the suppression of ACE-2/Ang-(1-7), thus resulting in further injury. It is believed that the presence of SARS-CoV-2 promotes an increased expression of the ACE/Ang II pathway, as it causes a down regulation of ACE-2 expression. This effect, causes a subsequent increase in Ang II concentrations in the lung and it also increases AT receptor activities thus resulting in lung injury.

Within the lung, the function of the ACE/Ang-(1-7)/Mas pathway may confer some protective effects. This axis aids in decreasing inflammation as well as preventing fibrosis and reducing pressures within pulmonary arteries. A study carried out on animals which involved the infusion of Ang-(1-7), demonstrated the following effects within the lungs: 1) decreased resistance and edema within pulmonary vessels, 2) increased partial pressure (PaO2) of oxygen within the lungs, 3) inhibition of tumour necrotic factor α (TNFα)
activities, 4) increased ratio of ACE-2/ACE, 5) increased ratio of Ang-(1-7)/Ang II, and 6) reduced inflammation

**Effects of COVID-19 on the nervous system**

ACE-2 is expressed in different regions of the brain including the cerebral blood vessels, choroid plexus and neurons of the neocortex. In the central nervous system (CNS) ACE-2 is also expressed in regions of the brainstem. Therefore, invasion and infection of the CNS by SARS-CoV-2 is quite possible. COVID-19 patients may present with symptoms of ageusia and anosmia. Many patients also report other neurological symptoms such as headaches and mental confusion.

Different routes have been theorized to explain the entrance of this virus into the nervous system. One of the potential routes considered is invasion of the olfactory bulb. An animal study investigating aspects of SARS-CoV infection of the brain demonstrated that SARS-CoV-1 initially infected the olfactory bulb, subsequently spreading transneurally. The SARS-CoV-2 virus may potentially utilize a similar route to enter the CNS. Entrance through the blood brain barrier (BBB) has also been considered. ACE-2 is found within the cerebral vasculature, therefore endothelial damage may potentially occur through the interactions of ACE-2 with SARS-CoV-2 thus resulting in a breach in the BBB subsequently allowing viral entrance into the CNS. The breach in the BBB commonly follows inflammation due to the release of inflammatory mediators such as interleukin 6, interleukin 8 and monocyte chemoattractant protein-1 (MCP-1) by immune cells triggered by the presence of the virus. Infected immune cells such as monocytes and T-cells may also serve as potential carriers of the SARS-CoV-2 virus into the CNS as these cells can potentially infiltrate the cerebral blood vessels, meninges and choroid plexus.

In patients diagnosed with COVID-19, evidence has already demonstrated the nucleocapsid protein of SARS-CoV-2 in CD68+ immune cells and the RNA of SARS-CoV-2 in macrophages obtained from bronchoalveolar lavage. However, further research is needed to exactly determine the interactions between the SARS-CoV-2 virus and immune cells as evidence from autopsy investigations have failed to significantly demonstrate a direct invasion of immune cells by this virus.

It is also postulated that the neurological manifestations in COVID-19 may be caused indirectly by the effects of the virus on the respiratory system. As the virus invades and destroys the lungs, hypoxemia occurs due to pure blood oxygenation. Hypoxemia can then lead to hypoxia within the brain, thus resulting in neurological symptoms such as altered levels of consciousness, coma or even death.

**Effects of COVID-19 on cardiovascular system**

ACE2 is expressed in the heart, thus rendering this organ quite susceptible to SARS-CoV-2 infections. Acute myocardial injury is very common in patients suffering from COVID-19 and it has been observed that this complication in COVID-19 patients is associated with an increased risk of mortality (7-11 fold increase in mortality rates). One study carried out to assess the incidence and significance of cardiac injury in patients with COVID-19 reported that cardiac injury was observed in 19.7% of patients that were hospitalized with this disease. This study also identified the presence of cardiac injury as an independent risk factor for determining mortality in patients that are hospitalized with COVID-19.

The exact mechanism by which the presence of SARS-CoV-2 induces this complication is not well understood; however, different factors have been proposed in an attempt to explain this pathology. Cardiac damage may occur as the SARS-CoV-2 virus directly invades and replicates within cardiac cells causing viral induced myocarditis. In addition, cytokines released in response to the presence of SARS-CoV-2, may induce systematic inflammation which may also lead to cardiomyopathy or cardiac injury. In the heart, ACE-2/Ang-(1-7)/Mas pathway may exhibit positive effects through promoting vasodilation and relaxation of cardiac vessels, reducing oxidative stress and enhancing cardiac function after an ischemic insult. Studies utilizing both human and animal subjects demonstrate that the presence of SARS-CoV-1 infection induces a reduction in ACE-2 expression in myocardial cells. In COVID-19, the increased levels of Ang II following a down-regulation of ACE-2 expression, causes an over stimulation of the RAS. The protective effects of the ACE-2/Ang-(1-7)/Mas pathway is reduced and cardiac injury may therefore be promoted.

ACE-2 can be found in the endothelium of blood vessels. It has been demonstrated that SARS-CoV-2 can potentially cause inflammation in the endothelium of blood vessels by directly infecting endothelial cells. The SARS RNA has been isolated from the cells lining small veins of various tissues in the body. The endothelium has the potential to produce Ang-(1-7) and within blood vessels, the ACE-2/ Ang-(1-7)/Mas pathway promotes vasodilation and also enhances anti-thrombotic effects. The plasma levels of D-dimer are significantly increased in severe cases of COVID-19 and severely ill patients commonly suffer from disseminated intravascular coagulation (DIC). D-dimers are present in the blood following fibrinolysis, a process which degrades blood clots. DIC in COVID-19 patients may occur due to the development of thrombosis in both veins and arteries. Thrombosis in arteries may lead to cerebrovascular accidents, myocardial infarctions and peripheral ischaemia. One study carried out to determine the incidence of thrombotic complications in critically ill intensive care unit (ICU) patients with COVID-19, demonstrated a 27% incidence of venous thromboembolism (VTE) and 3.7% incidence of arterial thrombosis. This study also reported pulmonary embolism (PE) (80%) as the most frequently observed thrombotic complication. In addition, through the observation of autopsies, thrombi have also been demonstrated within the pulmonary vasculature.

**Effects on the endocrine and reproductive system**

The endocrine system which consists of a series of organs is also affected by the SARS-Cov-2 virus. It is not yet fully understood how this virus gains entry into the CNS; however, the presence of the SARS-CoV-1 genome has already been demonstrated within the hypothalamus and one study has already shown that both the hypothalamus and pituitary gland are affected by SARS-CoV-1. It might be safe to assume that similarly to SARS-CoV-1, SARS-CoV-2 may also have some damaging effects on the hypothalamus and pituitary gland. The SARS-CoV-1 virus, potentially exhibits similar amino acid sequences to the adrenocorticotropic hormone (ACTH), a hormone secreted in the blood from the pituitary gland. The presence of viral particles in the blood that share similar structure to ACTH, results in the destruction of ACTH by antibodies that were initially formed against these viral particles. This leads to adrenal insufficiency. Since the proteins of SARS-CoV-1 and SARS-CoV-2 are quite similar, it is possible the SARS-CoV-2 may utilize a similar mechanism in disrupting the hypothalamic-pituitary-adrenal axis. With the involvement of this axis, blood cortisol levels may be severely lowered following an infection with SARS-CoV-2 virus; therefore causing psychological effects and tiredness.
Serum levels of free T3, T4, and TSH have been shown to be reduced in patients infected with SARS-CoV-1⁴. This may be attributed to the development of sick euthyroid syndrome or central hypothyroidism. Illnesses such as COVID-19 infections can disrupt the thyroid axis decreasing the blood levels of T4 and TSH. During a period of illness, like with SARS-CoV-2 infection, the tissue binding and uptake of thyroid hormones may be disrupted. In addition, hormones such as cortisol and inflammatory mediators like cytokines may interrupt the normal function of type I deiodinase, limiting the conversion of T4 to T3 thus reducing T3 levels. Furthermore, T3 levels may be further reduced due to the increased activity of type 3 deiodinase⁶². In addition to the mechanisms already outlined, thyroid hormone levels during COVID-19 illness, even though not yet demonstrated, may possibly be affected by the direct damaging effects of the SARS-CoV-2 virus on this organ. An autopsy study on 5 SARS patients reported significant destruction of the thyroid follicular and para-follicular cells by SARS-CoV-1. Destruction of the thyroid parenchyma causes decreased T3 and T4 levels while damaged para-follicular cells affects the blood levels of calcitonin⁶⁶. To date, much data has not yet been accumulated regarding the thyroid involvement in COVID-19; however, COVID-19 patients who present with a pre-existing history of thyroid diseases should continue medical treatment. Patients taking medications for hyperthyroidism should be closely monitored as they are at an increased risk for developing complications such as agranulocytosis⁶⁷.

Both the endocrine and exocrine pancreas express ACE-2 and damage to the exocrine pancreas can result in elevated levels of amylase and lipase⁶⁸. When the endocrine pancreas becomes involved, abnormal glucose metabolism is observed. A study which assessed 39 SARS-CoV-1 patients with no history of diabetes and no use of steroids showed significant increase in fasting plasma glucose as compared to their matched healthy siblings. During the follow up period, 20 patients were identified as having diabetes upon hospitalization and following a 3 year follow-up period, diabetes persisted in 2 patients. This study also concluded that through the use of ACE-2 expressed on pancreatic islet cells, SARS coronavirus enters and damages islet cells resulting in acute diabetes⁶⁹. SARS coronavirus induces an increase in fetuin A levels. Fetuin A is a glycoprotein that has been shown to be associated with abnormal insulin sensitivity; therefore, COVID-19 patients presenting with a previous history of type-2 diabetes mellitus (T2DM), may experience worsening of their insulin resistance due to increased levels of this glycoprotein⁷⁰.

Despite the availability of information regarding testicular involvement in COVID-19, there remains a deficiency of information regarding ovarian involvement in this disease⁷¹. ACE-2 is expressed in the testes and can be found on Leydig and Sertoli cells in addition to the spermatogonia. The blood testosterone levels may be altered in men suffering from SARS-CoV-2 infections. A study carried out comparing 81 males of reproductive aged diagnosed with SARS-CoV-2 infection to 100 healthy males, reported that the male subjects presenting with COVID-19 showed an increase in their serum levels of luteinizing hormone (LH); however, the ratios of testosterone to LH and follicle stimulating hormone (FSH) to LH were both significantly reduced. Even though inflammation caused by covid-19 infections may result in abnormal stimulations from the hypothalamus or pituitary gland⁷²; the findings from this study may support the notion that in COVID-19, disturbances in the male reproductive hormone levels may be more due to abnormalities at the level of the testes.

**Effects of COVID-19 on the gastrointestinal system**

SARS-CoV-2 RNA has already been identified from stool specimens⁷³. Patients diagnosed with COVID-19 commonly present with diarrhoea. Other gastrointestinal symptoms commonly observed include nausea, vomiting, anorexia and abdominal pain⁷⁴,⁷⁵. One study was carried out in China to investigate the clinical characteristics of patients presenting with COVID-19. This study which enrolled 1099 patients, from 552 hospitals, across 30 different provinces demonstrated that 3.8% of patients presented with diarrhoea and 5.6% of patients presented with nausea or vomiting or both nausea and vomiting⁷⁶. Diarrhoea may occur alone in the absence of respiratory symptoms. One study carried out to assess the clinical, pathologic, and virologic features of the intestinal involvement of the SARS-CoV-2 virus reported that watery diarrhoea was the most common gastrointestinal symptom observed and it was present in 20.3% of study subject while fever and diarrhoea with an absence of respiratory symptoms were reported in 5.8% of study participants who presented with COVID-19⁷⁷. It is postulated that the prognosis for COVID-19 infections can be predicted based on the presence or absence of gastrointestinal symptoms⁷⁸; however, more research in this regards is required as evidence from difference sources yields contradictory results⁷⁹,⁸⁰,⁸¹.

Different mechanisms have been postulated to explain the development of gastrointestinal symptoms in COVID-19 patients. In the digestive tract SARS-CoV-2 can potentially interact with ACE2 causing diarrhoea. Evidence has already been brought forward to support the presence of ACE-2 in the linings of the oesophagus, and the absorptive cells of small and large intestines⁸². The presence of ACE-2 in different regions of the digestive tract increases the likelihood that the SARS-CoV-2 virus may establish infections in this region of the body by directly binding to ACE-2, thus gaining entrance into intestinal cells. This may be followed by the development of diarrhoea as viral cellular invasion and subsequent infection may cause imbalances in intestinal secretions, impair absorption from the gastrointestinal tract and potentially activate the enteric nervous system (ENS). In addition, infection with COVID-19 also stimulates inflammatory responses that may lead to inflammatory induced damage to intestinal cells, thus resulting in diarrhoea⁸³. It is also theorized that when infected with the SARS-CoV-2 virus, diarrhoea may occur secondary to the use of antibiotics/antiretroviral drugs or due to the viral disruption of the normal flora of the gastrointestinal tract⁸⁴,⁸⁵. It is also important to note that the COVID-19 infections alter the normal function of ACE-2. ACE-2 regulates homeostasis within the gut; therefore, the disruption of the normal function of ACE-2 makes the gastrointestinal tract more vulnerable to the effects of inflammation thus contributing to the development of gastrointestinal symptoms including diarrhoea⁸⁶,⁸⁷.

The laboratory results of a patient suffering from COVID-19 may reveal elevated levels of aspartate aminotransferase (AST), alanine transaminase (ALT), Gamma Glutamyl Transferase (γ-GT), and Alkaline phosphatase (ALP). Patients may also present with hyperglycemia and increased clotting time⁸⁸. Different mechanisms for the cause of liver injury in COVID-19 have been theorized since the exact mechanism of injury is not yet known. It has been demonstrated that within the liver ACE-2 is mainly expressed on cholangiocytes⁸⁹. Therefore, the presence of ACE-2 serve as a potential receptor for the direct binding of SARS-CoV-2 within the hepatic system, thus inducing cellular damage⁹⁰. Evidence also suggests that damages within the hepatic system by SARS-CoV-2 infections may be due to inflammatory responses caused by the presence of the viral infection⁹¹. The use of high dose anti-viral drugs in addition to the use of antibiotics, antipyretics and steroids should also be investigated as potential causes of hepatic damage in patients suffering from COVID-19⁹²,⁹³.
Effects of COVID-19 on the renal system

ACE-2 has been identified in different regions of the kidneys therefore, this demonstrates a susceptibility of this organ to infections with SARS-CoV-2\(^\text{[5,6]}\). The presence of proteinuria and increased levels of creatinine and blood urea nitrogen have already been observed in patients diagnosed with COVID-19\(^\text{[9]}\). In addition, patients suffering from SARS-CoV-2 infections are also at an increased risk for developing acute kidney injury (AKI)\(^\text{[10]}\). A study designed to investigate the occurrence of AKI in hospitalized COVID-19 patients demonstrated that AKI occurred in 1,993 (36.6%) study participants out of a total of 5,499 subjects\(^\text{[11]}\). The exact mechanism by which the SARS-CoV-2 virus induces renal injury is not yet well understood; however, since ACE-2 is highly expressed in the kidneys, it is possible that injury may follow the binding and entrance of the virus into cells subsequently establishing an infection with eventually causing tissue damage\(^\text{[12]}\). Evidence from post-mortem discoveries demonstrates the presence of diffuse acute tubular injury (ATI), in addition to necrosis and damage to the brush border of the proximal renal tubules\(^\text{[13]}\). Therefore, it is evident that the effects of the SARS-CoV-2 virus damages the renal proximal tubules\(^\text{[14]}\) with secondary endothelial involvement\(^\text{[15]}\). It is also theorized that during an infection with SARS-CoV-2, renal injury may follow the deposition of immune complexes within the kidneys. In addition, it is believed that the presence of viral particles or antigen within the kidneys may induce the excess release of cytokines which potentially causes inflammation and subsequent tissue damage\(^\text{[16,17]}\).

Future direction and conclusion

Since the outbreak of COVID-19 in 2019, much research has been carried out, as means of developing effective methods for treating the disease and controlling its spread. To date, although much information has already been accumulated on COVID-19, this disease still place a great burden on healthcare facilities as the number of cases continue to rise in different countries around the world. Discoveries made on the mode of infection of the SARS-CoV-2 virus, have led to a promising future for the management and control of COVID-19. Evidence suggests that SARS-CoV-2 establishes an infection by binding to targeted cells that express ACE-2\(^\text{[18]}\). In addition to the lungs, various organs and tissues of the body also express ACE-2 and are therefore susceptible to SARS-CoV-2 infections\(^\text{[19]}\). This knowledge aids physician’s understanding on the clinical presentation of COVID-19 patients. Knowledge accumulation can also facilitate better understanding on the modes of transmission of SARS-CoV-2 as the RNA of this virus has already been isolated from stool samples and can therefore suggest an oral-faecal mode of transmission\(^\text{[20]}\).

Knowledge on the use of ACE-2 by SARS-CoV-2 as means of entering and infecting target cells has also raised interest in investigating effective methods for managing COVID-19. ACE-2 levels may be increased by the use of ACE inhibitors and angiotensin receptor blockers (ARBs)\(^\text{[21]}\). ACE-2 has protective effects on lung tissues as it decreases inflammatory effects by decreasing Ang II and increasing ang-(1-7)\(^\text{[22,23]}\). The inhibition of Ang II formation by ACE inhibitors or the blockade of AT1 receptors by ARBs also potentially decreases inflammation in the renal and cardiovascular systems and may therefore function to alleviate some of the major complications observed in COVID-19 patients\(^\text{[24,25]}\).

In conclusion, it is evident that SARS-CoV-2 establishes an infection by binding to ACE-2 expressed on target organs and tissues. Various regions of the body apart from the lung express ACE-2 and this therefore explains the common symptoms and complications that may accompany an infection with SARS-CoV-2.

Declaration of interest

The authors of this paper declare no conflict of interests.

References

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