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A Review on Post Covid Syndromes

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ABSTRACT:
COVID-19, a communicable disease caused by Corona virus 19 has claimed millions of life around the world. Some patients who were formerly affected by the disease are perceived as a population in need of consideration since certain symptoms as well as complications were reported to persist among them even after their recovery from the disease. This condition in which the symptoms does not cease for more than 3 months are termed as 'Post COVID-19 Syndrome' This review is aimed to describe about the Post COVID-19 Syndromes faced by the patients after recovering from COVID-19 as well it's pathogenesis and management.

KEY WORDS: COVID-19, Post covid sequelae, Symptoms, Pathophysiology, Management.

I. INTRODUCTION:

COVID-19, a multi-systemic disease which has been spread worldwide at a rapid pace with increasing morbidity as well as mortality among all populations is caused by the pathogen Novel Coronavirus 19 [1].This viral infection was first reported in December and has resulted in millions of death globally [2]. Although most of the people with COVID-19 have recovered, certain consequences that persist for months even after recovery were reported by a significant portion of patients who have suffered from the condition [3]. These symptoms which last for months after recovery are termed as "Post-COVID-19 Syndrome" [4]. 'Any signs and symptoms which develop in the course of the infection or following the infection accordant with COVID-19, unceasing for more than 3 months, and not described by an alternative diagnosis' is said to be Post COVID-19 syndrome.This is characterized by continuance of certain symptoms after recovery and any newly developed syndromes or amplification of chronic conditions within a month after recovery were included [5]. On top of that, these syndromes were not only reported in people with severe disease who needs to be hospitalized or in older people with pre-existing comorbidities but also in young, formerly healthy subjects with mild disease [6].Fatigue, dyspnea, chest pain, smell and taste dysfunction and psychological disorders [7] were found to be the persisting signs and symptoms reported by the patients who recovered from COVID-19. Moreover, it results in certain cardio endocrinal, autoimmune, neurological, liver and renalcomplications that lasts for months which lasts for months [8]. These symptoms which prolongs for several months interrupts with work activities and the quality of life of the people affected by it [9].

PATHOGENESIS

COVID-19 is an infection that affects multiple systems [10]. The principal target for SARS-CoV-2 binding and infection is the cell surface angiotensin-converting enzyme 2 (ACE2) receptor, which is widespread in cells of most organs [11,12]. Most patients recover without complications as a result of a monocyte-macrophage, CD4 and CD8 cellular response, and a regulated inflammatory response [10]. In patients with severe life-threatening infections, a SARS-CoV-2 immunological dysfunction is detected, which is associated with high levels of cytokines interleukin-1 (IL-1), IL-6, IL-2, and IL-10 ("cytokine storm") and significant inflammation [10]. The cause of post-COVID syndrome is not well understood. Prolonged inflammation appears to play a crucial role in the aetiology of most post-COVID symptoms, according to evidence.

PATHOPHYSIOLOGY

The following are the main pathophysiologic processes of acute COVID-19: endothelium damage and microvascular injury; immune system dysregulation and stimulation of a hyperinflammatory state; hypercoagulability with in situ thrombosis and macrothrombosis; and maladaptation of the angiotensin-converting enzyme 2 (ACE2) pathway [13] are all examples of direct viral toxicity.

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These are the potential mechanisms for the pathophysiology post acute COVID-19 (1) virus-specific pathophysiologic abnormalities; (2) immunological abnormalities and proinflammatory damages in response to the acute infection; and (3) predicted post-critical illness consequences are all potential pathways contributing to the pathophysiology of post-acute COVID-19. After a critical illness, post-intensive care syndrome encompasses new or increasing impairments in physical, cognitive, and mental domains [14,15,16,17,18]. The pathogenesis of post-intensive care syndrome is multifaceted, with microvascular ischemia and damage, immobilization, and metabolic changes during critical illness all being implicated [16]. Furthermore, survivors of acute COVID-19 may be at a greater risk of infections with bacterial, fungal (pulmonary aspergillosis), or other pathogens [19-21], similar to previous investigations of SARS survivors, in which 25–30 percent suffered subsequent infections [22,23].

POST–COVID-19 SYMPTOMS

FATIGUE

COVID-19 patients may develop chronic fatigue syndrome/myalgic encephalomyelitis, which manifests as a long-term relapse of exhaustion, cognitive impairment, depression, and other symptoms after only a small amount of exertion [24]. Fatigue is the most prevalent symptom of post-COVID syndrome, with rates ranging from 17.5 percent to substantially higher rates (up to 60.3 and 72.0 percent, respectively) among hospitalized COVID-19 patients in wards or critical care units [2,25-32]. Patients have experienced exhaustion lasting up to seven months after the onset of COVID-19, causing considerable disability, and many patients have reported fatigue lasting longer than seven months, necessitating further inquiry [27,32]. Male gender, as well as comorbidities such as hypertension and diabetes mellitus, have been linked to fatigue [25]. Because there is presently no widely accepted diagnostic procedure it is crucial to rule out any illnesses that share symptoms. Hormonal imbalances, immune system dysfunction, infection, and nervous system abnormalities are all possible causes in the pathophysiology of the disorder [25].

DYSPNEA AND CHEST PAIN

COVID-19 patients who were admitted to the hospital may have more respiratory and physical difficulties [32,33]. Symptoms of COVID-19, such as dyspnea and decreased exercise tolerance, can last for up to four months in a considerable percentage of patients hospitalized for COVID-19, with impaired exercise tolerance being the most common [32,33]. In rough, residual dyspnea persisted in 10% and 40% of COVID-19 survivors who reported having it during the acute phase of the disease, which lasted two and four months, respectively. [32,33]. Breathlessness was a prevalent symptom in hospitalized patients [27], even weeks after discharge, affecting up to 42.6 percent of ward patients and 65.6 percent of critical care unit patients, respectively [29]. Up to 22% of survivors developed chest pain after two months [2,26,30,31]. COVID-19 sequelae, such as respiratory and physical functional impairment, have been linked to residual lung injury and may have an impact on COVID-19 survivors' psychological health due to a worse quality of life [33]. COPD, or chronic obstructive pulmonary disease, has been established as a risk factor for serious lung disease.

OLFACTORY AND GUSTATORY DYSFUNCTION

Following the onset of smell and taste loss, recovery of olfactory and gustatory dysfunction can take up to a month [34,35,36], and it can affect up to 11% and 9% of patients six months after discharge, respectively [26]. Gender and age have never been found to be indicators of olfactory performance [35]. The peripheral expression of two known proteins employed by SARS-CoV-2 to infect human cells (ACE2 and TPMRSS2), as well as partial loss of olfactory receptor neurons in the olfactory epithelium, may be linked to the mechanism through which SARS-CoV-2 induces olfactory dysfunction. Taste loss is caused by SARS-CoV-2, however the exact mechanism is uncertain. Because ACE2 receptors have been discovered in the mouth and on the tongue, it is possible that direct damage to the gustatory organ is to cause [26]. Other common post-COVID syndrome symptoms include gastrointestinal problems such as vomiting and diarrhoea, which can last up to two months in one-third of patients [2,28,30].

POST COVID COMPLICATIONS IN VARIOUS ORGAN SYSTEM

CARDIO-VASCULAR COMPLICATIONS:

Corona virus (COVID – 19) enters into the cells by attaching it via a spike protein to the receptor of angiotensin-converting enzyme-II, the virus which is abundant in several different cell types and tissues that can cause injury in several organs [37]. The series of CV complications is huge, acute myocarditis with heart failure, right ventricular dysfunction (RVD), arrhythmias, myocardial ischemia and pulmonary

International Journal of Pharmaceutical Research and Applications
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thromboembolism are most significant case [38,39]. The prevalence of RVD was 14.4% in younger patients without previous history of CV disease after 6–10 weeks of discharge from the hospital [39]. Nitric oxide is a strong vasodilatory and anti-inflammatory signaling molecule which is produced by endothelial cells. Reduced capacity of nitric oxide production and/or decreased nitric oxide sensitivity is termed as Endothelial dysfunction. It causes heart failure with preserved ejection fraction (HFpEF) symptoms such as palpitations, exercise-related fatigue. This condition results in a procoagulant and proinflammatory situation [40]. Another mechanism by which COVID-19 may damage the cardiovascular system such as hyper-inflammation, hyper-coagulability with thrombosis and renin-angiotensin aldosterone system dysfunction [37]. Inflammation of circulatory system eventually results in inflammation of myocardium muscle (myocarditis), diffuse of thrombotic microangiopathic (TMA), cardiac arrhythmias, acute coronary syndrome(ACS) and heart failure [41]. Mildly infected patients were reported with dyspnea, fatigue and heart dysfunctions upto 8 months of follow-up [42]. 9% of patients report with palpitations upto 6 months as a post acute COVID-19 syndrome [37]. In addition, COVID-19 in cardiovascular, produces orthostatic syndromes including orthostatic hypotension, postural orthostatic tachycardia syndrome (POTS), chest pain, cardiac arrhythmias, and inappropriate sinus tachycardia (IST) due to autonomic nervous system (ANS) dysfunction such as dysautonomia [43]. Inappropriate sinus tachycardia can be triggered by viral infection that penetrates into the cells by attaching into the ACE-II receptor which influence the endogenous angiotensin-II synthesis, a hormone that activates the sympathetic nervous system (SNS). Renin–angiotensin–aldosterone system dysfunction with compensatory activation of the SNS may contribute to inappropriate sinus tachycardia (IST) [43]. Inappropriate sinus tachycardia is a prevalent among PCS patients [44], it is defined as within 24-hour of ECG monitoring the average heart rate exceeding 90 beats per minute or a resting heart rate >100 beats per minute which may cause gain-of-function mutation in the cardiac pacemaker HCN4 channel [37]. Some anti-COVID agents that produce potential cardiotoxicity includes macrolide antibiotic, azithromycin associated with a prolonged QT interval, chloroquine/ hydroxychloroquine produce conduction defects in the heart and prolong PR, QT intervals due to the protease inhibitors, lopinavir/ritonavir [44].

ENDOCRINOLOGICAL COMPLICATIONS:

The average incidence of T_1DM is increase globally in 3–4% per year [45]. New onset of diabetes mellitus rise in patients with long-COVID particularly in children without a history of diabetes [46,47] by affecting immune regulation causing direct damage to pancreatic β-cells or both [46]. New onset diabetes proposed by several mechanisms during COVID-19 pandemic whether the diabetes originated from the infection or the infection triggered autoimmunity [45]. SARS-CoV-2 enters the host cells by binding to angiotensin converting enzyme-II, a transmembrane glycoprotein with proteolytic activity in many tissue cells including pancreatic β-cells as well as exocrine pancreatic cells the viral replication in pancreatic cells, thereby altering pancreatic β-cell function directly and impairing insulin secretion [45] infection may trigger diabetic ketoacidosis (DKA) in patients with new-onset T_1DM [46]. While the infection induce inflammation, cytokine activation which result in insulin resistance could lead to stress hyperglycemia, it is unclear what extent the SARS-CoV-2 destroy the islet cells, which leading to decreased insulin secretion and production [46]. The patients with mild respiratory symptoms found with hyperglycemia, acute damage to β-cells strengthening the hypothesis due to viral replication in the pancreas, the episodes of respiratory infection within a nine-month period associated with subsequent onset of autoimmunity in the islet cells within the following three months [46]. Higher incidence of T_2DM, due to pandemic situations such as prolonged close of school, indoor stay with social distancing, high-calorie food consumption, reduction in physical activities like: exercise, genetic factors of obesity, and health disparities in the population may contributed towards it [45].

NEUROLOGICAL COMPLICATIONS:

A small percentage of the patients were diagnosed with new-onset of cerebrovascular diseases (e.g. ischemic stroke, hemorrhagic stroke and cerebral arteritis), changes in brain function (e.g. encephalitis, myoclonic seizure and encephalopathies), involvement in peripheral nervous system (e.g. Inflammatory myopathy and Acute inflammatory demyelinating polyradiculo neuropathy), and neuropsychiatric changes (e.g. depression, personality change) occurs in the people infected with severe forms of the SARS-CoV-2 infection [48] associated with neurological

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manifestations [7]. Higher probability of psychiatric symptoms, neurological, physical illnesses and inflammatory complications in post-COVID patients brain along with increased suicidal behavior and thoughts [7]. Neuropsychiatric symptoms includes sleeping disorders, psychosis, anxiety (26%) and depression (23%) may affect patients have been reported even upto six months follow up after infection [8,13]. In female gender persistent psychological symptoms such as depression, anxiety were high risk factors. Neurological complications are predominant in male gender including Guillain-Barre syndrome (Acute inflammatory demyelinating polyradiculoneuropathy) in post-COVID patients [7]. The condition of post-traumatic stress disorder under the psychiatric category which occurs after the recovery of patient from the life threatening COVID-19, this condition provoked by trauma or other life stressing factors in which the rate of prevalence ranges from 5.8–20%. Development of behaviors such as obsession, compulsions, annoyance, aggressive status, difficulty in concentration, distrust in other people, decreased social activity and defect in cognitive function were clinical manifestations of the stress disorders [7].

POST-COVID AUTOIMMUNE SYNDROME

According to several reports, coronavirus disease 2019 (COVID-19), a pandemic respiratory infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), can cause autoimmune and autoinflammatory diseases in children, including paediatric inflammatory multisystemic syndrome (PIMS; which includes diseases like Kawasaki disease shock syndrome, toxic shock syndrome, myocarditis, and macrophage activation syndrome) [49].

Contagious diseases have long been thought to be a common cause of autoimmune and auto-inflammatory diseases, largely because to molecular denial. A variety of infectious agents have been linked to the development of Kawasaki illness, an acute vasculitis with unclear aetiology that primarily affects children [49].

According to recent research, autoimmune and auto-inflammatory disorders in SARS-CoV-2-infected people respond well to intravenous immunoglobulin (IVIG) treatment. The early detection of COVID-19 linked autoimmune and auto-inflammatory disorders, as well as the timely initiation of treatment, are critical for a successful recovery and the avoidance of end-organ damage and death. Nonetheless, resistance to IVIG treatment was more likely in KD-COVID-19 than in traditional Kawasaki disease, necessitating the use of peripheral steroids [49].

Loss of immunological tolerance that leads to autoimmunity in SARS-CoV-2 infection could be linked to a loss of tolerance to certain self antigens as a result of transitory immunosuppression that occurs during sickness as well as a type of immune reconstitution following recovery. There is a significant reduction in lymphocytes from several lineages in COVID-19, including T lymphocytes (TL) CD4 +, CD8 +, and regulatory TL [50].

Genetic predisposition, which includes human leukocyte antigens (HLA) polymorphisms as well as some non-HLA genes; the influence of gender, which would be more prevalent in the female gender; age, which is more popular in reproductive age due to the impact of estrogens; a family medical history of autoimmune diseases; and an individual history of autoimmune disorders (which makes an individual more susceptible to developing another autoimmune disease). When assessing individual susceptibility to developing autoimmunity, which is a disorder characterised by a loss of immunological self-tolerance, each of these predisposing factors is additive [50].

However, some patients developed autoimmune diseases such as systemic lupus erythematosus, autoimmune hemolytic anaemia, autoimmune thrombocytopenia, Guillain-Barre syndrome, vasculitis, or multiple sclerosis as a result of SARS-CoV-2 infection. Several symptoms linked with systemic autoimmune illnesses, such as fatigue, joint pain, dry syndrome, and myalgias, may emerge during infection and linger after it is controlled [50].

POST COVID LIVER COMPLICATIONS

Increased cytokine levels have been linked to lung injury and multi-organ failure in COVID-19 infection [51], and a more severe cytokine storm may play a role in COVID-19 pathogenesis [51].

Hepatocytes (liver cells) are a major source of proteins that are involved in both innate and adaptive immune responses. The liver cells maintain immunological homeostasis by inhibiting the passage of microbial and food antigens from the gut to the rest of the body, as well as synthesizing soluble chemicals required for efficient immune responses. As a result of reduced hepatic synthesis of proteins involved in innate immunity and pathogen-associated molecular pattern recognition, liver damage can affect

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immune surveillance. Immune dysregulation is a feature of both CLD and cirrhosis [51].

COVID-19 severity and clinical outcomes have been linked to liver biochemistry. COVID-19 appears to have little effect on a healthy liver, and its use is restricted to cases of severe infection and multi-organ failure [51].

Surprisingly, people with cirrhosis have a lower risk of contracting SARS-CoV-2 [51]. Because liver injury and CLD are linked to COVID-19 severity and mortality, determining indicators of liver disease, such as liver enzymes, fibrosis, and steatosis, might be prioritized as COVID-19 severity diagnostic factors [51].

The viral infection of liver cells may directly induce liver damage in patients with coronavirus infections. Approximately 2–10% of COVID-19 patients have diarrhea, and SARS-CoV-2 RNA has been identified in stool and blood tests. This evidence suggests that the liver may have been exposed to a virus [52].

COVID-19 induced liver damage could be caused by a variety of reasons. These include direct virus damage into the hepatocytes via ACE-2, an uncontrolled inflammatory/immune response resulting in fibrosis or liver failure, or a liver lesion produced by anti-COVID-19 medication therapy [52].

DILI is a common cause of abnormal liver tests and a leading cause of acute liver failure, which can result in death or the need for a liver transplant. In people with symptomatic liver injury, DILI is a common useful diagnostic tool. Patients with COVID-19 positivity who are hospitalized to the hospital may be subjected to pharmacological polytreatment, rendering clinical management even more difficult [52].

A chronic COVID-19 patient is a difficult patient who may require therapeutic polypharmacy, raising the risk for liver damage [52].

Despite the lack of data on COVID-19-related liver problems in patients, liver injury is linked to prolonged hospitalization [53].

POST COVID RENAL COMPLICATIONS

AKI prevalence in COVID-19 was estimated to be 0.5–28 percent in China and Italy in early publications. In China, COVID-19 was used to examine the renal histopathology of 26 corpses. Acute tubular necrosis (ATN) was seen in all of the specimens, and 18 of them had moderate to severe ATN. Cellular edema was only seen on occasion in the distal tubules and collecting ducts. There were interstitial infiltrates, but they were generic and minor [54].

According to a survey study, breathing distress is highly linked to the development of AKI in COVID-19. In comparison to 21.7 percent of non-ventilated patients, 89.7% of mechanically ventilated patients suffered AKI [54].

Since SARS-CoV-2 affects the upper respiratory tract first, it must enter the bloodstream before reaching the kidney. SARS-CoV-2 RNAaemia has been found in 10–15 percent of COVID-19 patients, with a higher prevalence in severely sick individuals. According to a meta-analysis evaluation, the rate of SARS-CoV-2 present in the urine is 3.7 percent. As a result, SARS CoV-2 is thought to directly infect kidney host cells via the circulation [54].

Further study found that patients with severe COVID-19 had lower CD4+ T cell counts in their peripheral blood. Elevated NKG2A concentrations in COVID-19 patients indicate functional depletion of NK and CD8+ T cells. Given the amount of tubular necrosis, lymphocyte infiltration in the renal interstitium may be limited due to the viruses' ability to lower lymphocyte counts and produce T cell malfunction [54].

ATN is perhaps the most prevalent lesion, according to kidney biopsy and autopsy findings, and could be induced by acute SARS-CoV-2 infection on TECs [54].

People who are infected with COVID-19 or SARS-CoV-2 who have pre-existing liver or renal comorbidities are more likely to have a poor clinical prognosis. These patients are at a higher risk of developing a serious infection, and their mortality rate is higher than the overall population [55].

Post Covid Pulmonary Complications

The British Society of Thoracic Imaging (BSTI) published codes (0–3) for reporting changes in CT scans after COVID in May 2020. This has aided in the reporting of CT scans as well as the identification of post-COVID fibrosis on pulmonary CT scans [56].

Patients who received intrusive ventilation and have chronic dyspnea (particularly men), as well as those who had a high-risk inpatient CXR, high inpatient CT scores, and high cytokine storm indicators (CRP >171.5 mg/L and WBC 12 109 /L), are at likelihood of developing post-COVID fibrosis [56].

Patients who were intubated with acute respiratory distress syndrome (ARDS) and

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 148-158 www.ijprajournal.com ISSN: 2456-4494

undergone invasive mechanical ventilation (IMV) therapy may develop chronic respiratory failure and irreversible lung fibrosis. The most well-known problems were post-ARDS, post-mechanical ventilation (barotrauma, fibrosis, pneumothorax, and so on), and post-intubation [57].

Following discharge, approximately 10%–20% of COVID-19 hospitalized patients required rehospitalization. Around a third of the 47,780 patients discharged from hospital in the UK following acute COVID-19 who have been followed up for an average of 140 days were readmitted (total 14,060), and more than one in ten (total 5875) died following discharge. Patients at significant risk of long-term problems were treated in intensive care units (ICUs) or care units, where they received long-term high-flow oxygen treatment (HFO), non-invasive mechanical ventilation (NIMV, CPAP, BIPAP), and were released on oxygen therapy [57].

This hypercoagulability is expected to persist in the post-acute period, and D-dimer levels, as a marker of persistent fibrin production and breakdown, can provide insight into this process. There are examples of thromboembolism diagnosed in the post-acute and chronic stages of infection that have been published [57].

It has been observed that after COVID-19, a reduction in pulmonary function test readings occurs, which can last up to 12 months and potentially become chronic, especially in situations of fibrosis or in relation to angiopathic alterations. Unfortunately, the development of fibrosis is one of the most significant post-acute consequences. Fibrosis has been found to be detectable from an early stage, regardless of the lung's pre-disease health or the severity of the disease [57].

Shortness of breath and cough are the most prevalent pulmonary symptoms in post-COVID syndrome. Dyspnea and impaired exercise capacity develop 2–4 months after discharge in 10%–40% of COVID-19 patients hospitalized and discharged from the intensive care unit, while shortness of breath occurs in 65 percent of patients hospitalized and discharged from the ICU [57].

Despite the fact that the specific mechanism of some viral infections, such as HIV, is unknown, the prevalence of pulmonary arterial hypertension (PAH) has grown [57].

Cough, which is one of the first indications of acute COVID-19 disease, is also common in post-COVID syndrome, along with other symptoms like chronic fatigue, headache, and generalized discomfort. In two studies, the prevalence of cough was observed to be between 7% and 10% [57].

In the course of the disease, viral pneumonia is the most prevalent and dangerous complication. It's unclear whether distributed COVID-19 pneumonia can have long-term consequences, such as persistent lung fibrosis. Numerous studies and reviews on post-COVID pulmonary fibrosis is rapidly growing. Post-COVID pulmonary fibrosis is sometimes known as PCILD (post-COVID interstitial lung disease) [57].

COVID-19 disease is much more than an acute infection; it is a complex entity with post-infection consequences and long-term impacts, particularly in the pulmonary system, emphasizing the importance of continuing to treat this disease even after patients have been released [57].

MANAGEMENT:

Management choices for post COVID-19 syndrome is insufficient due to unknown mechanism. But, there are some optimal management for patients with long COVID-19, some of countries have produced clinical guidelines to assist clinicians [58].

REHABILITATION

In rehabilitation, Patients are advised to start some light aerobic exercise based on their own capacity. Exercising shows increased gradual improvements in fatigue and dyspnea for four to six weeks. And also breathing exercises helps to strengthen respiratory muscle, mainly the diaphragm. Light aerobic and breathing exercises should be performed daily atleast for 5–10 min. Complementary behavioural modification and mental support given to patients who are all having Psychological and mental health issues such as PTSD (Post-traumatic stress disorder), anxiety and depression. It may also help to improve the patient's well-being and their mental health. There must be also considered about the risk of physical rehabilitation because it may not be suitable for patients of critical COVID-19 with severe pulmonary or cardiac damage. Hence, there is some exclusion criteria for postCOVID-19 rehabilitation like patients with high resting heart rate (>100 beats/min), low or high blood pressure (<90/60 or >140/90 mmHg), low blood oxygen saturation (<95%), or other conditions like exercise is a contraindication. Conditions like myalgic encephalomyelitis or chronic fatigue syndrome (ME/CFS) or postural orthostatic tachycardia syndrome (POTS) with post-exertional malaise are not suitable for physical rehabilitation [59].

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 148-158 www.ijprajournal.com ISSN: 2456-4494

CARDIOVASCULAR MANAGEMENT:

Patients are presenting with Post-COVID cardiovascular complication due to pre-existing cardiac conditions such as myocardial infarction, tachyarrhythmia, pulmonary embolism etc. However, physical exercise like low level stretching, strengthening, slow walking for one week and increasing rest period will help with mild COVID-19 post recovery [4].

Continuous clinical and imaging study like ECG and ECHO for 4-12 weeks may be done in those with cardiac complication based on individual cardiac condition. Avoidance from sports or aerobic activity for 3–6 months until resolving of myocardial inflammation by cardiac MRI or troponin regularization are some of the suggestions for sportspersons with cardiovascular complications caused by COVID-19 [60].

Patients those who are presenting with cardiovascular disease should be under treatment of statins, antiplatelet medicines, and medications which control their risk factors, such as hypertension and diabetes. Angiotensin Converting Enzyme Inhibitors (ACE inhibitors)/ Angiotensin Receptor Blockers (ARB)/ Angiotensin Receptor-Neprilysin Inhibitor (ARNi), Beta blockers, diuretics and mineralocorticoid receptor blockers, these are the medications given in the guideline for the therapy of cardiac dysfunction [4].

Patients with inappropriate sinus tachycardia and postural orthostatic tachycardia syndrome may get improvement from low-dose beta blockers by managing their heart rates and reduce adrenergic activity. Anti-arrhythmic drugs (for example, amiodarone) should be used with caution in patients with fibrotic pulmonary changes after COVID-19 [60].

In patients with atrial fibrillation, anticoagulation therapy is necessary to prevent stroke based on the CHA2DS2Vasc score. And also anticoagulation prophylaxis is needed for patients those with confirmed DVT/pulmonary embolism, preferably with novel oral anticoagulants or warfarin, to keep the INR (international normalised ratio) within the value of 2-3.

Patients with congestive heart failure often benefit from non-pharmacological treatment, such as self-management education and limiting dietary sodium to 2 grams per day. They should report or reach cardiologist through telemedicine to prevent the worsening of cardiac symptoms and maintain the regular follow-up. Furthermore, people are advised to get vaccinated for COVID-19 and pneumococcal disease [4].

PULMONARY MANAGEMENT:

Professional organizations have recognized COVID-19 survivor's post-hospital discharge care as a leading research priority and guidance for their management. Home pulse oximetry using FDA-approved devices has been recommended as a useful equipment to monitor patients with persistent symptoms, but there is currently no supporting evidence. Patients presenting with prolonged dyspnea, recommend serial pulmonary function tests (PFTs) and 6-min walk tests (6MWT), along with high-resolution computed tomography (chest) at 6 and 12 months. According to a British Thoracic Society guidance document, assessing of COVID-19 patients in the first three months after hospital discharge based on the severity of acute COVID-19 is required. Clinical assessment and chest X-ray in all patients at 12 weeks are adviced for both severe and mild-to-moderate COVID-19 groups, A clinical judgement should be used in interpreting ECHO, 6MWTs, sputum samples, and PFTs. Patients should be checked with high-resolution computed tomography of the chest, pulmonary angiogram or ECHO or follow-upbased on this 12-week assessment. Patients those with severe acute COVID-19, severe pneumonia, required to get admitted in ICU, elder patients or those patients having multiple comorbidities are suggested a prior clinical assessment for respiratory, psychological and also rehabilitation for 4–6 weeks after discharge. In some cases, lung transplantation has previously been done for fibroproliferative lung disease after ARDS due to severe influenza A (H1N1) infection and COVID-19 [60].

RENAL MANAGEMENT:

The renal function recovery extent is unknown and also dialysis-dependent AKI (Acute kidney injury) is uncommon discharge. Post-acute COVID-19 patients who have chronically reduced renal function may acquire benefit, if they have regular follow-up with a nephrologist in AKI survivor centers, which has previously been provided better results [60].

ENDOCRINE MANAGEMENT:

For newly diagnosed diabetes mellitus patients who do not have type 2 diabetes risk factors, serologic testing for type 1 diabetes associated auto antibodies and repeat post-prandial C-peptide measurements must be acquired at follow-up, whereas it is appropriate to treat patients with such risk factors as if they had ketosis-prone

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 2 Mar-Apr 2022, pp: 148-158 www.ijprajournal.com ISSN: 2456-4494

type 2 diabetes. Corticosteroids can be used to treat incident hyperthyroidism induced by SARS-CoV-2-related destructive thyroiditis, but first make sure patient don't have Grave's disease [60].

NEUROPSYCHIATRIC MANAGEMENT:

Patients with neurologic complications, a standard therapy should be used with imaging evaluation and consultation to a physician. For cognitive impairment, a neuropsychological evaluation should be considered in the post-acute illness setting. Patients with sleep disturbances, PTSD, dysautonomia, anxiety, depression and fatigue should be identified using standard diagnostic method [60].

For fatigue, patient should get plenty of rest, enough sleep and should be stay hydrated. Patient should not take OTC analgesics unless there is absolutely necessary. For some patients, graded exercise therapy (GET) is the management protocol for chronic fatigue syndrome. Aerobic exercises, balance and breathing training can also help. Good sleep hygiene should be maintained those who are facing difficulty in sleeping. Avoid drinking coffee, alcohol and increasing use of phones and computers before bedtime, this can help improve sleep latency. Self medication with benzodiazepine should be avoided. It is important to seek proper medical advice than self-medication [4].

II. CONCLUSION:

In this review, a description about the Post COVID-19 Syndromes, its pathogenesis and management strategies have been provided. This long term consequence may cause physical, mental as well as financial stress upon the person. Hence a better understanding about these symptoms is needed to develop certain techniques to prevent as well as manage these Post COVID sequelae and to support the individual's experiencing these effects. Knowledge regarding all details about the COVID-19 together with these Post COVID Syndrome will let us to counter all the global health challenges, thus leading the way to a better public health.

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Volume 7, Issue 2 Mar-Apr 2022, pp: 148-158 www.ijprajournal.com ISSN: 2456-4494

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