

## Research Article

### Post-Covid-19 Long Haul Syndrome

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#### Abstract:

**Background:** People with post covid19 conditions may experience a wide range of symptoms lasting from 3 weeks to 6 months. Covid-19 is a rapidly onset illness in humans that results from the coronavirus. Originating in 2019, it was first discovered in China and later became a pandemic. Covid19 affects billions of people worldwide and most of the recovered patients show post covid19 effects.

**Objectives:** The goal of this study was to provide an estimate of the effects of Post Covid-19, also called Long Haul syndrome based on the published literature on the subject of chronic clinical presentations in long haulers.

**Methodology:** The articles were retrieved by searching relevant databases. Articles containing original work, both qualitative and quantitative, were searched for relevant content.

**Results:** Of the total 2920 articles from initial research, 20 were finalized to be researched for this comprehensive assessment. All of the research was based on hospitalized and non-hospitalized covid19 patients with proper follow-up history for more than a month. These study participants have multi-faceted effects, more than 35 types of symptoms, and multi-organ involvement in various diseases.

**Conclusion:** The incidence of multifaceted effects of post covid19 has continued to impact the victims for weeks or months. These include multi-organ diseases and need multidisciplinary care and proper follow-up treatment.

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## INTRODUCTION:

Long haul syndrome is a set of conditions that persist for more than 4 weeks after a confirmed diagnosis of Covid-19 (1). As covid-19 (named SARS-CoV-19 due to its resemblance with SARS-CoV (~80%) shows high mortality rates in 2002-03 first and then a worldwide outbreak in December 2019 onwards(2). Just like Covid-19 diverse symptomatology, the post-Covid19 syndrome also exhibits a diverse clinical spectrum including respiratory (fatigue, shortness of breath, sore throat), cardiovascular (chest pain, palpitations, tachycardia), physical (arthritis, myalgia, weakness), neurocognitive (sleep disorders, anxiety, mood swings, cognitive impairment) and multi-organ diseases (3).

There are certain criteria defining long haul syndrome or post-covid19 syndrome. It may be defined as “No recovery after symptoms appear for weeks to months regardless of confirmatory diagnostic testing.” (4)

Another definition by National Institute for Health and Care Excellence (NICE) says” Long haul is a generalized term for recovered people still showing signs and symptoms unexpectedly” (5) The exact reasons why it happens are not known. But certain factors ignite these symptoms. The incidence of post covid19 syndrome is 10 to 35% among covid19 victims and high up to 85% among hospitalized patients. (6)

There is an estimate that SARS-CoV-19 impacted billions of people worldwide across 200 countries since a large population is at risk of developing long-

haul covid19. Hence, it is a globally addressed issue of public health. Victims suffer functional impairment, low-quality life decrement, and encumbered socioeconomic status as well, leading to despair and collapse.

Despite emerging issues on a massive level, there are no proper defining grounds for labeling confirmed diagnosis, nor authorized treatment of it yet (7). However, potential interventions alongside research trials are underway targeting the underlying causes of emerging complications including, yet not limited to, affected organ pathology and neurological hormonal dysregulation (8). Due to globally acknowledged health issues, it gives a spur to evaluate all its diversifying effects and their impact on victims physically, mentally as well as socioeconomically so that these patients can be managed better (9). Evidence was keenly analyzed but no specific review related to this topic has been found so we systematically reviewed the effects of Post Covid19 Long haul syndrome.

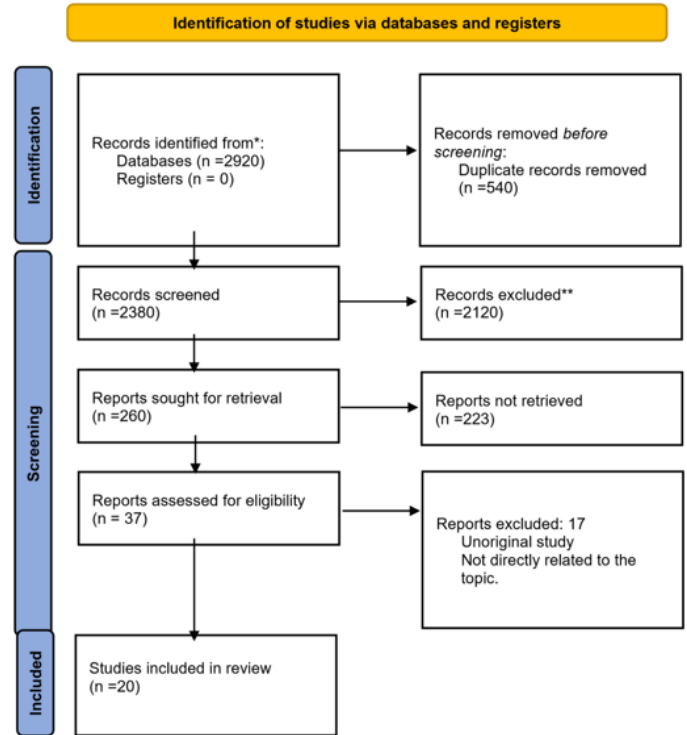
This review will be a nutshell of guiding information covering maximum dimensions from the basis of disease to its multifaceted effects. It will be a milestone in understanding the influence of this disease on the mental and physical agony of long haulers <sup>(10)</sup>. This systematic review covers the inquisitive plunge of the extent of post-covid19 effects and their further consequences.

## OBJECTIVES:

To determine the effects of the long-haul syndrome.

## METHODS AND METHOD:

A comprehensive evaluation was conducted in line with the Recommended Reporting Items for Systematic. Review and Meta-analysis Guidelines (PRISMA). Clinical symptoms have been seen in Covid19 patients for weeks to months following recovery. A thorough literature search will be carried out from March 22 to October 22. A comprehensive search of databases such as PubMed, Medline, and PakMediNet was carried out. First, all articles on long-distance syndrome will be collected. There will be no limitations on the publications retrieved based on their publication date, research method, language spoken by the authors, or country of origin. After that, all available data will be changed depending on inclusion-exclusion criteria. Citations found in search results will be transferred to Endnote X20.0 for reference management. Inclusion Criteria: The articles will be in English or have a translation available. According to research on covid-19 victims, symptoms might continue for weeks to months after a negative covid19 screening test. Only one-of-a-kind research articles, such as randomized controlled trials and cohort studies, will be considered. Review articles, editorials, case reports, and case series were all barred from consideration. Apart from English, the material is written in a variety of languages. Titles that did not match ours, duplicate articles and incomplete articles were also removed.



## Data extraction:

Extractions from the research included the following pieces of information i.e the study design, sample size, study participants' age, and symptomology of long haul patients.

## RESULTS:

A total of 2920 articles were obtained for this review. After removing duplicates, 2380 articles undergo title and full-text availability screening. 37 publications were evaluated for eligibility, and 17 studies were excluded because they contained unoriginal research and were not directly related to the topic. According to inclusion-exclusion criteria, the screening process ended up with a total of 20 articles excluding acute covid19 symptomatology-based articles. Hence, 20 articles were studied for final analysis and review. The general features of all

20 studies are shown in Table 1. A sum of 6 studies was from Bangladesh, Victoria, Mexico, China, Nigeria, and the Mediterranean region. Others include the US, the UK, and different populations.

All the studies were based on hospitalized and non-hospitalized covid19 patients with proper follow-up history for more than a month. These study participants have multi-faceted effects, more than 35 types of symptoms, and multi-organ involvement in various diseases.

COVID-19 survivors reported symptoms of post-viral disease, the most common of which were fatigue (17 studies). Fatigue, dyspnea, memory loss, concentration problems, and sleep issues were the most commonly reported chronic complaints. The most typical symptoms included sleep problems and fatigue or muscle weakness. Patients stated having anxiety or depression. A small percentage of the participants reported experiencing serious symptoms; including infarction, kidney failure, myocarditis, and respiratory failure. The severity of the condition was associated with the existence of other comorbidities.

**Table 1:**

Article Name	Study Participants	Symptomatology
<p><i>„Long-COVID“: a cross-sectional study of persisting symptoms, biomarker, and imaging Abnormalities following hospitalization for COVID-19 <sup>(11)</sup></i></p>	<p>Discharged COVID-19 patients. This report summarizes the clinical assessment of 384 patients. reviewed a median of 54 days following hospital discharge with COVID-19.</p>	<p>53% reported persistent breathlessness, 34% persistent cough, and 69% persistent fatigue. 15% were depressed. Of people who attended for repeat imaging and blood tests because investigations on discharge had been abnormal, 9% had a deteriorating chest radiograph appearances at follow-up, and 30.1% and 9.5% had persistently elevated d-dimer and CRP concentration respectively. COVID-19 is associated with an increased risk of thrombosis<sup>5</sup> but the significance of the persistent elevation in d-dimer is unclear. Deteriorating chest radiograph appearances raise the possibility of developing lung fibrosis.</p>
<p><i>Persistent Poor Health after COVID-19 Is Not Associated with Respiratory Complications or Initial Disease Severity <sup>(12)</sup></i></p>	<p>Participants who had a positive SARS-CoV-2 polymerase chain reaction result at the institution in the 3 months from March to May 2020 was recruited from the post-COVID-19 outpatient clinics. This included those managed as inpatients and staff members in whom COVID-19 was diagnosed at the center but who self-managed at home.</p> <p>The median age of the outpatient cohort was 48 years (range, 35– 59 yr.)</p>	<p>Little evidence was found for post-infectious pulmonary fibrosis on chest X-rays or for hypoxia during 6MWTs. However, 62% of patients did not feel back to full health, and this was associated with an increased perception of exertion. A total of 47% of the cohort met the diagnostic criteria for fatigue, independent of the initial severity of the infection. This the study highlights the persistence of ill health after SARS-CoV-2 infection that presents a serious a burden to quality of life. The lack of association with infection severity highlights that this may be an issue for a large number of patients, and this should be used to inform management strategies for convalescent patients.</p>

<p><i>Persistent Symptoms in Patients After Acute COVID-19</i> <sup>(13)</sup></p>	<p>Discharged COVID-19 patients who met World Health Organization criteria for discontinuation of quarantine (no fever for 3 consecutive days, improvement in other symptoms, and 2 negatives test results for severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] 24 hours apart).</p> <p>143 patients were included. The mean age was 56.5 (SD, 14.6) years (range, 19-84 years), and 53 (37%) were women</p>	<p>87.4% reported the persistence of at least 1 symptom, particularly fatigue, and dyspnea. Limitations of the study include the lack of information on symptom history before acute COVID-19 illness and the lack of details on symptom severity.</p>
<p><i>6-month consequences of COVID-19 in patients discharged from hospital: a cohort study</i> <sup>(14)</sup></p>	<p>Discharged COVID-19 patients. Patients had a median age of 57.0 (IQR 47.0–65.0) years 897 (52%) were men and 836 (48%) were women.</p>	<p>Fatigue or muscle weakness 1038/1655 (63%), Sleep difficulties 437/1655 (26%), Hair loss 359/1655 (22%), Smell disorder 176/1655 (11%), Palpitations 154/1655 (9%), Joint pain 154/1655 (9%), Decreased appetite 138/1655 (8%), Taste disorder 120/1655 (7%), Dizziness 101/1655 (6%), Diarrhea or vomiting 80/1655 (5%), Chest pain 75/1655 (5%), Sore throat or difficulty to swallow 69/1655 (4%), Skin rash 47/1655 (3%), Myalgia 39/1655 (2%), Headache 33/1655 (2%), Low-grade fever 2/1655 (&lt;1%).</p>

<p><i>Post-COVID-19 syndrome among symptomatic COVID-19 patients: A prospective cohort study in a tertiary care center of Bangladesh <sup>(15)</sup></i></p>	<p>Discharged COVID-19 patients aged &gt; 18 years, total 355 in number</p>	<p>Post-viral fatigue was the most prevalent feature (117 [33%]). Other features included persistent cough (8.5%), post-exertional dyspnea (7%), headache (3.4%), vertigo (2.3%), and sleep-related disorders (5.9%)</p> <p>Symptoms with less incidence include Rash (0.6%), Pneumonia (0.6%), Restless-leg syndrome (0.6%), Bradycardia (0.6%), Palpitation (1.4%), Anosmia (2%), Tinnitus (0.3%), Nasal blockade (0.3%), Chest pain (0.8%), Adjustment disorder (1.4%), Arthralgia (1.4%), New-onset diabetes (0.3%), New-onset hypertension (0.6%), Non-ulcer Dyspepsia (1.4%), Excessive sweating (1.4%), Myalgia (0.6%), Burning feet (0.6%), Disturbance of memory (0.6%), Precipitation of gout (0.3%)</p> <p>Thus, this study revealed that the patients did not completely recover, even after apparent clinical recovery. COVID-19 also caused long-term sequelae and distress in nearly half of the patients.</p>
<p><i>Post-COVID-19 Fatigue and Anhedonia: A Cross-sectional Study and Their Correlation to Post-recovery Period <sup>(16)</sup></i></p>	<p>200 patients of COVID-19 after 2 consecutive negative PCR tests who attended for pulmonology clinic for follow-up and psychiatric department for assessment</p>	<p>(SD ± 20.72), mean total frequency score of 229.89 (SD ± 18.80), mean total change score of 234.87(SD ± 16.58), and mean total anhedonia score and 688.41(SD ± 52.9 224.02 (SD ± 20.72) fatigue which on the fatigue assessment scale showed a mean Fatigue score of 40.81(SD ± 5.75).</p>

<p><i>(Assessment and Characterization of Post-COVID-19 Manifestations<sup>(17)</sup>)</i></p>	<p>The study involved 287 recovered COVID-19 subjects, 103 of them were males and 184 females. The age of involved subjects is expressed as Mean <math>\pm</math> SD was <math>32.3 \pm 8.5</math> and ages ranged from 20 to 60 years old. Mean <math>\pm</math> SD weight, height, and body mass index (BMI) were <math>77 \pm 16.4</math>, <math>162.9 \pm 15.3</math> and <math>28.5 \pm 5.2</math>, respectively. Percent of smokers among male subjects was 27.2%, while all females were non-smokers</p>	<p>Most subjects suffered from fatigue (72.8%), anxiety (38%), joints pain (31.4%), continuous headache (28.9%), chest pain (28.9%), dementia (28.6%), depression (28.6%), and dyspnea (28.2%). A few percent of recovered subjects have newly diagnosed with diabetes (2.4%) Other mild symptoms like joint and muscle pain were also reported by many subjects and it could be classified as mild manifestations. It was noted that many manifestations are related to the central nervous system such as continuous headaches, migraine, depression, anxiety, and obsessive-compulsive disorder. Few percent of subjects have suffered from critical complications such as stroke, myocarditis, renal failure and pulmonary fibrosis which could be reversible and required extra investigation. Regarding obesity as a factor affecting disease severity or post disease symptoms, it was shown that the majority of subjects were overweight or obese but there is no significant effect on the severity grade or type of post-COVID-19 symptoms. Obsessive-compulsive disorder (OCD) was diagnosed for a few percent of subjects and it was mainly reported by female subjects.</p>
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<p><i>Smell and taste loss in COVID-19 patients: assessment outcomes in a Victorian population <sup>(18)</sup></i></p>	<p>A total of 150 patients were contacted with 102 (68%) agreeing to participate in the survey. Among the 102 study participants, there were 40% male and 60% female patients. The mean age of the study population was 45 years (range 17 – 87 years).</p>	<p>No patient reported anosmia or ageusia preceding the illness. Comorbidities included hypertension in 23% of patients, respiratory disease (e.g. asthma, COPD) in 12%, chronic rhinosinusitis in 9%, cardiac disease in 7% (e.g. coronary artery disease, congestive heart failure, arrhythmia, peripheral vascular disease, hypercholesteremia) and diabetes type 1 or 2 in 6%. Other noted comorbidities included obstructive sleep apnea, anxiety/depression, cancer, rheumatoid arthritis and inflammatory bowel disease. At the time of data acquisition, all patients had clinically recovered from an acute COVID-19 infection. Our dataset was collected with a mean of 83 days (range 5–132, SD 19.21) following initial PCR diagnosis.</p> <p>We noted high rates of smell (65%) and taste disturbance (63%) in our cohort. Further, 74% of participants reported either smell or taste disturbance with 36% reported both smell and taste disturbances. 38% and 18% of participants reported smell and taste disturbance respectively, in the absence of any nasal obstruction during their illness.</p>
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<p><i>Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19</i> (19)</p>	<p>Of the 279 hospitalized patients between March 15th and April 14th, 2020 in our COVID-19 unit, 48 were admitted to ICU, and 57 patients died within the three months following admission (43 in the ward group and 14 in the ICU group) After having excluded demented or bedridden (n = 18), unreachable (n = 69), non-French speaking patients (n = 12), and those declining participation (n = 2), 120 patients answered the phone questionnaire after a mean (<math>\pm</math>SD) of 110.9 (<math>\pm</math>11.1) days following admission: 96 in the ward group and 24 in the ICU group for artificial ventilation.</p>	<p>After a mean of 110.9 days, the most frequently reported persistent symptoms were fatigue (55%), dyspnea (42%), loss of memory (34%), concentration and sleep disorders (28% and 30.8%, respectively). Loss of hair was reported by 24 (20%) patients, including 20 women and 4 men. Comparisons between ward- and ICU patients led to no statistically significant differences regarding those symptoms. Thirty-five (29%) patients had anmMRC grade <math>\geq</math>2 (“Walks slower than people of the same age because of dyspnea or has to stop for breath when walking at own pace”).</p>
<p><i>Post-acute COVID-19 syndrome. Incidence and risk factors: A Mediterranean cohort study</i> (20)</p>	<p>Two hundred seventy-seven patients recovered from mild (34.3%) or severe (65.7%) forms of SARSCoV2 infection</p>	<p>Post-COVID syndrome includes pneumonia, fatigue, anosmia, myalgia, and pneumatological symptoms including cough, neurological symptoms including headache and others such as diarrhea, calin features, visual loss, fever, and laboratory features</p>
<p><i>Sixty-Day Outcomes Among Patients Hospitalized With COVID-19</i> (21)</p>	<p>Patients hospitalized with COVID-19 (discharged between 16 March and 1 July 2020) at 38 hospitals participating in the MI-COVID19 initiative.</p>	<p>Mortality and patients who survived showed the symptoms of morbidity including cardiopulmonary symptoms, the inability to return to normal activities, physical and emotional symptoms, and financial loss,</p>

<p><i>Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation</i> <sup>(22)</sup></p>	<p>All patients discharged from LTHT following a positive COVID-19 test</p>	<p>Fatigue, Breathlessness, Neuropsychological Symptoms, Speech and Swallowing problems, weight Loss/gain, bowel/bladder Incontinence, Perceived Health, quality of life, change since COVID-19 illness</p>
<p><i>Attributes and predictors of long COVID</i> <sup>(23)</sup></p>	<p>Mobile health app Users with PCR positive COVID-19 patients/ Negative matched Controls</p>	<p>Symptoms of, abdominal pain, hoarse voice, diarrhea, chest pain, skipped meals, unusual muscle pains, fever, sore throat, persistent cough, loss of smell, shortness of breath, headache, and fatigue.</p>
<p><i>Follow-up of adults with noncritical COVID-19 two months after symptom onset</i> <sup>(24)</sup></p>	<p>The study was based on clinical follow-up of 150 patients with non-critical COVID-19 confirmed with real-time PCR150</p>	<p>Weight loss (&gt;5%), grade 2-4 dyspnea, persistent chest pain, palpitation, anosmia/ageusia, headache, cutaneous signs (free description), arthralgia, myalgia, persisting digestive disorders (i.e. diarrhea, vomiting, pain), fever (temperature &gt;38°C) or sick leave.</p>
<p><i>Persistence of COVID-19 Symptoms after Recovery in the Mexican Population</i> <sup>(25)</sup></p>	<p>This study was conducted in the state of Zacatecas Mexico, which has a population of approximately 1.5 million people, with a population of 5432 Covid-19 recoveries at the time of recruitment. Data were collected from 25 July to 20 September 2020</p>	<p>COVID syndrome in which symptoms persist with different frequencies after recovering from their initial illness. Several studies have analyzed different symptoms or conditions that are presented in recovered patients, exhibiting multi-organ manifestations like into the the gastrointestinal tract, kidney, heart, brain, eyes, and lungs, respectively, which demonstrate evidence of this collateral damages within recovered patients</p>

<p><i>Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-center longitudinal study</i> <sup>(26)</sup></p>	<p>Covid 19 patients hospitalized and discharged from Renmin Hospital of Wuhan University, Wuhan China before 1 march 2020</p>	<p>General symptoms (49.6%) including physical fatigue sweating myalgia arthralgia chills limb edema dizziness, Respiratory symptoms (39%) including post-activity polypnea nonmotor polypnea chest distressed chest pain cough sputum throat pain, Cardiovascular symptoms (13%) including resting heart rate increase discontinuous flushing of newly diagnosed hypertension, psychological symptoms (22.7%) including somnipathy depression anxiety dysphoria feelings of inferiority, and alopecia.</p>
<p><i>Post-acute COVID-19 syndrome and its prolonged effects: An updated systematic review</i> <sup>(27)</sup></p>		<p>The most common manifestations were fatigue (54.11%), dyspnea (24.38%), alopecia (23.21%), hyperhidrosis (23.6%), insomnia (25.98%), anxiety (17.29%), and arthralgia (16.35%). Thirteen studies reported fatigue and anosmia, 15 dyspnea, 12 chest pain, and 11 non-productive coughs and 5 studies showed more than one symptom. Apart from constitutional symptoms of COVID-19, personality and sleep disorders, bladder and bowel incontinence, new-onset hypertension, and diabetes</p>

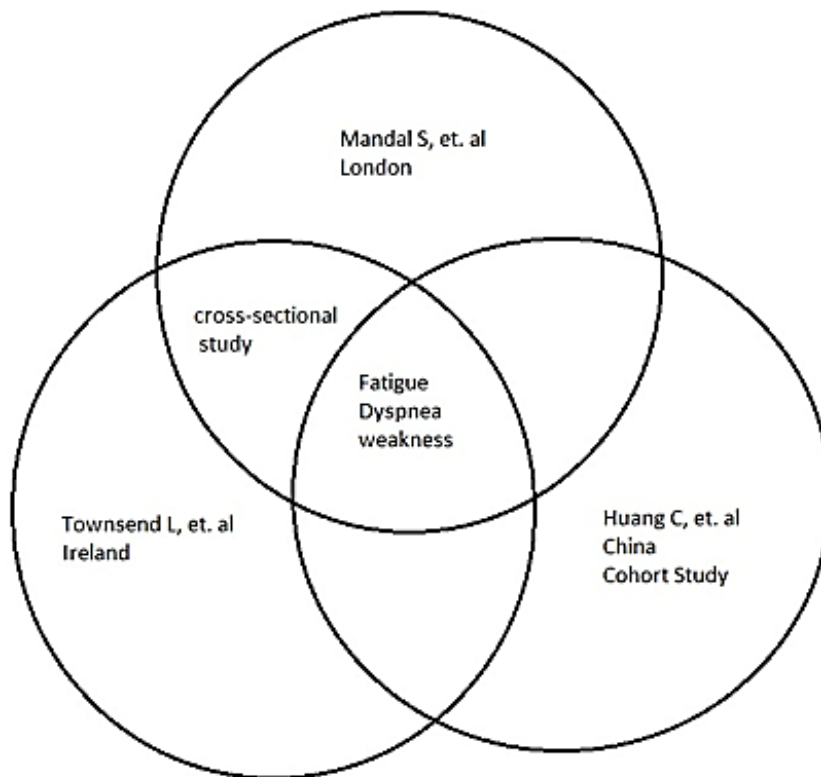
<p><i>6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: a retrospective cohort study using electronic health records</i> <sup>(28)</sup></p>	<p>Study participants were COVID-19 patients. The COVID-19 cohort was divided into subgroups of patients who were not hospitalized (190 077 patients), those who were hospitalized (46 302 patients) ITU admission (8945 patients) and those who received a diagnosis of encephalopathy (6229patients).</p>	<p>Intracranial hemorrhage ischemic stroke, Parkinson’s disease, and parkinsonism, Guillain-Barré syndrome, nerve root, and plexus disorders , myoneural junction, and muscle disease (neuromuscular disorders, encephalitis, dementia , psychotic, mood, and anxiety disorders, insomnia</p>
<p><i>(Patient Outcomes after Hospitalization with COVID-19 and Implications for Follow-up: Results from a Prospective UK Cohort</i> <sup>(29)</sup></p>	<p>Patients were recruited from the Diagnostic and Severity markers of COVID-19 to Enable Rapid triage (DISCOVER) the study, a single-center a prospective study (Bristol, UK) recruiting consecutive patients (≥18 years of age) admitted with COVID-19). The inclusion criteria were a positive PCR result for SARSCoV-2 or a clinic radiological diagnosis of COVID-19 disease.</p>	<p>Although most symptoms were improving, 81 (74%) patients reported at least one ongoing symptom: 39% breathlessness, 39% fatigue and 24% insomnia Sixteen (59%) patients in the mild The COVID-19 group reported ongoing symptoms compared with 49 (75%) and 16 (89%) in the moderate and severe groups, respectively.</p>
<p><i>„Long COVID“: persistent COVID-19 symptoms in survivors managed in Lagos State, Nigeria</i> <sup>(30)</sup></p>	<p>A total number of 274 COVID-19 survivors were assessed in this study. The mean age of respondents was 41.8 years (SD ± 11.8) with a range of 10 to 83 years. The majority of respondents were male (66.1%) and aged between 36 and 49 years (38.3%). The median number of days after discharge with COVID-19-like symptoms was 15 days (IQR 14– 17 days) (Table 1). Among the study participants, a majority (50.7%) had a mild form of the disease at the initial time of COVID-19 diagnosis.</p>	<p>Easy fatigability, headaches, chest pain, and insomnia, were the most common symptoms. System Symptoms cough dyspnea chest pain, sore throat, dysgeusia, excessive sweat, weight loss, loss of appetite, palpitations, abdominal discomfort, vomiting, and nausea.</p>

**Table 2:**

Authors and References	Participants	No. of Days of Post-covid19 symptoms	Risk factors and Alarming Effects reported	Total no. of patients	Type of Study
Mandal et al. <sup>(11)</sup>	Discharged hospitalized covid19 patients	Average 58 days	Increased risk of thrombosis and lung fibrosis	384	Cross-sectional
Liam et al. <sup>(12)</sup>	Self-managed home covid19 survivors	3 months	Breathlessness upon little exertion (6-minute walk test)	487	Cross-sectional
Carfi et al. <sup>(13)</sup>	Discharged hospitalized patients	60 days	Interstitial pneumonia	143	Case series
Huang et al. <sup>(14)</sup>	Symptomatic covid19 patients in Bangladesh	6 months	Impaired pulmonary diffusion capacities and sleep difficulties	1733	Cohort study
Mahmud et al. <sup>(15)</sup>	Recovered covid19 patients	1 month	Post-viral-fatigue syndrome and myalgic encephalomyelitis	355	Prospective cohort study
Samir et al. <sup>(16)</sup>	Psychiatric covid19 patients	–	Fatigue and anhedonia	200	Cross-sectional study
Marwa et al. <sup>(17)</sup>	Recovered covid19 patients		Obsessive-compulsive disorder	287	-----
Horvath et al. <sup>(18)</sup>	Victorian population with smell and taste loss	83 days	Comorbidities like obstructive sleep, IBD, HTN	150	Retrospective descriptive study
Garrigues et al. <sup>(19)</sup>	Hospitalized post-discharge patients	110 days	Loss of hair	279	-----
Moreno-Perez et al. <sup>(20)</sup>	Mediterranean post covid19 patients	10-14 weeks	Lymphopenia, anosmia Dysgeusia	277	Mediterranean cohort study
Vineet et al. <sup>(21)</sup>	60 days Postdischarged hospitalized Follow-up patients	60 days	Cardio-pulmonary and emotional symptoms	488	Descriptive clinical follow-up
Halpin et al. <sup>(22)</sup>	Discharged covid19 patients	29-71 days	Breathlessness and psychological; distress	100	Cross-sectional evaluation
Sudre et al. <sup>(23)</sup>	Post covid19 patients	More than 28 days	Anosmia and dyspnea	558	Prospective cohort study
Carvalho Schneider et al. <sup>(24)</sup>	Non-critical covid 19 patients	2 months	Weight loss, palpitations, anosmia	150	Descriptive clinical follow-up

Galvan-Tejada et al. <sup>(25)</sup>	Recovered covid19 patients in the Mexican population	31-60 days	Multi-organ manifestations like GIT, kidney, and heart collateral damage	219	Case-control study
Xiong et al. <sup>(26)</sup>	Covid19 survivors in Wuhan	More than 3 months	Increased resting heart rate, post activity polypnoea	538	Cross-sectional study
Almas et al. <sup>(27)</sup>	----	More than 60 days	Immune system dysregulation		Systematic review
Taquet et al. <sup>(28)</sup>	Survivors of covid19	6 months	Neurological and Psychiatric symptoms like shock hemorrhage	236,379	Retrospective Cohort study
David et al. <sup>(29)</sup>	Hospitalized survivors of covid19 in the UK	80-97 Days	Breathlessness and insomnia	110	Prospective cohort
Osikomaiya et al. <sup>(30)</sup>	Covid19 survivors in Nigeria		Increased coagulability and fatigue	274	Case-control study

Venn Diagram:



## **DISCUSSION:**

Twenty papers met our inclusion criteria and were included in this review. Throughout the research, more than 35 post-covid19 symptoms were recognized. Most of the signs and symptoms mirrored those of the first stages of acute covid-19. There is, however, still room for the identification of additional impacts in long-haul vehicles at a later date.

In the following discussion, we will focus on the various effects of the long-haul syndrome in detail. TABLE 1 describes the study participants and symptomatology in detail as reviewed in 20 articles. Overall, the most important and alarming effects seen among long haulers are due to endothelial damage and micro-vascular injury during their acute attack of the coronavirus. This direct viral toxicity later causes immune system dis-regulation, hyper-inflammatory, and hypercoagulability states in long haulers.

However, potential mechanisms behind post covid19 effects are multi-factorial including sequelae of recovery from critical illness and other pathophysiological changes caused by the coronavirus (31).

This systematic review demonstrated that post covid19 syndrome affected most of the systems of the human body. Hence, this discussion elaborates on the maximum number of diseases of an organ system involved.

Overall, the most common symptom among long haulers was a feeling of tiredness, body ache, and fatigue. (11—15, 17, 19, 20, 22, 27, 29, 30). Among hospitalized-discharged patients, more than 85% suffer from fatigue and tiredness (13).

Neuropsychiatric symptoms were also often reported symptoms, such as headache, migraine, sleeplessness, agitation, anxiousness, depression, and dementia. (11, 15, 17, 18, 19, 22, 24, 27, 28, 29). In post-covid-19, the cause and pathogenesis of neuropsychiatric disorders were unknown. Alopecia is also reported in three studies. 14, 18, 26. Although it is self-limiting, it can lead to serious emotional stress.

Among the most prominent pulmonary symptoms, dyspnea and cough commonly prevail. Long-term effects of covid19 seem to be caused by decreased diffusion capacity owing to a reduction of lung volume. (11, 12, 17). Patients with critical covid19 have a much higher risk of pulmonary vascular micro and macro thrombosis than those with ARDS caused by other viruses because of the severity of the endothelial destruction and the extensive nature of the microangiopathy.

In addition to these, other constitutional symptoms include a decrease in appetite, the onset of diabetes or hypertension (27), eyesight changes, or dry eyes. (22, 24).

Among cardiovascular diseases, by comparing pre-pandemic and post-pandemic times, it has been shown that the incidence of takotsubo cardiomyopathy is higher during this pandemic. Decreased expression of the Renin-Angiotensin-Aldosterone pathway, cytokine-derived storm degradation of myocardial integrity, and a variety of arrhythmias all seem to play a role in the development of cardiovascular sequelae in long haulers.

According to a cross-sectional study, among discharged long haulers, post covid19 is associated



with an increased risk of thrombosis. 11 Palpitations, flushing, new onset hypertension, peripheral vascular disease, and other mild symptoms were also noticed (14, 15, 18, 26). However, critical conditions like stroke and myocarditis were also reported.

Metabolic disorders seen in long haulers include new-onset diabetes, excessive sweating, hypercholesterolemia, weight gain/loss, loss of appetite, abdominal discomfort, and nausea. (14, 15, 18, 26, 30).

Musculocutaneous symptoms include easy fatigability, recurrent muscle cramping, myalgia, arthralgia, alopecia, skin rash, and restless leg syndrome (14)

Other post covid19 effects reported include dry eyes, ear problems, renal failure, and many more complications causing serious burdens to quality of life.

There should be management strategies for better control of these deteriorating health effects.

TABLE 2 categorizes the 20 studies based on the author's name, the total number of participants, no. of days of reporting, and the type of study. Hence, summarizes the alarming effects reported.

## **CONCLUSION:**

The victims' lives have been significantly altered over the course of several weeks or months as a result of the emergence of post-covid19 effects, which include a variety of facets. These disorders may impact many organs and need treatment from several experts, in addition to the provision of proper follow-up therapy. This review offers light on a broad array of symptoms as well as the influence that the protracted COVID-19 illness has on a person's capacity to function physically, mentally, and socially. This study also

highlights the need for further research to be undertaken to fully understand the long-term repercussions of COVID-19 and to provide suitable treatments and management strategies for those who have been exposed to COVID-19 for a prolonged length of time.

## **LIMITATIONS:**

Many issues hampered the usefulness of this systematic study. A variety of factors contribute to the incongruity across studies' findings. They include small sample sizes and differences in stated outcomes. Almost all research included COVID-19 individuals with mild, moderate, and severe illness and varied follow-up intervals, and many studies relied on self-reporting methods, which may lead to interobserver bias. Several outcomes may emerge as a consequence of this. In every research we looked at, symptoms were evaluated according to a set of criteria, which might mask unreported results. There is no clear description of the impact of COVID-19 and its symptoms in the long term; however, a high viral load has been linked to the complications. It is possible for a patient who has survived a severe illness to have persistent symptoms for a longer period than a patient with a milder form of the same disease. Thus, prospective investigations are required to identify and characterize post-acute COVID-19.

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