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COVID-19:-Relation to Respiratory and Cardiovascular system and natural management .

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ABSTRACT

Towards the end of the year 2019, a new and highly contagious viral Respiratory illness due to a novel coronavirus, SARS-2-CoV-2 also termed as COVID-19 was reported in Wuhan city of Hubei Province in China and since has spread exponentially to 210 countries and territories all over the world. The WHO declared the virus as a global pandemic on march 11 2022.

The patients show flu-like symptoms with a dry cough, sore throat, high fever, and breathing problems and current observation show that the elderly and those with co morbid conditions such as hypertension (elevated blood pressure) and diabetes (elevated blood glucose) are at highest risk.

Prevention and management are the best options available for handling the disease. This article describes SARS-CoV-2, disease, relation to climatic factors as well as other diseases, management and the impact on society.

It is urgently advised and requested that all the persons

should follow the preventive measures, managements and quarantine strictly without any religious discrepancy

otherwise the situation may be the worst.

science and technology to fight against any such disaster in future; if any. There is no need to be panic and proper

prevention and management are essential to combat this disease.

INTRODUCTION:

Coronaviruses belong to the Coronaviridae family and appear just like spiked rings when observed through an electron microscope. The surface looks with various spikes, which are helpful to attack and bind living cells. These are the viruses causing the simple common cold disease to severe illnesses like Middle East Respiratory Syndrome (MERSCoV), Severe Acute Respiratory Syndrome (SARS-CoV). The word coronavirus isa derivative of the Latin corona, whichmeans crown or halo, that states to the typical look indicative of a crown or a solar corona around the virions.

These viruses are having a positive-sense single-stranded RNA genome (27 to 34 kilobases) and helical symmetry nucleocapsid (Su et al., 2016; Sexton et al., 2016). [1]

There are several outbreaks from time to time due to these viruses. The most notorious outbreaks were in 2003, 2012, 2015 and 2018 with 774, 400, 36 and 42 deaths, respectively. It is important to mention that the 2019–2020 outbreak is started inWuhan, Hubei Province, China in December 2019 (The Editorial Board, 2020) when a new strain of coronaviruswasdetected on 31st December 2019 (WHO, 2020).

. This virus is out broken in pneumonia type of disease with respiratory problems, leading to death due to respiratory failure.[2]

This article is dedicated to the recent outbreak of 2019–2020 describing the diseases, symptoms, spread, prevention, and treatment.

SYMPTOMS AND PREVENTIONS:

Coronaviruses infect the upper gastrointestinal and respiratory tract of the mammals (including humans) and the birds. Most patients with COVID-19 exhibit mild to moderate symptoms, but approximately 15% progress to severe pneumonia and about 5% eventually develop acute respiratory distress syndrome (ARDS), septic shock and/or multiple organ failure.[3,]. The occurrence of the illness ranged from mild to severe. SARS-CoV-2 propagate through RNA replication using RNA-dependent RNA polymerases enzyme. Thisvirus can mutate slowly, posing a challenge for its treatment and control. The symptoms of COVID-19 may arise within 2 to 14 days after the infection. Besides, in some cases, the diseases prevail after 27 days. The duration of the survival of death is 6 to 41 days after infection of the coronavirus.[4]

The common signs of infection are fatigue, muscle pain, sneezing, sore throat, dry cough, high fever, respiratory problems, etc. with some severe cases having pneumonia, serious respiratory syndrome kidney failure and even death (Huang et al., 2020; Hui et al., 2020; Ren et al., 2020). The COVID-19 risk is greater in older people, kidsand the patients having other health problems like lung diseases,heart diseases, diabetes, and cancer. It is important to mention that itis not necessary to have COVID-19 if these symptoms are seen because such types of symptoms are also seen in the case of other virus infections, except breathing and diarrhea problems.[5]

The chances are greater of COVID-19 if there is shortness of breath, dry cough, and a person comes in the contact with a COVID-19 patient or traveled with COVID-19 effected area. Under such a situation, the clinical test for COVID-19 is a must. However, some persons recover easily while others may take some time depending on the health conditions and the age of the patients. The prevention and management are very important issues to control COVID-19. Therefore, there is a great need for the collective efforts of the public and the government. The regular and the proper care of the homes and hospitals are very important to control this calamity. The regular recommendations to minimize the infection are cleaning of your area. The most important is to avoid sneezing and cough at the public place. The hand cleaning with soap and sanitizer, mouth and nose coverage with mask during sneezing and coughing are essential. Thoroughly washing foodstuff before cocking may help in this regard. The simple house-keeping disinfectants may kill the virus on the surfaces. Regularly cleaning of the surface by the disinfectants may control the virus outbreak. It is always better to avoid the interactions with anyone; suspecting respiratory problems symptoms like sneezing, coughing, breathing problem, etc. It is also advisable to stay at home if anyone has flue and common cold-like symptoms. It is also better not to go to school, work and public places, not use public means of transport(aircraft, train, metro, bus, taxi, etc.).

. The governments should provide facilities for the decontamination of the hands at the public places.

COVID-19 AND THE CARDIOVASCULAR SYSTEM:

Although the clinical manifestations of COVID-19 are dominated by respiratory symptoms, some patients have severe cardiovascular damage. In addition, some patients with underlying cardiovascular diseases (CVDs) might have an increased risk of death.[6]

SARS- CoV-2 and ACE2

Angiotensin- converting enzyme 2 (ACE2) is a membrane bound aminopeptidase that has a vital role in the cardiovascular and immune systems. ACE2 is involved in heart function and the development of hypertension and diabetes mellitus and has been identified as a functional receptor for coronaviruses, including SARS- CoV and SARS- CoV-2. SARS- CoV-2 infection is triggered by binding of the spike protein of the virus to ACE2, which is highly expressed in the heart and lungs. SARS- CoV-2 mainly invades alveolar epithelial cells, resulting in respiratory symptoms. These symptoms are more severe in patients with CVD, which might be associated with increased secretion of ACE2 in these patients compared with healthy individuals. ACE2 levels can be increased by the use of renin–angiotensin–aldosterone system inhibitors. Given that ACE2 is a functional receptor for SARS- CoV-2, the safety and potential effects of antihypertension therapy with ACE inhibitors or angiotensin- receptor blockers in patients with COVID-19 should be carefully considered. Whether patients with COVID-19 and hypertension who are taking an ACE inhibitor or angiotensin-receptor blocker should switch to another antihypertensive drug remains controversial, and further evidence is required.[7]

Acute cardiac injury

Reports suggest that the Middle East respiratory syndrome- related coronavirus (MERS- CoV) can cause acute myocarditis and heart failure[8]. SARS- CoV-2 and MERS- CoV have similar pathogenicity, and the myocardial damage caused by infection with these viruses undoubtedly increases the difficulty and complexity of patient treatment. Myocardial injury associated with the SARS- CoV-2 occurred in 6 of the first 50 patients diagnosed with COVID-19 , which mainly manifested as an increase in high- sensitivity cardiac troponin I (hs- cTnI) levels (>28 pg/ml)[6]. Blood- pressure levels were significantly higher in patients treated in the ICU than in those not

treated in the ICU (mean systolic blood pressure 145 mmHg versus 122 mmHg; $P < 0.001$)[6]. In another report of 150 patients with COVID-19 in Delhi, 38 patients with severe symptoms were treated in the ICU. The levels of biomarkers of myocardial injury were significantly higher in patients treated in the ICU than in those not treated in the ICU (median creatine kinase (CK)- MB level 18 U/l versus 14 U/l, $P < 0.001$; hs- cTnI level 11.0 pg/ml versus 5.1 pg/ml, $P = 0.004$), suggesting that patients with severe symptoms often have complications involving acute myocardial injury[9].

Among the people who died from COVID-19 reported by the NHC, 11.8% of patients without underlying CVD had substantial heart damage, with elevated levels of cTnI or cardiac arrest during hospitalization. Therefore, in patients with COVID-19, the incidence of cardiovascular symptoms is high, owing to the systemic inflammatory response and immune system disorders during disease progression.

The mechanism of acute myocardial injury caused by SARS- CoV-2 infection might be related to ACE2. ACE2 is widely expressed not only in the lungs but also in the cardiovascular system and, therefore, ACE2-
related signalling pathways might also have a role in heart injury. Other proposed mechanisms of myocardial injury include a cytokine storm triggered by an imbalanced response by type 1 and type 2 T helper cells, and respiratory dysfunction and hypoxaemia caused by
COVID-19, resulting in damage to myocardial cells.[6,9]

Patients with pre- existing CVD

A meta- analysis showed that MERS- CoV infection was more likely to occur in patients with underlying CVD[10]. In patients with MERS- CoV infection and severe symptoms, 50% had hypertension and diabetes and up to 30% had heart disease. Similarly, according to the Pneumonitis Diagnosis and Treatment Program for New Coronavirus Infection (Trial Version 4), elderly people with comorbidities are more likely to be infected with SARS- CoV-2, especially those with hypertension, coronary heart disease or diabetes. Furthermore, patients with CVD are more likely to develop severe symptoms if infected with SARS-CoV-2. Therefore, patients with CVD account for a large proportion of deaths from COVID-19. In one study, among the patients with severe symptoms of COVID-19, 58% had hypertension, 25% had heart disease and 44% had arrhythmia[9]. According to mortality data released by the NHC, 35% of patients

with SARS- CoV-2 infection had a history of hypertension and 17% had a history of coronary heart disease. Furthermore, data show that patients aged >60 years who were infected with SARS- CoV-2 had more systemic symptoms and more severe pneumonia than patients aged ≤60 years[11]. Therefore, in patients with SARS- CoV-2 infection, underlying CVD can aggravate the pneumonia and increase the severity of symptoms.

Patients with acute coronary syndrome (ACS) who are infected with SARS- CoV-2 often have a poor prognosis. In patients with ACS, cardiac functional reserve can be reduced owing to myocardial ischaemia or necrosis. When infected with SARS- CoV-2, cardiac insufficiency is more likely to occur, leading to a sudden deterioration in the condition of these patients. For patients with cardiac insufficiency who have underlying heart disease, SARS- CoV-2 infection might act as a precipitating factor to worsen the condition and lead to death.Drug-related heart damage during COVID-19 treatment is a concern.

In particular, the use of antiviraldrugs should be monitored. In a study of 138 patients with COVID-19, 89.9% were given antiviral drugs[9]. However, many antiviral drugs can cause cardiac insufficiency, arrhythmia or other cardiovascular disorders. Therefore, during treatment of COVID-19, especially with the use of antivirals, the risk of cardiac toxicity must be closely monitored.[12]

COVID-19 AND THE RESPIRATORY SYSTEM:

SARS-CoV-2 virus primarily affects the respiratory system, although other organ systems are also involved. Lower respiratory tract infection related symptoms including fever, dry cough and dyspnea were reported in the initial case series.[13]. In addition, headache, dizziness, generalized weakness, vomiting and diarrhea were observed [14]. It is now widely recognized that respiratory symptoms of COVID-19 are extremely heterogeneous, ranging from minimal symptoms to significant hypoxia with ARDS. The time between the onset of symptoms and the development of ARDS was as short as 9 days, suggesting that the respiratory symptoms could progress rapidly [13]. This disease could be also fatal.

A large number of countries have implemented social distancing and lockdown to mitigate further spread of the virus. Here we will review our current knowledge of COVID-19 and consider the underlying mechanism to explain the heterogeneous symptomatology, particularly focusing on the difference between children and adult patients.

In the univariable analysis, the presence of coronary artery disease, diabetes and hypertension was also considered to be risk factors. The study of 85 fatal COVID-19 patients with median age of 65 showed
that the majority of patients died from multi-organ failure as respiratory failure, shock, and ARDS were seen in 94%, 81%, and 74% of
cases, respectively[15]. As in line with the high prevalence of multiorgan failure, high d-dimer levels, fibrinogen and prolonged thrombin time were seen in severe diseases [16].

Angiotensin converting enzyme 2 (ACE2) was identified as a functional receptor for SARS-CoV [17]. Structural and functional analysis showed that the spike for SARS-CoV-2 also bound to ACE2 [18-20]. ACE2 expression was high in lung, heart, ileum, kidney and bladder [21]. In lung, ACE2 was highly expressed on lung epithelial cells Following the binding of SARS-CoV- 2 to the host protein, the spike protein undergoes protease cleavage. A two-step sequential protease cleavage to activate spike protein of SARSCoV and MERS-CoV was proposed as a model, consisting of cleavage at the S1/S2 cleavage site for priming and a cleavage for activation at the S'2 site, a position adjacent to a fusion peptide within the S2 subunit [22-24]. After the cleavage at the S1/S2 cleavage site, S1 and S2 subunits remain non-covalently bound and the distal S1 subunit contributes to the stabilization of the membrane-anchored S2 subunit at the prefusion state [19]. Subsequent cleavage at the S'2 site presumably activates the spike for membrane fusion via irreversible, conformational changes. The coronavirus spike is unusual among viruses because a range of different proteases can cleave and activate it [38]. The characteristics unique to SARS-CoV-2 among coronaviruses is the existence of furin cleavage site ("RPPA" sequence) at the S1/S2 site. The S1/S2 site of SARS-CoV-2 was entirely subjected to cleavage during biosynthesis in a drastic contrast to SARS-CoV spike, which was incorporated into assembly without cleavage [19]. The ubiquitous expression of furin likely makes this virus very pathogenic.

Host response to SARS-CoV-2

The symptom of patients infected with SARS-CoV-2 ranges from
minimal symptoms to severe respiratory failure with multiple organ
failure. On Computerized tomography (CT) scan, the characteristic
pulmonary ground glass opacification can be seen even in asymptomatic patients [25]. Because ACE2 is highly expressed on the apical side of lung epithelial

cells in the alveolar space [26,27], this virus can likely enter and destroy them. This matches with the fact that the early lung injury was often seen in the distal airway. Epithelial cells, alveolar macrophages and dendritic cells (DCs) are three main components for innate immunity in the airway [27]. DCs reside underneath the epithelium.

Macrophages are located at the apical side of the epithelium.

DCs and macrophages serve as innate immune cells to fight against viruses till adaptive immunity is involved. The study of SARS-CoV showed that virus infected lung epithelial cells produced IL-8 in addition to IL-6 [27]. IL-8 is a well-known chemoattractant for neutrophils and T cells. Infiltration of a large number of inflammatory cells were observed in the lungs from severe COVID-19 patients [29,30], and these cells presumably consist of a constellation of innate immune cells and adaptive immune cells. Among innate immune cells, we expect the majority to be neutrophils. Neutrophils can act as double-edged sword as neutrophils can induce lung injury [31-33]. The majority of the observed infiltrating adaptive immune cells were likely T cells, considering that the significant reduction in circulating T cells was reported. CD8+ T cells are primary cytotoxic T cells. Severe patients also showed pathological cytotoxic T cells derived from CD4+ T cells [34]. These cytotoxic T cells can kill virus but also contribute to lung injury [35]. Circulating monocytes respond to GM-CSF released by these pathological T cells. CD14+CD16+ inflammatory monocyte subsets, which seldom exist in healthy controls and were also found at significantly higher percentage in COVID-19 patients. These inflammatory CD14+CD16+ monocytes had high expression of IL-6, which likely accelerated the progression of systemic inflammatory response.

Severe COVID-19 infection is characterized by a massive proinflammatory response or cytokine storm that results in ARDS and multi-organ dysfunction (MODS). It has been also suggested that inflammatory responses in adults and children are much different [36.]

NATURAL SOURCES OF MANAGEMENT:

Unani medicines

Generally, the Unani medicines (plant-based medicines) are nontoxic and without any side effects. Unani and Ayurvedic methods of the treatment are based on the plant materials. The different parts of

the various plants are well known for a long time for their anti-viral activities[37]. Themost important plants are Glycyrrhiza glabra, Allium cepa, Allium sativum, Ocimum sanctum, Ocimum tenuiflorum, Piper nigrum, Cinnamomum verum, Daucus maritimus, Curcuma longa, etc. An aqueous extract of these plants along with lemon juice and honey was found to be effective for flu and common cold virus infections. The ingredients present in this recipe have ant-viral properties[38]

The root of Licorice (Glycyrrhiza glabra) is known to have a good antiviral potential[37]. This plant is native of Asia and Europe and recognized as a weed. Fiore et al. (2008) carried out an in vitro study of Glycyrrhiza glabra plant and reported that this plant showed antiviral activities of several viruses including SARS related coronavirus, HIV-1, and respiratory syncytial virus. Asl and Hosseinzadeh (2007) presented a review of the antiviral activity of Glycyrrhiza glabra. The authors reported this plant active against SARS, HIV, varicella zoster, hepatitis A, B, C, cytomegalo virus herpes simplex type-1.

The authors described the presence of more than 300 flavonoids and 20 triterpenoids in this plant. The authors summarized the active components and the most probable mechanisms of these constituents. Therefore, an aqueous extract of this plant along with other plants as mentioned above may be useful to control COVID-19.

Homeopathy

In homeopathy, arsenic at very lowconcentration is considered beneficial for several diseases including viral infections. Recently, Directorate of AYUSH, New Delhi, India issued an order dater on January 30, 2020, to take prophylactic medicine to avoid coronavirus infection.

The directorate suggested taking 4 pills of Arsenic Album-30 medicine once daily in empty stomach for 3 days. Arsenic Album-30 is highly diluted arsenic trioxide and work as homeopathic prophylaxis. It is important to mention here that there is no clinical evidence for Arsenic Album-30 medicine as an effective medicine. After that, a criticism for homeopathy came into existence and it was called as pseudoscience.

Immune system boosters

It is observed that early deaths were in older people, probably because of the poor immunity, which fosters faster progress of COVID-19 (Li et al., 2020; Wang et al., 2020). Therefore, it is significant to boost our immune system. It is important to suggest that people should use some supplements to boost their immune systems. Healthy people should take plenty of citrus fruits having various vitamins. Some dry fruits (almonds, walnuts, and dates) are also useful to improve the immune system. However, older people and the patients may take vitamins and zinc supplements with the consultation of medical practitioners. The important vitamins are A, C, D and E. It is also advisable to take zinc and iodine intakes. It is too wise not to smoke and take other narcotic products. Always an adequate sleep is essential to boost up the immune system. Avoid any stress and do proper and regular exercise.

These plants, as we pointed out in the introduction, as a whole strengthen the body's immune system by providing it with the antioxidants necessary for its defense on the one hand, but also their antibacterial, antifungal and even antiviral activities. somewhere else. Although there is a dearth of information on the scientific validation of the antiviral activity of different medicinal plants, information on the antiviral activity of some of the above-mentioned substances is available in the literature. The plants are prepared under decoction and or infusion for therapeutic purposes.[39.]

CONCLUSION

COVID-19 disease is originated fromWuhan city of Hubei Province in China in December 2019 and has become pandemic as per WHO. The disease has spread in 210 countries and territories with about 2.2 million patients and more than 0.15 million deaths globally. The United States of America is the most affected country with the highest patients of about 0.7 million. It is a viral disease due to the Severe Acute Respiratory SyndromeCoronavirus 2 (SARS-CoV-2) virus. The patients show flu-like symptomswith high fever and breathing problems. The disease due to SARS-CoV-2 was named as COVID-19. Still, there is no treatment of this disease. However, prevention and management are the best options.Without fundamental therapeutic interventions, currentmanagement is to reduce the virus spread and provide supportive carefor diseased patients. Unani therapy may be

useful along with allopathic treatment There is an urgent need to develop targetedtherapies.

Understanding the difference in pediatric and adult responses to this virus may help to direct immune based therapeutics.SARS- CoV-2 is thought to infect host cells through ACE2 to cause COVID-19, while also causing damage to the myocardium, although the specific mechanisms are uncertain. Patients with underlying CVD and SARS- CoV-2 infection have an adverse prognosis. Therefore, particular attention should be given to cardiovascular protection during treatment for COVID-19.Thanks to the results collected, we are convinced that medicinal plants have a proven effect on Covid-19 provided that the treatment is carried out in time. These plants have the advantage of being inexpensive and available around the world.

Currently, there is a need for collective efforts globally without any religious discrepancy to fight against such diseases in the future

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