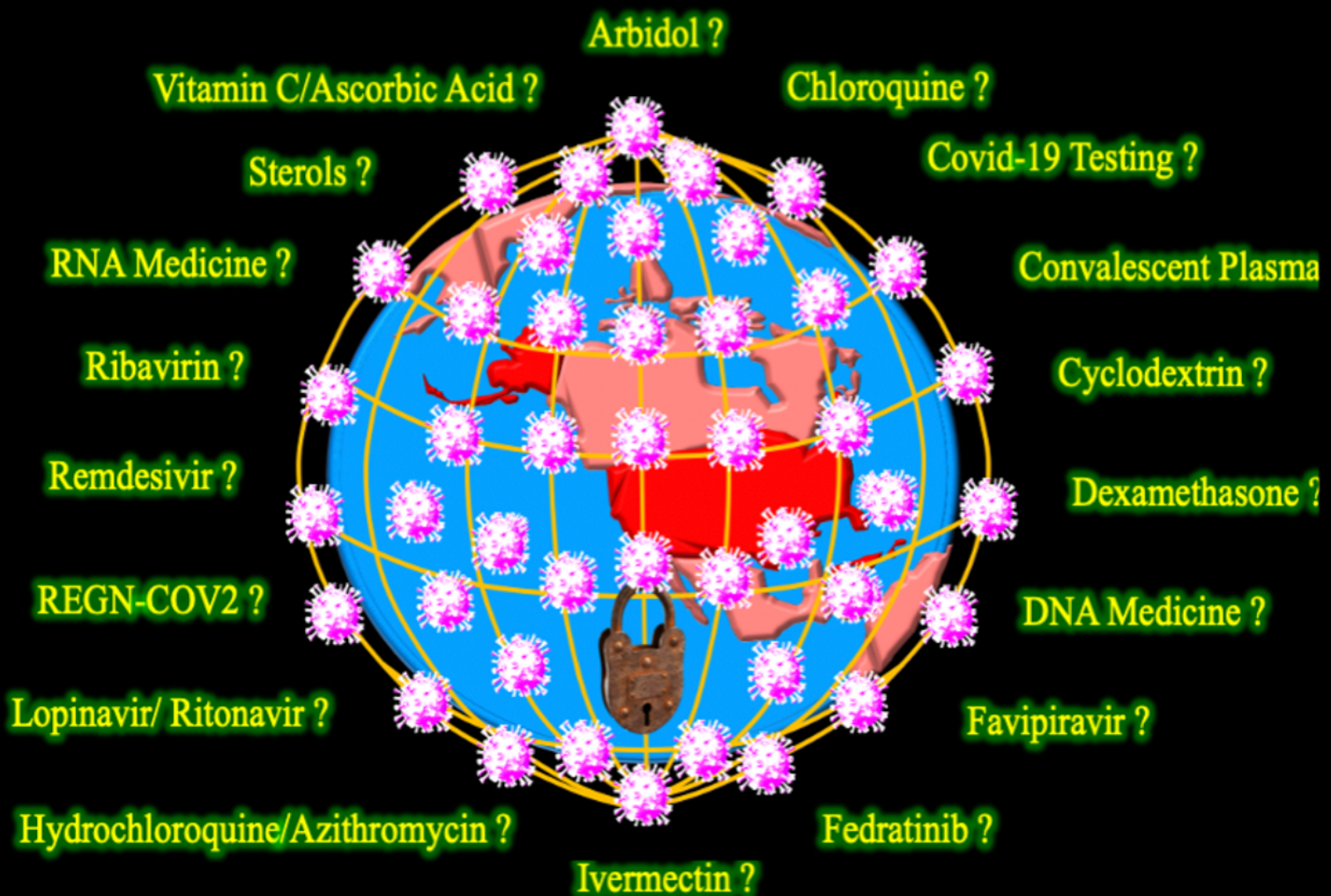




# Science Documents®



Fear of coronavirus locks down the world  
and resets activities on the earth

## Implications of SARS-CoV-2 (COVID-19) pandemic and fatal outcomes of patients with Lifestyle disorders and NCDs

Kaiser Jamil<sup>1\*</sup>, Javeed Ahmed Tantray<sup>2</sup> and Rabbani Syed<sup>3</sup>

<sup>1</sup>Department of Genetics, Bhagwan Mahavir Medical Research Center, Hyderabad, India, <sup>2</sup>Department of Zoology, University of Kashmir, Kashmir, India and <sup>3</sup>Department of Pharmaceutics, King Saud University, Riyadh, Saudi Arabia

\*Corresponding author: [Kaiser.jamil@gmail.com](mailto:Kaiser.jamil@gmail.com)

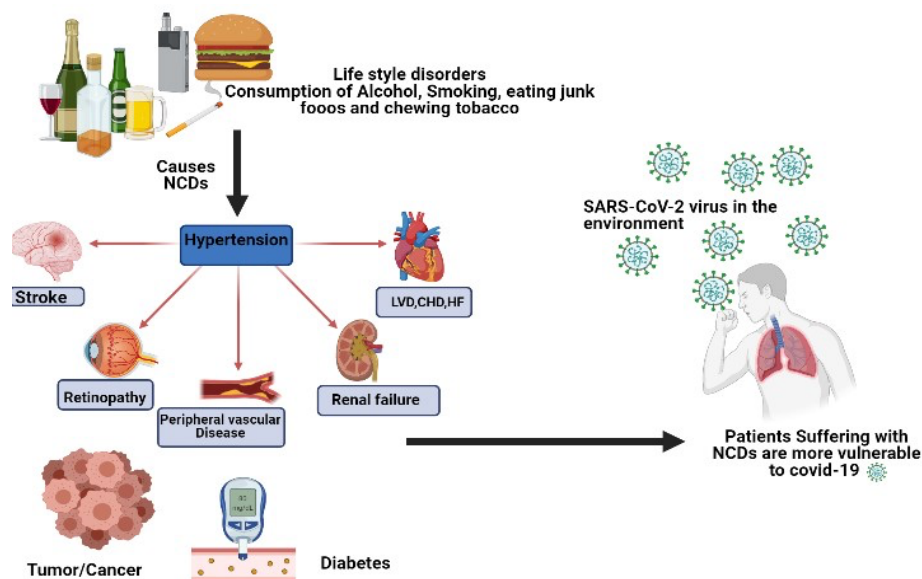
Recent reports have estimated that 1.7 billion people that is more than 20 percent of the world's population is at risk of becoming severely infected with COVID-19 due to their underlying health problems such as diabetes, obesity, heart disease, and other immune-compromised conditions. Further, COVID19 also affects people suffering from lifestyle disorders. Lifestyle disorders relate to our habits or our addictions to: Cigarettes, Beedi, ghutka (Indian tobacco), Alcohol, etc. The consumers of these items are likely to suffer from- Non-communicable diseases (NCDs) such as: Cancers, Cardiovascular diseases, Diabetes, Hypertensions, etc. and around 40 million people are estimated to die each year, that is around 70% of all deaths globally. They are a result of a combination of factors including genetics, physiology, environment, and behaviors and now the corona virus pandemic. NCDs are more vulnerable to COVID-19, a lethal disease of a novel coronavirus renamed as SARS-CoV-2. These Coronaviruses are enveloped viruses, minute in size (65–125 nm in diameter) and contain a single-stranded RNA as a nucleic material, size ranging from 26 to 32kbs in length. Increasing evidence shows that these coronaviruses are not always confined to the respiratory tract but, they may also be neuroinvasive and neurotropic, with potential consequences in vulnerable populations. The aim of this study was to evaluate the correlation between comorbidities related to lifestyle diseases and their role in the exacerbation of disease in COVID-19 patients leading to fatal outcomes. The pathogenesis of COVID-19 is overtly complex, with multiple factors involved. In addition to the direct viral effects and inflammatory and immune factors, the downregulation of ACE2 and imbalance between the RAS and ACE2/angiotensin-(1–7)/MAS axis may also contribute to the multiple organ injuries in COVID-19. After binding of SARS-CoV-2 to the ACE-2 receptor of the host cell, the S protein of the virus undergoes activation at a position adjacent to a fusion peptide within the S<sub>2</sub> subunit leading to viral and host cell membrane fusion. The spike glycoprotein of SARS-CoV-2 is a potential target for the development of specific drugs, antibodies, and vaccines. In the longer term –this disease is likely to continue to spread rapidly into and within cities and countries hence – it is suggested that there is a need to change the way we live and adopt to new normal.

**Key words:** COVID-19, SARS-CoV-2, lifestyle diseases, NCDs, risk factors, ACE2 receptor, comorbidities.

### Introduction

World has witnessed how COVID19 has crashed economies, disrupting our everyday life and challenged the normal health care systems. People suffering from cancers, heart patients, renal dialysis, complicated diabetic patients, chronic liver patients, asthmatics and hypertensive patients have all been devastated and shattered due to non-availability of their standard health

care facilities. In this review we attempt to describe the impact of COVID19 on vulnerable and immuno-compromised population. The vulnerable include those suffering from NCDs and other normal population who are children or pregnant mothers. The effects of this pandemic have also been seen on senior citizens exposing them to unimaginable situations never faced



**Fig. 1.** Schematic diagram of Life style disorders leads to NCDs and COVID-19 exposure to NCDs patients.

by them before. Moreover, Lancet has predicted that globally 1 in 5 will be affected by coronavirus who are suffering from lifestyle disorders.<sup>1</sup> The heightened risk of COVID-19 was also reported by a team of experts from the London School of Hygiene who analyzed patients suffering from comorbidities, lifestyle diseases like diabetes, lung disease, HIV etc. They also found that the COVID-19 had killed 420,000 people globally during the first wave could adversely affect the vulnerability of comorbid patients having at least one underlying health problems. Pulmonary studies have detailed the pathological mechanisms due to SARS-CoV-2 infections, but a detailed understanding remains elusive. A few autopsy studies of patients with COVID-19 have shown that congested lungs had a patchy distribution of abnormalities on gross examination. Further, microscopic findings included diffuse alveolar damage with hyaline membrane formation, pneumocyte activation, microvascular thrombi, lymphocytic inflammation, and proteinaceous edema.<sup>2,3</sup> The impact of measures taken to contain COVID-19 on lifestyle-related behaviour is undefined. Their risk factors can be divided into three primary risk sets: modifiable behavioral risk factors, non-modifiable risk factors and metabolic risk factors, many of which are common for several diseases. The current study reviewed the impact of COVID-19 on lifestyle-related diseases and many of these are immune-compromised as mentioned above.

#### **Route of infection of coronavirus (SARS-CoV-2) in humans**

One question which everybody is worried about is -Can asymptomatic person transmit the diseases? this has been proven right in a Chinese study.<sup>4</sup> It has been reported that transmission appears to have happened during the incubation period of the virus from an asymptomatic patient. This finding came to light when the world was witnessing an exponential spread of the virus and the question was why is the spread so rapid? General belief which went viral was that active sneezing and coughing was the route of contaminating the surrounding and the people in its vicinity but now it is much more difficult to stop the spread because people who look well may be transmitters of the deadly virus.<sup>5</sup>

Once the virus enters a new host, it seeks a receptor to attach itself to the host and this is the ACE2 receptor of the host cell. The chemistry between the virus spike protein and the ACE receptor fuse and then virus enters the cell makes millions of copies of itself by the mechanisms beautifully described by a host of Scientists<sup>6,7</sup> and the consequences results in diseases prevalence. The result could be morbidity, mortality or recovery. ACE-2 has been identified as a functional receptor for SARS-CoV-2 and is highly expressed on the pulmonary epithelial cells. Restoring the balance between the RAS and ACE2/angiotensin-(1-7)/MAS may help attenuate organ injuries in COVID-19.

#### **Host's defense system**

The immune system is instrumental in protecting and fighting any external invaders of every shape and tries to destroy it. Hence when the virus appears the T cells quickly multiply to attack the virus and recruit B cells to produce antibodies which provide protection from future attacks. This is significant because antibody signals for SARS-CoV-2 have been reported by many researchers to decline over time. Additionally, recent research has shown that the T-cell response can persist even when antibodies wane.<sup>8,9</sup> And when the cells became infected with the virus, immune genes that fight viral infection, interferon-stimulated genes, get activated.

#### **Clinical symptoms and pathology**

The clinical spectrum of COVID-19 is quite heterogeneous, ranging from mild flu-like symptoms to acute respiratory distress syndrome, multiple organ failure and death. The organs like brain, heart, oral and nasal mucosa, kidney, nasopharynx, colon, lymph nodes, small intestine, stomach, thymus, skin, spleen, bone marrow, liver and blood vessels, are all susceptible to be infected by COVID-19, on account of presence of abundant ACE2 in these areas of the body.<sup>10</sup> This is especially visible in older age, diabetes and in other comorbidities that are reported as significant predictors of morbidity and mortality. The significant defense mechanism is described as the "Cytokine Storm",<sup>11</sup> which results in chronic inflammation, increased coagulation activity, immune response impairment, and potential direct pancreatic damage by SARS-CoV-2. Early in the pandemic, high levels of inflammatory cytokines such as interleukin-6 (IL-6) were observed in patients with poor outcomes. This could be among the underlying mechanisms of the association between diabetes and COVID-19. Another devastating event which takes place in addition to the direct viral effects and inflammatory and immune factors, the downregulation of ACE2 and imbalance between the RAS and ACE2/angiotensin-(1-7)/MAS axis may also contribute to the multiple organ injuries in COVID-19 patients.

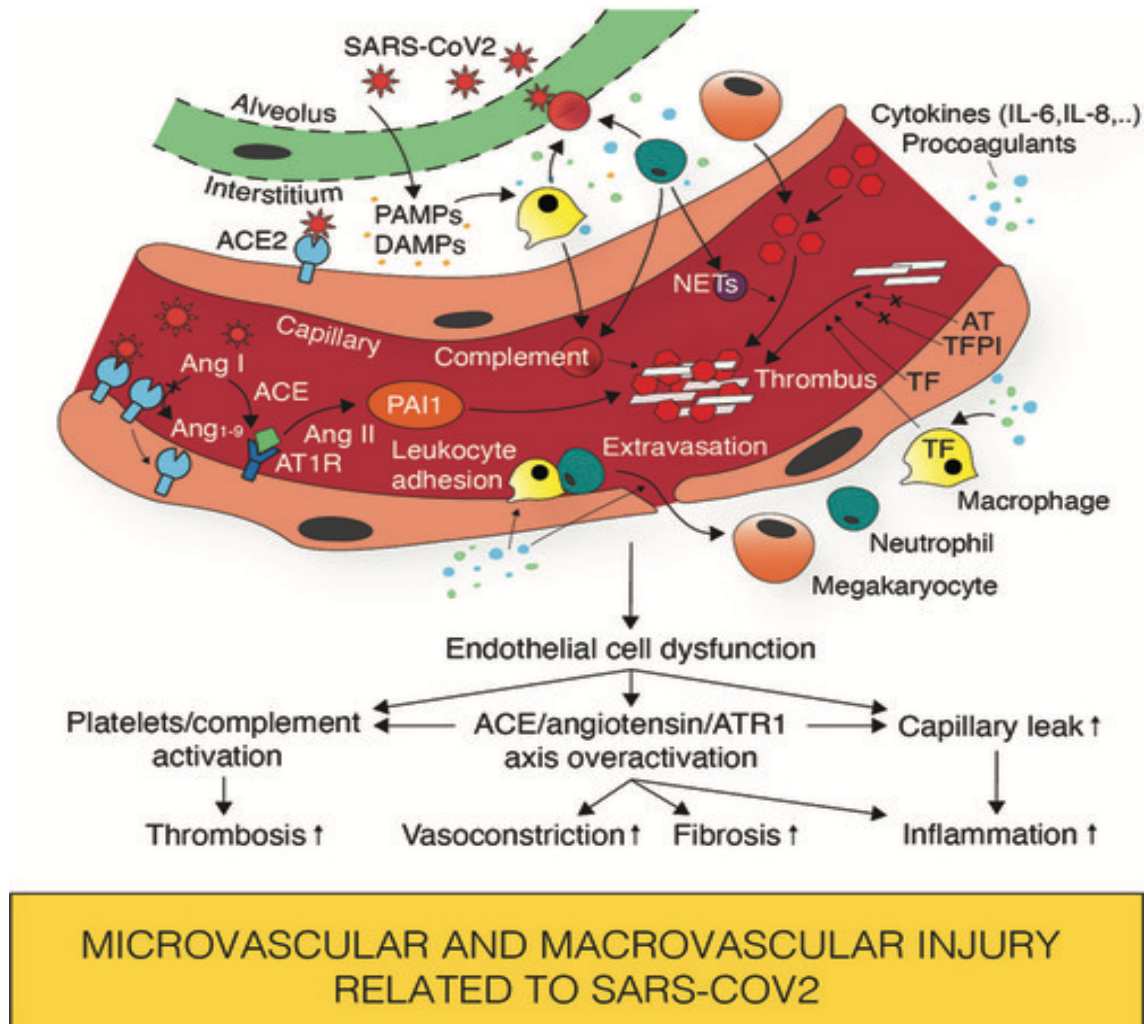
#### **Implications of COVID19 on comorbid patients**

The comorbid patients have complex etiologies which are driven by the unrelated causes such as unhealthy lifestyles, ageing or obesity or even due to environmental or climate change. In such cases there are huge possibilities of apparent high blood pressure, increase in blood glucose levels, elevated blood lipids and may be representations of deep lying lifestyle habits.

A systematic review and meta-analysis was conducted to evaluate comorbidities associated with severe and fatal cases of COVID-19.<sup>12,13</sup> Thus, it is obvious that there are a number of multiple risk factors that contribute to the development of NCDs. The various

types of risks can be divided into three primary risk sets: modifiable behavioural risk factors, non-modifiable risk factors and metabolic risk factors, many of which are common for several diseases. The thought remains whether diabetes mellitus patients or hypertensive patients are at increased risk for COVID19 in this era of pandemic.<sup>14</sup>

and lipoprotein (a). These conditions in patients considerably weaken their immune systems and such patients become susceptible to infections, and exposure to SARS-CoV-2. Preexisting heart disease poses additional burden for COVID19 patients, moreover, discontinuing their ACE and ARB inhibitors could be injurious to the patients.<sup>15</sup> COVID-19 causes coagulation abnormalities in a substantial proportion of



Song W, et al., Xiang Y: Cryo-EM structure of the SARS coronavirus spike glycoprotein in complex with its host cell receptor ACE2. 2018, *PLoS Pathology*; 14:e1007236.

### (i) Heart disease and COVID19:

The number one cause of deaths globally is heart diseases (Cardiovascular Diseases- CVDs) which account for 17 million deaths per year. The number is predicted to sore by 2030 to more than 23 million a year. CVDs are a group of disorders of the heart and blood such as arrhythmia's, Ischaemic heart disease; Stroke; Peripheral arterial disease and congenital heart disease. The modifiable risk factors which could help in disease prevention include: high blood pressure, abnormal blood lipids, tobacco use, physical inactivity, obesity, unhealthy diet (salt), diabetes, heavy alcohol use. And other factors which can be controlled through intervention include excess homocysteine in blood, inflammatory markers (C-reactive protein), abnormal blood coagulation (elevated blood levels of fibrinogen),

patients, which can lead to thromboembolic events. ACE2 is a key surface protein for virus entry and is part of the renin–angiotensin–aldosterone system (RAAS). COVID-19 can also cause disorders such as myocardial injury, arrhythmias, ACS and thromboembolism. Details of CVD disorders have been elegantly described by Nishiga et al.<sup>16</sup>

### (ii) Diabetes and COVID19:

Among the lifestyle diseases Diabetes is listed as a metabolism disorder syndrome that affects the way the body uses food for energy and physical growth.<sup>17</sup> There are 4 types of diabetes: Type 1, Type 2, Gestational, and Pre-Diabetes (Impaired Glucose Tolerance). Type 2 is the most common diabetes in the world and is caused by modifiable behavioral risk factors such as, high

cholesterol, unhealthy diets, physical inactivity, obesity, high blood pressure, alcohol use, psychological stress, high consumption of sugar, and low consumption of fiber. In this disease presence of autoantibodies makes the patients susceptible to the prevailing coronavirus infections.<sup>18</sup>

### (iii) Hypertension and COVID19:

The majority of the population aged over 60 years have hypertension, and it has been suggested that they may be at increased risk from the effects of COVID-19.<sup>19</sup> Recent studies have demonstrated that comorbidity of Arterial Hypertension as a risk factor associated with COVID-19 pathology. Progression of SARS-CoV-2 infection in the development of cardiovascular comorbidities has been observed and its mechanisms are undoubtedly complex and may well be related to underlying causes of lifestyle behaviours. Approximately 50% of US patients with hypertension are prescribed angiotensin converting enzyme inhibitors (ACE-I), aldosterone receptor blockers (ARB) and aldosterone antagonists, collectively called RAAS inhibitors, and are among the most frequently prescribed anti-hypertensive medications. These medications may impact the Coronavirus infections in the individuals. The latest evidence shows that people with uncontrolled or untreated high blood pressure may be at risk of getting severely ill with COVID-19 than those whose high blood pressure is managed with medication.<sup>20</sup> Further a few reports from Cardiologists indicate that the most prevalent comorbidities in COVID19 patients were hypertension (42%) diabetes (23%). Hypertension alone was linked to diabetes with increased rates of mortality is not fully confirmed.<sup>21</sup>

### Cancers and COVID19

Cancer affects different parts of the body and is characterized by a rapid creation of abnormal cells in that part and can invade other parts of the body as well. More than 7 million people die of cancer each year and 30% of those diseases are attributed to lifestyle choices. Most people with cancer are at an increased risk from coronavirus because they have weak immune systems because of their current cancer treatments. This is because cancer and its treatment can weaken your immune system and reduce the ability to fight infections. Some types of cancers can also lower the ability to fight infection. The cancer that affects the immune system, include leukaemia or lymphoma and a many other malignancies such as cervical cancer due to human papilloma virus infection; Lung cancer due to exposure of living in air-polluted places and smoking; breast cancer due to hormonal therapies, obesity due to varied food habits, and people with less of physical activity. People suffering from prostate and colon cancer also belong to high-risk group susceptible to COVID19 due to anaemia and unhealthy diet and low fibre intake. Specific risk groups are cancer patients with an impaired immune system such as:

Leukocytopenia, and low immunoglobulin levels, also long lasting immunosuppression (steroids, antibodies). It should also be proposed to patients in follow-up or cancer survivors if they present with symptoms suggestive of COVID-19 infection

### (iv) Lung Diseases and COVID19:

The Forum of the International Respiratory Society identified, in 2017, five major lung diseases, the “big five”, which include asthma, chronic obstructive pulmonary disease (COPD), acute lower respiratory tract infections, lung cancer and tuberculosis. These diseases are among the most common causes of severe illness and deaths worldwide. Among the “big five” lung diseases, except lung cancer, have increased during COVID-19 epidemics. COVID-19 is a serious respiratory disease, but how it really affects the lungs is still being investigated. The coronavirus infects the upper or lower part of the respiratory tract and travels down the airways to the alveoli. The lining of the respiratory tract becomes irritated and inflamed. About 14% of COVID-19 cases are severe, with an infection that affects both lungs. As the swelling gets worse, the lungs fill with fluid and debris causing serious pneumonia. As the sacs get filled with mucus it becomes harder for breathing, hence oxygen is generally provided to such patients. The most common clinical presentation of severe COVID-19 is acute respiratory failure consistent with the acute respiratory distress syndrome.<sup>22</sup> Airway, lung parenchymal, pulmonary vascular and respiratory neuromuscular disorders all feature in COVID-19. One report has observed that people in the extremely vulnerable group include those :

- having chemotherapy
- having radical radiotherapy for lung cancer
- with cancers of the blood or bone marrow such as leukaemia, lymphoma or myeloma who are at any stage of treatment
- having immunotherapy or other continuing antibody treatments for cancer
- having other targeted cancer treatments which can affect the immune system, such as protein kinase inhibitors or PARP inhibitors
- who have had bone marrow or stem cell transplants in the last 6 months, or who are still taking immunosuppression drugs
- taking medicine such as high doses of steroids

### (v) COPD & COVID19:

Chronic respiratory diseases are the most under-diagnosed conditions; chronic respiratory diseases (CRD) are a potent cause of death globally with 90% of the deaths taking place in low-income countries. Chronic obstructive pulmonary disease (COPD) and asthma are the two main types of CRDs. Exposures to cigarette smoke, dust and chemicals and environmental exposures, tobacco smoke, air pollution infections are all related to risk of lung diseases. Smokers are likely to be more vulnerable to COVID-19 as the act of smoking

means that fingers (and possibly contaminated cigarettes) are in contact with lips which increases the possibility of transmission of virus from hand to mouth. Smokers may also already have lung disease or reduced lung capacity which would greatly increase risk of serious illness. Smoking products such as water pipes often involve the sharing of mouth pieces and hoses, which could facilitate the transmission of COVID-19 in communal and social settings. Conditions that increase oxygen needs or reduces the ability of the body to use it properly will put patients at higher risk of the consequences of bilateral viral pneumonia.

The presence of chronic obstructive pulmonary disease (COPD) is associated with an increased risk of mortality in patients with community-acquired pneumonia because of local/systemic inflammation, compromised host response, or increased mucus production in patients with COPD. Smoking, which represents the most important risk factor for COPD, is also an established risk factor for COVID-19 infection. Higher expression of angiotensin-converting enzyme 2 receptors has been reported in smokers and patients with COPD, facilitating the entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into the cell. In this regard, it should be noted that a comparison between non-smokers, ex-smokers, and current smokers indicated similar risk levels in the ex-smokers and in those who never smoked.

### Discussion

The SARS-CoV-2 from WUHAN caused the disease COVID19, is still causing concern in the health sector as the virus continues to trouble the medical fraternity. Most importantly the cause of concern is its everchanging etiology and epidemiology on a daily basis. This study, while dealing with lifestyle disorders has also correlated the impact of comorbidities in Covid patients. This study may be important to clinicians who are attending to the patients, so they could modify their treatment strategies. Further it may give a correct picture to the governments to impose their role in not segregating those with Covid plus disease patients and only disease patients.<sup>23</sup>

Thousands of publications have appeared in literature that pertains to the disease and its causes, but there are no concrete steps to combat it – hence everyone is looking forward to its vaccine. Nevertheless, no one is sure whether it will hold well for the new mutated and more virulent forms of the virus. In one report as many as 50% of patients were suffering from at least one. Comorbidity during hospital admissions, these included hypertension, diabetes, COPD, CVD, Obesity. Hence it was observed the comorbidities were contributing to the disease burden. Further about 70% of the patients who required ICU care have been observed with comorbidities.<sup>24</sup>

Our 2020 scenario has witnessed older people, and people with preexisting conditions (such as heart diseases, diabetes, respiratory conditions, and cancers) appear to be more susceptible to becoming severely ill upon the virus attack. We have seen the silent deaths of the elderly in long-term-care facilities during the Covid-19 pandemic. Over the past year; several lockdowns have taken place in the hope of mitigating the virus spread. But there was more of economic losses and maybe social isolation may have helped in decreasing the disease burden to some extent. We adopted new habits, learned, and worked through videoconferences, made social distancing an everyday habit and mask a fashion item. All this was done due to dire necessity to minimize the infections. So, now we have a chance to end the pandemic, I'd say we should go for it. Scientists are working on the virus to provide evidence for every public-policy issue from stay-at-home orders to vaccine production. Most people default to either local or national news, which are both entirely consumed by how COVID-19 is impacting domestic issues. With all of the best and brightest minds in the world working on the same issues, the public is gaining an in-depth understanding of the virus and its consequences, very quickly. Soon after, multiple reports of cases came from across Europe and the United States, even here some Paediatric multisystem inflammatory syndrome temporally associated with COVID-19 (PIMS) were found to carry the virus causing COVID-19 and some had proteins in their body showing that they previously had the infection. A significant number of patients were exposed to someone with COVID-19 infection. Severe abdominal pain and diarrhea is another common complaint with PMIS. So far, we know the similarities between these two diseases, but we do not have sufficient information to fully understand the differences. This article discussed the potential role of lifestyle factors in regard to immune functioning and prevention of severe outcomes of COVID-19.<sup>25</sup>

The information on demographic variation in lifestyle practice during COVID-19 can help to devise user-friendly behavioral support interventions using fitness applications, video streaming and motivation support. The results of such a study indicates a mixed effects of the preventive measures that can be adopted to control coronavirus on the lifestyle related behaviour with an improvement in regular meal consumption pattern and healthy eating behaviour and reduction in unhealthy food intake as positive indicators and significant reduction in physical activity and increase in sitting time, screen time and stress as negative indicator. COVID-19 infection is associated with an increased tendency of thrombosis in both arterial and venous systems owing to inflammation, endothelial dysfunction, hypoxemia, and stasis. Severe cases can lead to hypoxemic respiratory failure with features of the acute respiratory distress syndrome, but the

mechanisms are not fully understood, however the disease progressed aggressively till death occurred. In Children's cases if the child has persistent fevers over 101°F as well as severe abdominal pain, diarrhea, or rash that could not be explained by another cause seeking medical evaluation is the only solution. Unusual numbers of children and teenagers living in COVID-19 hotspots have been reported to develop an inflammatory condition (officially called Multisystem Inflammatory Syndrome in Children, or MIS-C) that looks a lot like Kawasaki disease. In many cases, the children have also tested positive for COVID-19 antibodies, suggesting the syndrome followed a viral infection.<sup>26</sup>

It is a tragedy to realize that this virus that we thought was going to spare our most vulnerable citizens—our children—is not. But it has suddenly presented the opportunity to actually understand Kawasaki disease. Kawasaki disease has a well-defined set of symptoms, including a persistent high fever, bloodshot eyes, redness around the mouth, a body rash and redness and swelling of the feet and hands. Only a few thousand cases of Kawasaki are diagnosed each year in the U.S., mainly in children ages 5 and younger.<sup>27</sup> JAMA med data was the first one to publish a 60% reduction in Oncology trials globally during the first wave of COVID-19 pandemic. In an effort to stop the virus spread, save lives and reduce pressure on hospitals, other diseases like cancers and dialysis patients', diabetic patients got neglected. The corona pandemic has disrupted the healthcare system of the general public, which has influenced the patient-physician decisions. For instance the patients seeking cardio care and dialysis conditions declined, further outcomes of diseases like cancer have worsened and hospital beds and ICU units were all for COVID19 patients.<sup>28</sup>

Assessment of severity by clinical, radiological, lung function and biological tests is vital for patients. Evaluation for the need of hospitalisation in dedicated units for cancer patients has been much neglected during the pandemic period. Serology tests to identify previous COVID-19 infection in all cancer patients were also neglected. Further, the critical tests for confirmation using RT-PCR for all patients undergoing surgery, radiotherapy, chemotherapy or immunotherapy has also been ignored may be due to non-availability of relevant technical staff. This failure of Health Care system to such patients has been of much inconvenience and hazardous to not only cancer patients, but also to those needing dialysis or flu type illness or respiratory illnesses. The diversion of healthcare professionals to attend to the more pressing COVID 19 patients has been the cause.

In addition to serious pathology in the respiratory tract, COVID-19 appears to cause extrapulmonary mani-

festations affecting the cardiovascular, gastrointestinal, urinary and nervous systems. Mental health problems associated with the pandemic include depression, anxiety, fatigue and post-traumatic stress disorder. Psychological distress due to SARS-CoV-2 may be associated with an increase in energy intake and a decrease in physical exercise, resulting in weight gain and increased rates of overweight and obesity.<sup>29</sup> ACE2 is expressed in many human tissues including the nasal epithelium, heart, kidneys, and lungs, and inactivates angiotensin II diminishing its vasoconstrictive and myoproliferative effects. SARS-CoV-2 binds to the ACE2 receptor via its spike (S) protein to allow entry into host cells. This complex is endocytosed leading to down-regulation of ACE2 and resulting in local accumulation of angiotensin II enzyme. Severe respiratory illness is a hallmark of COVID-19 and a primary cause of morbidity- and mortality, local activation of the RAAS is proposed as a mechanism for severe lung injury.

### Conclusion

2020 has brought previously unseen challenges upon humankind. A virus that, due to globalization, spread at an unprecedented speed, stormed the entire planet and there is only one thing that can stop it as it is now: a vaccine. At present, physical distancing and face masks are undoubtedly the best preventive measures to avoid exposure to the novel coronavirus. However, appropriate lifestyle changes in regard to nutrition, exercise, sleep, smoking and alcohol intake may contribute to shifting the population distribution of infection risk and preventing severe outcomes of COVID-19. Studies are underway to explore whether hypertension is an independent risk factor for COVID-19. Given the theoretical risks of RAAS inhibition, randomized trials have been initiated to evaluate clinical outcomes for COVID-19 patients treated with ACE-Is or ARBs. Behavioural risk factors related to disease are quantitative and not categorical phenomena and constitute a continuous distribution. The introduction of community-wide measures reducing these risk factors may be capable of shifting the population distribution of risk. This approach may be able to significantly reduce the burden of disease.

Widespread and prolonged closures of schools and businesses lead to dramatic changes in daily routines and lifestyle behaviours. Harmful health behaviours, such as overeating, smoking and excessive alcohol consumption, may be more likely to be initiated by individuals affected by economic shutdowns, quarantines and curfews. At present, the most effective measure in halting the transmission of COVID-19 and preventing associated chronic complications is unarguably the avoidance of exposure to the virus through physical distancing, face masks and eye protection. In addition, changes in lifestyle factors, including nutrition, exercise, smoking, alcohol

consumption, screen time and sleep, may be able to contribute to shifting the risk distribution for COVID-19.

**Conflict of interest:** none declared

## References

- Lange KW, Nakamura Y: Lifestyle factors in the prevention of COVID-19. 2020, *Global Health Journal*; 4:146-52.
- Wichmann D, et al., Kluge S: Autopsy findings and venous thromboembolism in patients with COVID-19: A prospective cohort study. 2020, *Ann Intern Med*; 173:268-77.
- Ackermann M, et al., Jonigk D: Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. 2020, *Engl J Med*; 383:120-28.
- Bhatia A, Edited By: Sonia Bhaskar: Coronavirus explainer: What we know about asymptomatic COVID-19 infections so far? Sept 9<sup>th</sup>, 2020, ICMR – Delhi-Report .
- Rallia M, et al., Ercolub L: Asymptomatic patients as a source of transmission of COVID-19 in homeless shelters, short communication. 2021, *Intl J Infect Dis*; 103:243-45.
- Ni W, et al. Gao Z: Role of angiotensin-converting enzyme 2 (ACE2) in COVID-19. 2020, *Crit Care*; 24:422.
- Katsi V, et al., Tousoulis D. The role of angiotensin-(1-7)/Mas axis and angiotensin type 2 receptors in the central nervous system in cardiovascular disease and therapeutics: a riddle to be solved. 2019; *Curr Vasc Pharmacol*; 17:319-25.
- Swadling L, Maini MK: T cells in COVID-19-United in diversity. 2020, *Nat Immunol*; 21:1307-8.
- Ng WH, Mahalingam S. Comorbidities in SARS-CoV-2 patients: A systematic review and meta-analysis. 2021, *mBio*; 12:e03647-20.
- Huang C, et al., Cao B: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. 2020, *Lancet*; 395:497-506.
- Tang Y, Wen C: Cytokine storm in COVID-19: The current evidence and treatment strategies. 2020, *Front Immunol*; 11:1708.
- Gold MS, et al., Ben-Shoshan M. COVID-19 and comorbidities: A systematic review and meta-analysis. 2020, *Postgrad Med*; 132:749-55.
- Bajgain KT, et al., Santana MJ: Prevalence of comorbidities among individuals with COVID-19: A rapid review of current literature. 2021, *Am J Infect Control*; 49:238-46.
- Fang L, et al., Roth M: Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? 2020, *Lancet Respir Med*; 8: e21.
- Mai F, Ferri C: COVID-19 and cardiovascular diseases – Review. 2020, *J Cardiology*; 76 453-58.
- Nishiga M, et al., Wu JC: COVID19 and Cardiovascular disease: from basic mechanisms to clinical perspectives. 2020, *Nat Rev Cardiol*; 17:543-58.
- Ghosh A, et al., Misra A. Effects of nationwide lockdown during COVID-19 epidemic on lifestyle and other medical issues of patients with type 2 diabetes in north India. 2020, *Diabetes & Metabolic Syndrome Clin Res Rev*;14:917-20.
- Chopra S, et al., Baitha U: Impact of COVID-19 on lifestyle-related behaviours- a cross-sectional audit of responses from nine hundred and ninety-five participants from India. 2020, *Diabetes Metab Synd*; 14:2021-30.
- Clark CE, et al., Martin U: COVID-19 and hypertension: risks and management. A scientific statement on behalf of the British and Irish Hypertension Society Christopher. 2021, *J Human Hypertension*; 35:304-7.
- Shibata S, et al., Itoh H: Hypertension and related diseases in the era of COVID-19: A report from the Japanese Society of Hypertension Task Force on COVID-19. 2020, *Hypertension Res*; 31:1–19.
- Dobkowski D: Studies find hypertension most prevalent comorbidity in patients hospitalized for COVID-19. Joint Hypertension Scientific Sessions, Venkata VRS, et al. Presentation, P135. Presented at: American Heart Association Hypertension Scientific Sessions; Sept.10-13, 2020 (virtual meeting).
- Xu Z, et al., Wang FS: Pathological findings of COVID-19 associated with acute respiratory distress syndrome. 2020, *Lancet Respir Med*; 8:420–2.
- Gold MS, et al., Ben-Shoshan M: COVID-19 and comorbidities: a systematic review and meta-analysis. *Postgraduate Medicine*; 132:749-55.
- Gasmi A, et al., Bjørklund G. Interrelations between COVID-19 and other disorders. 2021, *Rev Clin Immunol*; 224:108651.
- Pietrobelli A. et al., Zoller T: Effects of COVID-19 lockdown on lifestyle behaviors in children with obesity living in Verona, Italy: a longitudinal study. 2020, *Obesity*; 28:1382-5.
- Joseph R. Hageman, MD What Are the Newest Effects of COVID-19 in Children? 2020, *Pediatric Annals*; 49:e242-e243,
- Revenco N, et al., Vasiliev I: SARS-COV-2/COVID19 Induce Kawasaki-Like Disease in Children Experience of Republic of Moldova: A Report of Five Cases. *Biomed Res and Clin Rev*; 3(3) DOI: 10.31579/2692- 9406/055.

**Acknowledgements:** thanks to the Research Director and Management of Bhagwan Mahavir Medical Research Center- Hyderabad for their support and encouragement.



28. Shioda K, *et al.*, Mori M: Navigating Through Health Care Data Disrupted by the COVID-19 Pandemic. 2020, *JAMA Intern Med*;180:1569-70.
29. Ranjan P, *et al.*, Vikram NK: Is excess weight a risk factor for the development of COVID 19 infection? A preliminary report from India. *Diabetes & Metabolic Syndrome*; 14:1805-7.
30. Song W, *et al.*, Xiang Y: Cryo-EM structure of the SARS coronavirus spike glycoprotein in complex with its host cell receptor ACE2. 2018, *PLoS Pathology*; 14:e1007236.

