wjpmr, 2022,8(7), 69-75

SJIF Impact Factor: 5.922

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Review Article

ISSN 2455-3301

WJPMR

COVID-19 MANAGEMENT AND POST COVID SYSTEMIC COMPLICATIONS: A REVIEW

Naveen Gautam[1]*, Subhash Upadhyay[2] and Sunayana Sharma[3]

[1]PG Scholar, P.G. Department of Swasthavritta and Yoga, Sri Ganganagar College of Ayurvedic Science & Hospital, Sri Ganganagar Rajasthan, India.

[2]Principal, College of Ayurvedic Science and Hospital, Sri Ganganagar Rajasthan, India.

[3]Associate Professor, Department of Swasthavritta and Yoga, Sri Ganganagar College of Ayurvedic Science and Hospital, Sri Ganganagar Rajasthan, India.

***Corresponding Author: Dr. Naveen Gautam**
PG Scholar, P.G. Department of Swasthavritta and Yoga, Sri Ganganagar College of Ayurvedic Science & Hospital, Sri Ganganagar Rajasthan, India.

Article Received on 08/05/2022 **Article Revised on 29/05/2022** **Article Accepted on 19/06/2022**

ABSTRACT

The COVID-19 epidemic has infected millions of people throughout the world, putting a strain on long-term care for COVID-19 survivors. As a result, it's critical to investigate both post-COVID (short-term) and long-term (long-term) effects, especially since the local and systemic pathophysiological outcomes of other coronavirus-related diseases (such as Middle East Respiratory Syndrome (MERS) and severe acute respiratory syndrome (SARS) have been well-documented. We noticed that such negative results were not isolated. The immunological system, haematological system, pulmonary system, cardiovascular system, gastrointestinal, hepatic, and renal system, skeletomuscular system, and neurological system were all damaged. Natural products have been in use since ancient times and have been demonstrated to be beneficial throughout time.

KEYWORDS: Covid-19, Post Covid-19 complications, Covid-19 management.

INTRODUCTION

Coronavirus disease (COVID-19), often known as SARS-CoV-2, is a rapidly spreading viral illness caused by the SARS-CoV-2 virus (subacute respiratory syndrome coronavirus).[1] The World Health Organization (WHO) classified it as a pandemic since it spreads internationally in a short period. This illness was originally discovered in Wuhan, China, and has flu-like symptoms that affect the entire body, including the lungs, kidneys, liver, arteries, and heart, among other organs. However, it mostly affects the respiratory system.[2] The most common consequences linked with the dangerous COVID-19 infection are acute respiratory distress syndrome (ARDS) and respiratory failure. Serious lung damage, haemolytic anaemia, and deadly multi-organ failure are among the other recorded consequences among hospitalised patients. Certain studies have also mentioned some common symptoms such as acute liver injury, renal injury, superinfections, shock, cardiac injuries, rhabdomyolysis, and hypoxic encephalopathy. Certain investigations have found that cardiac muscles are directly implicated in some people, causing conduction system failure and cardiomyopathy, whereas infectious myocarditis is the most common cardiac consequence seen in COVID-19 patients to date.[3] According to several investigations, the SARS-CoV-2 virus uses angiotensin-converting enzyme 2 (ACE2) receptors to cause cardiac damage and pneumonia. The SARS-CoV-2 virus was discovered to target organs with a larger number of ACE receptors, such as the lungs, heart, intestinal epithelium, intravascular endothelium, and kidneys.[4]

The neurological system has recently been implicated in COVID-19 patients, according to several investigations. The coronavirus has impacted neural tissues such as astrocytes, macrophages, and microglia, resulting in nerve injury and infection. Nerve injuries are characterised by headaches, convulsions, dizziness, acute cardiovascular illnesses, olfactory dysfunction, dysgeusia, ataxia, visual impairment, and decreased awareness. Also, as a late consequence of COVID-19 infection, subacute thyroiditis has been documented, highlighting the importance of a thyroid check-up in discharged patients.[5] Infected patients had an unexpected rise in biological parameters such as albumin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), lactate dehydrogenase (LDH) levels, and serum ferritin levels, as well as a fall in lymphocyte count and haemoglobin level, leading to multiorgan failure, according to one study.[6]

COVID-19 is a contagious illness that spreads from one person to another when they come into touch with a polluted environment. Fever, shortness of breath, dry cough, sore throat, muscular discomfort, disorientation, weariness, headache, dyspnea, and loss of taste and smell are some of the clinical signs and symptoms of COVID-19 infection.[7] The government advises using hand sanitiser and wearing protective equipment such as a mask. Although no successful therapy has been documented yet, antiviral medications, respiratory medicines, and chloroquine/hydroxychloroquine are all recommended.[8] Although the long-term implications of these infections are unknown, the SARS-CoV-2 virus has the potential to harm several organs, including the heart, brain, and lungs, resulting in major health issues in the future. Although the majority of infected individuals recovered rapidly, there is still a need to research its late consequences and create appropriate remedies. We concluded the therapeutic herbs, yoga's impact, and post-covid problems linked with this pandemic in this review.

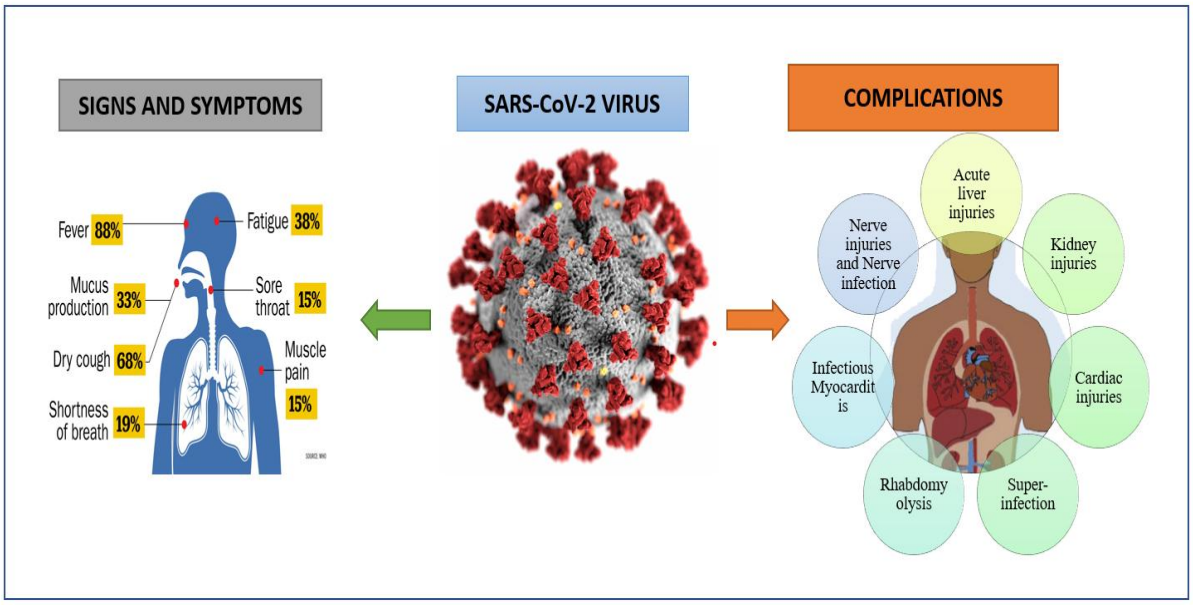

Figure 1: Depicts The Anatomy of The Sars-Cov-2 Virus, As Well As The Illness's Signs and Symptoms and Consequences.

Medicinal plants employed for covid-19

There is no particular therapy for COVID-19 infection at this time. Furthermore, researchers and community members are employing herbal remedies in a variety of methods to treat this ailment. Natural products with immunomodulatory capabilities have been shown to play a significant role in reducing disease development, as immunity was crucial in COVID-19 infection.[9]

COVID-19 has no particular therapy at the moment. Furthermore, residents and researchers are attempting to determine the best method for curing or preventing the ailment, which includes the use of herbal medicine. Because the immunological condition of patients is so important in COVID-19 infection, a herbal remedy with an immunomodulatory action might be useful as a preventative and possibly therapeutic treatment for COVID-19 infection patients. Consumption of herbal remedies containing active chemicals with antibacterial or antiviral, anti-inflammatory, and immunostimulatory properties, such as echinacea, quinine, and curcumin, is a recent trend in the community. These herbal substances are thought to have the ability to alter immune responses, and as a result, they may be useful in preventing or treating COVID-19.[9]

Respiratory disorders can be treated using traditional plant-based remedies. Some of the most well-known plants used to treat respiratory problems include *Artemisia vulgaris, Boerhavia procumbens, Capparis spinosa L., Carum copticum, Cistanche tubulosa, Euphorbia hirta.* Aside from these, there are hundreds of plants that are used to cure or reduce the symptoms of respiratory issues like cough, asthma, colds, bronchitis, flu, respiratory tract infections, whooping cough, and breathing difficulties. Herbs are commonly used in the treatment of respiratory issues in the form of decoction, powder, juice, tea, or oil investigated the effects of *Alstonia scholaris* leaves on asthma in rats and guinea pigs. Leaf extracts of *A. scholaris* were shown to have prostaglandin-mediated broncho-vasodilatory action. The findings show that the root extract of A. scholaris relaxes calcium chloride-induced contractions in the ileum of guinea pigs, indicating that the extract interferes with calcium ion entry into cells.[3]

Ficus religiosa leaf extracts show that it reduced histamine and acetylcholine-induced pre-convulsive dyspnoea (shortness of breath) in guinea pigs. This means that a comprehensive assessment of significant herbs backed by scientific research might aid in the

discovery of a naturally occurring, biocompatible cure for COVID-19 sufferers' respiratory difficulties

Antiviral Plants

Medicinal herbs have been used to treat human infections for a long time. Many herbal plants are effective against viral infections in the form of leaf powder, decoctions, infusions, pastes, and tablets. There are hundreds of plants that have antiviral activities in humans. Human viruses such as influenza virus, human immunodeficiency virus (HIV), Hepatitis C virus , and Herpes simplex virus type 1 (HSV-1) have all been treated with antiviral plants such as *Sambucus nigra, Withania somnifera, Sylibum marianum*.[10]

There are a plethora of herbs that have been demonstrated to have potent anti-VRI properties. These plants have antiviral action (*Glycyrrhiza spp.),* analgesic activity (*Calendula officinalis*), anti-inflammatory activity (*Hedera helix*), and immunological stimulatory activity (*Hedera helix*) (*Andrographis paniculate*). *Lomatium dissectum* (desert parsley) and *Osmorhiza occidentalis* (western sweet Cicely) from the Apiaceae family, *Rosmarinus officinalis* (rosemary), and *Prunella vulgaris* (heal-all) from the Lamiaceae family are among the most significant antiviral herbs, for example, found that aqueous extracts of five traditionally used herbal medicines had significant anti-influenza A properties *(Duchesnea indica, Fragaria indica, Liquidambar formosana, Lithspermum erythrorhizon, Melia toosendan* and *P. vulgaris*). Tian et al. discovered that extracts from various plants, including *P. vulgaris*, had potent anti-neuraminidase activity and may effectively combat influenza virus. For example, Sornpet et al. showed that crude extracts of five Asian medicinal herbs (*Andrographis paniculata, Curcuma longa, Gynostemma pentaphyllum, Kaempferia parviflora,* and *Psidium guajava*) have biological activity against highly pathogenic avian influenza virus (H5N1).[10]

Chathuranga et al. also looked at the anti-RSV activity of the plants *Plantago asiatica* and *Clerodendrum trichotomum.* Lower quantities of *P. asiatica* and *C. trichotomum* extract dramatically reduced RSV gene replication and transcription, which in turn lowered RSV protein synthesis and hence reduced RSV-induced cell death.[11]

Furthermore, during the first SARS-CoV outbreak, researchers discovered that Glycyrrhizin, a saponin derived from Liquorice roots, can suppress the replication of SARS-associated coronavirus with an EC50 value ranging from 300 to 600 mg/L. (during and after virus adsorption, respectively). The CC50 was measured at more than 20,000 mg/L. This indicates that at a dosage of 20,000 mg/L, there was only a 20–30% drop in cell viability, showing the compound's low cytotoxicity. It was shown that giving infected cells 4000 mg/L of glycyrrhizin stopped the virus from replicating. The study also found that Glycyrrhizin is a safer option than antiviral drugs like Ribavirin, which can cause haemolysis and a significant drop in haemoglobin levels in SARS patients. Although there are certain risks associated with utilising untested herbal items, phytochemicals are generally considered fundamentally safe due to their biocompatibility, lower toxicity than xenobiotics, and environmental friendliness. The mechanism of action of phytochemicals like Glycyrrhizin remained unclear during the SARS pandemic in 2002. Further research on Glycyrrhizin aimed to figure out how it works and create a more effective version of the phytochemical to fight coronaviruses. According to However et al. adding 2-acetamido—D-glucopyranosylamine to the glycoside chain of glycyrrhizin increases its antiviral activity by tenfold.[12,13]

POST COVID COMPLICATIONS

The Immune System's Complications

The development of adaptive immunity (mediated by T and B cells) to the virus characterises the sequence of immunological processes associated with SARS-CoV-2. COVID-19 has been linked to Guillain-Barré Syndrome (GBS).[14] Polyneuropathy (loss of the myelin sheath) and an inflammatory cascade of peripheral nerves define this disease's rapid progression. Clinical trials of adult, young, and child patients during or after coronavirus infection have documented GBS.[15] The signs and symptoms varied from severe respiratory problems to muscular paralysis. Different publications have linked these symptoms to the physiological activation of inflammatory cells during COVID-19 infection. Nonetheless, further research is needed to figure out how the COVID-19 virus causes this illness. Rheumatoid arthritis (RA) caused by COVID-19 has been extensively documented in case reports and observational research. In addition, a cross-sectional investigation of COVID-19's influence on rheumatic patients found that those who were impacted had arthralgia, myalgia, and weakness, which appeared before COVID-19 respiratory symptoms.[16] In children, autoinflammatory disorders such as Kawasaki disease have been documented. This condition primarily affects children under the age of five and is defined as an acute inflammatory process in small and medium-sized arteries, with increased cardiac involvement and a higher inflammatory response with macrophage activation. In addition, myocarditis was discovered in young individuals with no previous cardiac morbidity, with patients classed as critical and high cytokine production, demonstrating acute respiratory distress syndrome.[17]

Nervous System Complications

COVID-19 infection has unknown short- and long-term effects on the central nervous system. The first investigation to investigate neurological signs in COVID-19 was a retrospective multicentre analysis by Mao et al. They were discovered in 36.4% of the 214 participants in the study. CNS signs were the most prevalent (24.8%), followed by peripheral nervous

system abnormalities (8.9%). Loss of taste, smell, and hearing, headaches, spasms, convulsions, confusion, visual impairment, nerve pain, disorientation, decreased awareness, nausea and vomiting, hemiplegia, ataxia, stroke, and cerebral haemorrhage were the most often reported symptoms in COVID 19.[17,18]

In most COVID 19 patients, anosmia and ageusia are the first basic neurological symptoms. The United States Centers for Disease Control and Prevention (CDC) has officially included abrupt loss of taste and smell as symptoms of COVID-19. Researchers discovered alterations in smell in 35.8% of patients (and taste in 38.5%) in a meta-analysis study. These symptoms are most likely caused by a pathogenic infection of the gustatory or olfactory systems.[19]

Patients infected with SARS-CoV-2 have also experienced hearing loss. Almufarrij *et al*. in review research looked at the likelihood of the novel coronavirus affecting the vestibular system, similar to how ototoxic medicines like azithromycin and hydroxychloroquine might cause changes in this system. Furthermore, Saniasiaya *et al.* showed that SARS-propensity CoV-2's to deoxygenate erythrocytes can induce hearing loss by fostering a hypoxic condition in the auditory centre, which can lead to irreparable damage.

In certain investigations, nonspecific neurological symptoms such as myalgia, headache, and dizziness were described, with myalgia accounting for 1.8–62.5%, headache for 0.6–70.3%, and dizziness for 0.6–21%. COVID-19 has also been linked to epileptic episodes. Stroke in COVID-19 is an uncommon but well-documented complication.[20]

It's possible to have an ischemic stroke, which involves the anterior circulation and the obstruction of major arteries. It usually occurs during the early phases of recovery, although it can also occur later. In hospitalised patients with pneumonia, however, an unusual rise in the incidence of arterial-venous sinus thrombosis (TSA) (from 7.7% to 28.0%) was documented and linked to COVID-19.[21]

The Haematological System's Complications

Several critical organic processes for regulating homeostasis are involved in the pathophysiology of COVID-19 infection. Hyperinflammation caused by SARS-CoV-2 causes the synthesis of endogenous chemical compounds that enhance vascular haemostasis disruption. The release of procoagulant and proinflammatory cytokines, which activate disseminated intravascular coagulation and the formation of thromboembolic states that can aggressively affect various tissues, particularly those that are more sensitive to ischemic processes, such as pulmonary, cardiovascular, and cerebrovascular tissues, has a direct effect on blood coagulation.[22,23]

The Pulmonary System's Complications

The pathophysiology of SARS-CoV-2 is complicated, involving a variety of organs and systems; however, the cardiopulmonary system is particularly vulnerable. The lungs, as target organs of the respiratory system, suffer from progressive functional loss, as evidenced by hypoxia and pathological findings from limited, non-invasive autopsies. SARS-CoV-2 infection has been shown to damage the pulmonary system, causing severe respiratory failure, as well as causing extrapulmonary clinical symptoms.[24,25]

Respiratory system dysfunction is one of the most aggressive outcomes linked to increased immune responses generated by viral infection. The cytokine storm stimulates defence mechanisms, boosting biochemical pathways and causing tissue damage indicators to be produced as well as lung tissue collapse. Respiratory failure, pulmonary thromboembolism, pulmonary embolism, pneumonia, pulmonary vascular damage, and post-viral pulmonary fibrosis are some of the most common related diseases. Pulmonary vein thrombosis is uncommon, although it can occur in the presence of dyspnea, cough, chest discomfort, and/or haemoptysis, resulting in systemic arterial embolism. In COVID-19 patients with hypercoagulable conditions, systemic arterial embolism is linked to venous and arterial thromboembolism aetiology.[26,27]

In 35.7% of patients, pulmonary thrombi in medium-sized arteries were found, resulting in pulmonary infarction and/or pulmonary haemorrhage. COVID-19 is a disease with a systemic nature, according to the autopsy results of individuals with post-viral infection. Because the lungs are heavily involved in the infection, there is a higher risk of cardiac and vascular consequences, such as acute myocardial infarction and thrombotic/thromboembolic events that can impact other organs. Although subsequent acute bronchopneumonia has been linked to pathological abnormalities, it has been identified as one of the most prevalent consequences in COVID-19 patients and may be the major cause of death.[28]

Cardiovascular System Complications

Both SARS-CoV and MERS-CoV are linked to myocardial damage, myocarditis, and heart failure, according to pathophysiological findings in SARS-CoV and MERS-CoV patients. The major causes causing myocardial damage, on the other hand, are diverse, mostly involving the cardiopulmonary and vascular systems. Severe infection in the acute respiratory tract induced by SARS-Cov-2 affects the cardiovascular system in numerous ways in these situations. COVID-19 detects myocardial damage in 25% of hospitalised patients, which is linked to an elevated risk of death. The risk of cardiac damage is greatly increased when SARS-Cov-2 infection is linked with serious cardiovascular events such as acute myocardial infarction Type I and II. As a result, there is a poor prognosis. Patients'

cardiovascular comorbidities have been linked to an elevated risk of mortality from COVID-19, according to growing clinical data and epidemiological results. Furthermore, necropsy results of individuals with COVID-19 revealed indications of chronic heart disease, including myocardial hypertrophy (92.9%), mild to severe coronary artery atherosclerosis (100%), and localised myocardial fibrosis (21.4%). Acute myocardial infarction was revealed to be a cause of mortality in 21.4% of patients with ATTR-positive cardiac amyloidosis, and substantial cardiac hypertrophy was detected in 7.15 of patients with ATTR-positive cardiac amyloidosis.[23,29]

The risk of cardiac damage, functional failure, and mortality is increased when adverse pathophysiological responses are combined with additional variables such as age, sex, cardiovascular, and metabolic comorbidities. Furthermore, treatment regimens that need polypharmacy (most notably, the use of antiviral medicines) might result in mitochondrial dysfunction and cardiotoxicity. Several medication classes used in COVID-19 treatment procedures have been shown to enhance the risk of heart damage. Chemotherapeutic cardiotoxicity is related to COVID-19 infection in patients with particular clinical situations, such as cancer therapy. In the presence of additional clinical diseases such as arrhythmia, thrombosis, pericardial illness, myocarditis, heart failure, and cardiac damage might worsen.[30,31]

Skeletomuscular System Complications

The occurrence of central and peripheral neurological symptoms may be linked to musculoskeletal problems. Neurological problems can damage the central nervous system (24.8%) and peripheral nervous system (8.9%), as well as induce skeletal muscle injuries (10.7%) according to studies.[32] SARS-CoV-2 infections have been linked to immune-mediated skin disorders. The use of immunosuppressants to reduce hyperinflammatory reactions (characterised by hyperactivation of macrophages and elevated levels of pro-inflammatory cytokines in COVID-19 was linked to the dermis' indirect involvement, with skin manifestations occurring regardless of disease stage or severity. Immune-mediated diseases including psoriasis and lupus have also been linked to an increased risk of viral infection. These might include dermatomyositis, an inflammatory myopathy that affects the skin and other organs, causing weakness and rashes, as seen in SARS-CoV-2 patients. COVID-19 epithelial features, which present as damage to the perifollicular levels and erythematous plaques induced by the response mediated by primary cells, might develop after the onset of the disease's general symptoms most commonly in adult diverse individuals. Rashes, hives, and acrocyanosis can be seen in these individuals of all ages.[33,34]

Gastrointestinal, Hepatic, and Renal System Complications

In those who are infected with COVID-19, inflammatory problems involving the digestive tract are prevalent. In epidemiological investigations of people infected with the new coronavirus, clinical symptoms such as diarrhoea, nausea, vomiting, abdominal discomfort, anorexia, acid reflux, gastrointestinal bleeding, loss of appetite, and constipation have been described. These symptoms can appear in the early stages of the disease, known as the viral phase, or as long-term gastrointestinal problems. Gastrointestinal symptoms have been linked to the immune system and changes in the intestinal flora, as well as comorbidities in individuals who have been infected with the virus. Obesity, advanced age, diabetes, a poor diet, and malnutrition are among the conditions that might cause systemic inflammation and intestinal metabolite dysfunction.[35]

COVID-19-induced hyperinflammatory alterations in the cardiopulmonary vasculature can lead to prothrombotic conditions, obstructing blood flow to other organs. Renal infarctions (mostly due to thromboembolism) are uncommon in COVID-19 patients. Ischemic episodes are uncommon, with a reported prevalence of 0.1–1.4%, and splenic thrombosis is uncommon. COVID-19 infections have been shown to produce macro and micro thromboembolic renal impairment, as well as microvascular blockage and infarction. Perfusion deficits in the lungs and kidneys were detected in a substantial proportion of patients with mild to moderate COVID-19, which might indicate the existence of systemic microangiopathy with micro thrombosis.[36]

CONCLUSION

All of the symptomatology and systemic pathophysiological alterations associated with COVID-19 have one thing in common: they all engage organic systems in conjunction with haematological and vascular dynamics. Viral infection triggers an intense immune response, which affects the cardiopulmonary system both directly and indirectly. Haematological alterations generated by vascular inflammation, on the other hand, create a milieu conducive to the production of thromboembolism, impacting other essential organs such as the brain system, gastrointestinal tract, liver, and kidneys. Furthermore, this viral infection can cause liver instability, which indicates a high level of vigilance throughout the body and results in an increase in plasma biochemical indicators of tissue aggressiveness generated in response to tissue-damaging substances. The long-term degenerative consequences and sequelae of COVID-19 systemic disease, as manifested in perennial (myocardium and brain) and stable (soft tissue) organs, are being assessed. Late viral infection has also been linked to various illnesses, including pathophysiological abnormalities in pregnant women and babies, changes in memory and reasoning profiles, muscle and joint discomfort, and changes in the cardiac QT wave interval. Some of these may be involved in sensitising the

immune system to virus particles, allowing them to maintain a latent immunological memory long after they have been removed from the organisms. This is now one of the most popular concepts for explaining the late-COVID-19 effects on some organs. Because of their capacity to infiltrate vascular tissue, virus particles can be discovered even in more protected tissues (arteries and veins).

REFERENCES

1. Orlandi M, Lepri G, Bruni C, Wang Y, Bartoloni A, Zammarchi L, et al. The systemic sclerosis patient in the COVID-19 era: the challenging crossroad between immunosuppression, differential diagnosis and long-term psychological distress. Springer, 2020; 2043-7.
2. Wang X, Fang X, Cai Z, Wu X, Gao X, Min J, et al. Comorbid chronic diseases and acute organ injuries are strongly correlated with disease severity and mortality among COVID-19 patients: a systemic review and meta-analysis. Research, 2020; 2020.
3. Mehraeen E, Behnezhad F, Salehi MA, Noori T, Harandi H, SeyedAlinaghi S. Olfactory and gustatory dysfunctions due to the coronavirus disease (COVID-19): a review of current evidence. Eur. Arch. Oto-Rhino-L., 2021; 278(2): 307-12.
4. Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol, 2020; 5(7): 819-24.
5. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ., 2020; 369.
6. Coperchini F, Chiovato L, Croce L, Magri F, Rotondi M. The cytokine storm in COVID-19: An overview of the involvement of the chemokine/chemokine-receptor system. Cytokine Growth Factor, 2020; 53: 25-32.
7. Panyod S, Ho C-T, Sheen L-Y. Dietary therapy and herbal medicine for COVID-19 prevention: A review and perspective. J. Tradit. Complement. Med., 2020; 10(4): 420-7.
8. SeyedAlinaghi S, Afsahi AM, MohsseniPour M, Behnezhad F, Salehi MA, Barzegary A, et al. Late complications of COVID-19; a systematic review of current evidence. Arch. Acad. Emerg. Med., 2021; 9(1).
9. Heneka MT, Golenbock D, Latz E, Morgan D, Brown R. Immediate and long-term consequences of COVID-19 infections for the development of neurological disease. Alzheimer's Res. Ther., 2020; 12(1): 1-3.
10. Akram M, Tahir IM, Shah SMA, Mahmood Z, Altaf A, Ahmad K, et al. Antiviral potential of medicinal plants against HIV, HSV, influenza, hepatitis, and coxsackievirus: A systematic review. Phytother Res., 2018; 32(5): 811-22.
11. Chathuranga K, Kim MS, Lee H-C, Kim T-H, Kim J-H, Gayan Chathuranga W, et al. Anti-respiratory syncytial virus activity of Plantago asiatica and Clerodendrum trichotomum extracts in vitro and in vivo. Viruses, 2019; 11(7): 604.
12. Khan T, Khan MA, Ullah N, Nadhman A. Therapeutic potential of medicinal plants against COVID-19: The role of antiviral medicinal metabolites. Biocatal. Agric. Biotechnol, 2021; 31: 101890.
13. Luo P, Liu D, Li J. Pharmacological perspective: glycyrrhizin may be an efficacious therapeutic agent for COVID-19. Int. J. Antimicrob. Agents, 2020; 55(6): 105995.
14. Loarce-Martos J, García-Fernández A, López-Gutiérrez F, García-García V, Calvo-Sanz L, del Bosque-Granero I, et al. High rates of severe disease and death due to SARS-CoV-2 infection in rheumatic disease patients treated with rituximab: a descriptive study. Rheumatol. Int., 2020; 40(12): 2015-21.
15. García-Manzanedo S, de la Oliva Calvo LL, Álvarez LR. Guillain-barre syndrome after Covid-19 infection. Med Clin., 2020; 155(8): 366.
16. Haberman RH, Castillo R, Chen A, Yan D, Ramirez D, Sekar V, et al. COVID-19 in patients with inflammatory arthritis: a prospective study on the effects of comorbidities and disease-modifying antirheumatic drugs on clinical outcomes. Arthritis Rheum, 2020; 72(12): 1981-9.
17. Sadanandam A, Bopp T, Dixit S, Knapp DJ, Emperumal CP, Vergidis P, et al. A blood transcriptome-based analysis of disease progression, immune regulation, and symptoms in coronavirus-infected patients. Cell Death Dis., 2020; 6(1): 1-14.
18. Samaranayake LP, Fakhruddin KS, Panduwawala C. Sudden onset, acute loss of taste and smell in coronavirus disease 2019 (COVID-19): a systematic review. Acta Odontol. Scand, 2020; 78(6): 467-73.
19. Saniasiaya J. Hearing loss in SARS-CoV-2: what do we know? J ENT, 2021; 100(2): 152S-4S.
20. Karimi-Galougahi M, Naeini AS, Raad N, Mikaniki N, Ghorbani J. Vertigo and hearing loss during the COVID-19 pandemic–is there an association? Acta Otorhinolaryngol Ital., 2020; 40(6): 463.
21. Tu TM, Goh C, Tan YK, Leow AS, Pang YZ, Chien J, et al. Cerebral venous thrombosis in patients with COVID-19 infection: a case series and systematic review. J Stroke Cerebrovasc Dis., 2020; 29(12): 105379.
22. Jin Y, Ji W, Yang H, Chen S, Zhang W, Duan G. Endothelial activation and dysfunction in COVID-19: from basic mechanisms to potential therapeutic approaches. Signal Transduct Target Ther., 2020; 5(1): 1-13.
23. Giustino G, Pinney SP, Lala A, Reddy VY, Johnston-Cox HA, Mechanick JI, et al. Coronavirus and cardiovascular disease, myocardial injury, and arrhythmia: JACC focus seminar. J. Am. Coll. Cardiol, 2020; 76(17): 2011-23.

24. Cobos-Siles M, Cubero-Morais P, Arroyo-Jiménez I, Rey-Hernández M, Hernández-Gómez L, Vargas-Parra DJ, et al. Cause-specific death in hospitalized individuals infected with SARS-CoV-2: more than just acute respiratory failure or thromboembolic events. Intern Emerg Med., 2020; 15(8): 1533-44.
25. Shi S, Qin M, Cai Y, Liu T, Shen B, Yang F, et al. Characteristics and clinical significance of myocardial injury in patients with severe coronavirus disease 2019. Eur. Heart J., 2020; 41(22): 2070-9.
26. Khan MZ, Jamal Y, Sutton B, Rauf F. Venous thromboembolism in patients with COVID-19 and correlation with D-dimers: a single-centre experience. BMJ Open Respir, 2020; 7(1): e000779.
27. D'Errico S, Zanon M, Montanaro M, Radaelli D, Sessa F, Di Mizio G, et al. More than pneumonia: distinctive features of SARS-CoV-2 infection. From autopsy findings to clinical implications: a systematic review. Microorganisms, 2020; 8(11): 1642.
28. George PM, Barratt SL, Condliffe R, Desai SR, Devaraj A, Forrest I, et al. Respiratory follow-up of patients with COVID-19 pneumonia. Thorax, 2020; 75(11): 1009-16.
29. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. Clin Res Cardiol, 2020; 109(5): 531-8.
30. Moderato L, Monello A, Lazzeroni D, Binno S, Giacalone R, Ferraro S, et al. Takotsubo syndrome during SARS-CoV-2 pneumonia: a possible cardiovascular complication. G. Ital. Cardiol (2006), 2020; 21(6): 417-20.
31. Teixeira R, Santos M, Gil V. COVID-19 and cardiovascular comorbidities: An update. Rev Port Cardiol, 2020; 39(8): 417.
32. Singh AK, Bhushan B, Maurya A, Mishra G, Singh SK, Awasthi R. Novel coronavirus disease 2019 (COVID-19) and neurodegenerative disorders. Dermatol. Ther., 2020; 33(4): e13591.
33. Niaki OZ, Anadkat MJ, Chen ST, Fox LP, Harp J, Micheletti RG, et al. Navigating immunosuppression in a pandemic: A guide for the dermatologist from the COVID Task Force of the Medical Dermatology Society and Society of Dermatology Hospitalists. J. Am. Acad. Dermatol, 2020; 83(4): 1150-9.
34. Sanghvi AR. COVID-19: an overview for dermatologists. Int. J. Dermatol, 2020; 59(12): 1437-49.
35. Weber TK, Leandro-Merhi VA, Bernasconi I, Oliveira MRMd. Nutritional therapy in hospital care of in-patients with Covid-19: evidence, consensus and practice guidelines. Rev. de Nutr., 2020; 33.
36. Silva Andrade B, Siqueira S, de Assis Soares WR, de Souza Rangel F, Santos NO, dos Santos Freitas A, et al. Long-COVID and post-COVID health complications: an up-to-date review on clinical conditions and their possible molecular mechanisms. Viruses, 2021; 13(4): 700.