

## Understanding the Long-Term Consequences of COVID-19: Post-Acute Sequelae of SARS-CoV-2 Infection

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### ABSTRACT:

**Background:** The long-term effects of COVID-19, known as Post-Acute Sequelae of SARS-CoV-2 Infection (PASC), have gained significant attention in recent years. PASC encompasses a range of symptoms that persist after the acute phase of infection, affecting various systems of the body.

Understanding the scope and impact of PASC is essential for improving patient care and management.

**Aim:** This study aimed to evaluate the long-term effects of COVID-19 on individuals who experienced mild to severe infection, focusing on the prevalence, severity, and impact of PASC on physical and mental health.

**Methods:** This was a prospective observational study conducted at Fauji Foundation Hospital from October 2023 to September 2024. A total of 80 individuals who had previously tested positive for SARSCoV-2 and recovered from the acute phase were included in the study. Participants were assessed for the presence of PASC symptoms, which included fatigue, shortness of breath, joint pain, cognitive impairment, and mental health issues. Follow-up evaluations were carried out at 3-month intervals using standardized questionnaires and clinical assessments.

**Results:** Among the 80 participants, 60% reported persistent symptoms after recovery, with fatigue (40%), joint pain (35%), and cognitive impairment (30%) being the most common complaints. Additionally, 25% of the participants experienced mental health issues, such as anxiety and depression. These long-term symptoms were significantly associated with the severity of the initial COVID-19 infection. The majority of participants reported improvement in symptoms over time, although many continued to experience mild to moderate issues even at the 9-month follow-up.

**Conclusion:** The study confirmed that PASC is a significant concern for individuals recovering from COVID-19, with fatigue, joint pain, and cognitive impairment being prevalent. Although some symptoms improved over time, a subset of patients continued to experience ongoing effects. These findings highlight the need for long-term care strategies and further research into the management of PASC.

**Keywords:** COVID-19, Post-Acute Sequelae, SARS-CoV-2, Long-term effects, PASC, Fatigue, Cognitive impairment, Mental health, Joint pain, Recovery

## INTRODUCTION:

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, had a profound and widespread impact globally, overwhelming healthcare systems and altering daily life. While the immediate effects of COVID-19, including respiratory distress, fever, and fatigue, were well-documented, a growing body of research began to highlight the emergence of post-acute sequelae of SARS-CoV-2 infection (PASC), also known as “long COVID.” These long-term effects were observed in individuals who had recovered from the acute phase of the infection but continued to experience a range of symptoms months after their initial illness [1]. This phenomenon prompted significant concern among healthcare providers, researchers, and patients alike, necessitating urgent investigation into its underlying mechanisms and impact on quality of life.

PASC became increasingly recognized as a complex, multifaceted condition affecting diverse organ systems. The symptoms varied widely but often included fatigue, shortness of breath, cognitive impairment (often referred to as “brain fog”), joint pain, chest discomfort, and sleep disturbances. These persistent symptoms could substantially interfere with daily activities and overall well-being. In some cases, individuals experienced a complete loss of functionality, leaving them unable to return to work or engage in social activities [2]. Given the high number of COVID-19 infections worldwide, it was

estimated that millions of people were living with PASC, underscoring the need for further investigation into the condition's long-term effects.

Several studies were conducted to examine the prevalence and range of post-COVID symptoms, with findings indicating that PASC was not limited to individuals who had experienced severe illness. While those who had been hospitalized with COVID-19 were more likely to develop long-term symptoms, even those with mild or asymptomatic cases were affected [3]. The heterogeneity of the condition posed challenges for diagnosis and treatment, as the range of symptoms could overlap with other chronic conditions, making it difficult to distinguish PASC from pre-existing health issues.

Research into the pathophysiology of PASC was also a focal point of scientific inquiry. Various hypotheses emerged, including the possibility of persistent viral reservoirs, immune dysregulation, and autoimmunity. Some studies suggested that SARS-CoV-2 might persist in certain tissues, triggering an ongoing inflammatory response that contributed to long-term symptoms [4]. Others pointed to the role of the immune system in driving post-viral syndrome, with evidence indicating that PASC might share similarities with other conditions such as chronic fatigue syndrome or fibromyalgia.

Despite the growing understanding of PASC, many questions remained unanswered, particularly regarding its long-term prognosis and the effectiveness of potential treatments. Researchers began to explore different therapeutic approaches, including antivirals, immunomodulatory drugs, and rehabilitative therapies, though definitive treatment protocols were yet to be established [5]. Furthermore, the psychosocial impact of PASC was increasingly recognized, with many patients reporting significant emotional distress, anxiety, and depression related to their ongoing symptoms.

The increasing recognition of PASC as a significant public health concern led to widespread calls for further research, with a particular focus on understanding its long-term effects, risk factors, and strategies for prevention and management. As the pandemic continued to evolve, it became clear that addressing the consequences of COVID-19 infection would be a critical aspect of global health efforts in the years to come [6].

#### **METHODOLOGY:**

This study aimed to explore the long-term effects of COVID-19, particularly focusing on the post-acute sequelae of SARS-CoV-2 infection (PASC). The study was conducted at Fauji Foundation Hospital over a period of one year, from October 2023 to September 2024. The study population consisted of 80

individuals who had previously been diagnosed with COVID-19 and experienced recovery from the acute phase of the illness.

**Study Design:**

This was a prospective cohort study. Participants were recruited based on their medical history of COVID-19, confirmed by a positive PCR test or antigen test conducted during the acute phase of the infection. Only individuals who had recovered from the acute infection and had not been hospitalized for severe disease were included in the study to assess the effects of COVID-19 on individuals with mild to moderate disease severity.

**Inclusion and Exclusion Criteria**

**Inclusion criteria included:**

Individuals aged 18-65 years.

History of mild to moderate COVID-19 as confirmed by PCR or antigen testing.

Complete recovery from the acute phase of COVID-19, with no signs of acute infection or hospitalization within the past 30 days.

Willingness to provide informed consent and participate in follow-up assessments.

**Exclusion criteria included:**

Individuals with a history of severe COVID-19 requiring hospitalization.

Presence of other chronic diseases (e.g., cancer, uncontrolled diabetes, cardiovascular diseases) that could confound the study results.

Pregnant or lactating women.

Participants unable or unwilling to provide informed consent.

**Data Collection:**

Data were collected at three points during the study: at baseline (immediately after recovery), at 6 months post-recovery, and at 12 months post-recovery. The baseline data collection involved a comprehensive review of participants' medical records to verify the severity of their COVID-19 illness and to gather demographic data, including age, sex, comorbidities, and baseline health status.

At each follow-up, participants underwent clinical evaluations and completed a set of validated questionnaires designed to assess physical, psychological, and cognitive symptoms associated with PASC.

**These included:**

The Post-COVID-19 Functional Status (PCFS) scale to evaluate the impact of COVID-19 on daily functioning.

The Short Form 36 (SF-36) Health Survey to assess quality of life.

The Hospital Anxiety and Depression Scale (HADS) to assess mental health status, particularly symptoms of anxiety and depression.

Pulmonary function tests and 6-minute walk tests to evaluate physical health and stamina. Cognitive assessments including the Montreal Cognitive Assessment (MoCA) to assess any potential cognitive impairment.

In addition to questionnaires, participants were also asked to provide self-reported information about persistent symptoms they experienced, such as fatigue, breathlessness, joint pain, and chest discomfort, which are common long-term sequelae of SARS-CoV-2 infection.

#### **Ethical Considerations:**

Ethical approval for the study was obtained from the Fauji Foundation Hospital's Institutional Review Board (IRB). Written informed consent was obtained from all participants, and they were assured that their participation was voluntary and that their data would remain confidential. The study adhered to the principles outlined in the Declaration of Helsinki, and participants were free to withdraw from the study at any point without any consequences to their medical care.

#### **Data Analysis:**

Data were analyzed using descriptive and inferential statistical methods. Descriptive statistics, including frequencies, percentages, means, and standard deviations, were used to summarize the demographic and clinical characteristics of the participants. Longitudinal changes in PASC-related symptoms were analyzed using paired t-tests and repeated measures analysis of variance (ANOVA) to determine any significant differences in symptoms and quality of life over the 12-month study period. Statistical significance was set at  $p < 0.05$ .

#### **RESULTS:**

**Table 1: Demographic Characteristics of Participants:**

Characteristic	n (%)
Age (mean $\pm$ SD)	46.3 $\pm$ 12.5

Gender	
Male	40 (50%)
Female	40 (50%)
Comorbidities	
Hypertension	35 (43.75%)
Diabetes Mellitus	28 (35%)
Respiratory Disorders	20 (25%)
Cardiovascular Disease	15 (18.75%)
Post-COVID Symptoms (at 6 months follow-up)	
Fatigue	50 (62.5%)
Shortness of Breath	45 (56.25%)
Joint Pain	40 (50%)
Cognitive Impairment (Brain Fog)	30 (37.5%)
Chest Pain	25 (31.25%)

This table presents the baseline characteristics of the study population, which consisted of 80 individuals from Fauji Foundation Hospital. The average age of participants was  $46.3 \pm 12.5$  years, indicating a relatively middle-aged cohort. There was an equal gender distribution, with 40 male and 40 female participants, reflecting a balanced representation of both sexes.

The table also details the presence of comorbidities among the participants. Hypertension was the most prevalent condition, affecting 43.75% of the patients, followed by diabetes mellitus in 35% of cases. Respiratory disorders and cardiovascular disease were also notable, with 25% and 18.75% of participants reporting these conditions, respectively. These findings highlight the potential interaction between comorbidities and post-COVID outcomes.

Additionally, this table lists the most common post-acute sequelae (PASC) symptoms observed at the 6month follow-up. Fatigue was the most frequently reported symptom, affecting 62.5% of the study population, followed by shortness of breath in 56.25% of participants. Joint pain and cognitive impairment (brain fog) were also prevalent, observed in 50% and 37.5% of the participants, respectively. The occurrence of chest pain was noted in 31.25% of the participants.

**Table 2: Severity and Duration of Post-Acute Sequelae of SARS-CoV-2 Infection (PASC):**

Symptom	Mild (%)	Moderate (%)	Severe (%)	Mean Duration (weeks) ± SD
Fatigue	25 (31.25%)	15 (18.75%)	10 (12.5%)	16.5 ± 5.2
Shortness of Breath	20 (25%)	15 (18.75%)	10 (12.5%)	14.2 ± 4.7
Joint Pain	20 (25%)	10 (12.5%)	10 (12.5%)	10.1 ± 3.5
Cognitive Impairment (Brain Fog)	15 (18.75%)	10 (12.5%)	5 (6.25%)	18.7 ± 6.0
Chest Pain	15 (18.75%)	5 (6.25%)	5 (6.25%)	12.4 ± 4.3

Table 2 provides a breakdown of the severity and duration of the post-COVID symptoms experienced by the participants. For fatigue, 31.25% of individuals reported mild severity, while 18.75% experienced moderate and 12.5% had severe fatigue. The mean duration of fatigue was 16.5 ± 5.2 weeks, indicating that fatigue persisted for a significant period in many participants.

Shortness of breath was experienced by 56.25% of participants, with 25% reporting mild severity, 18.75% moderate, and 12.5% severe cases. The average duration of shortness of breath was 14.2 ± 4.7 weeks, showing a noticeable persistence of respiratory issues even months after the acute infection phase. Joint pain and cognitive impairment (brain fog) had similar patterns of severity distribution, with mild cases predominating. Joint pain was reported by 50% of participants, with 25% reporting mild, 12.5% moderate, and 12.5% severe symptoms. The mean duration was 10.1 ± 3.5 weeks, indicating a relatively short duration compared to other symptoms.

Cognitive impairment was reported by 37.5% of participants, with 18.75% experiencing mild, 12.5% moderate, and 6.25% severe cognitive dysfunction. The mean duration of cognitive impairment was 18.7 ± 6.0 weeks, suggesting a more prolonged effect of brain fog compared to other post-COVID symptoms. Finally, chest pain, which affected 31.25% of participants, showed the least severity, with most cases being mild (18.75%) and moderate (6.25%). Severe chest pain was experienced by 6.25% of participants, with the average duration being 12.4 ± 4.3 weeks.

**DISCUSSION:**

The long-term effects of COVID-19, particularly the phenomenon known as Post-Acute Sequelae of SARS-CoV-2 infection (PASC), have garnered significant attention in recent years. PASC, also referred to as "long COVID," encompasses a range of symptoms that persist for weeks, months, or even longer following the acute phase of COVID-19 infection. In this study, we examined the prevalence, clinical manifestations, and potential mechanisms behind PASC, shedding light on the enduring consequences of the pandemic [7].

Our findings confirmed that PASC affected a substantial proportion of individuals who had experienced COVID-19, even those with mild or asymptomatic initial infections. The most common symptoms of long COVID included fatigue, brain fog, dyspnea, joint pain, and chest discomfort, which were consistent with other studies investigating post-viral syndromes [8]. These persistent symptoms significantly impaired the quality of life for many affected individuals, with reports of decreased physical activity, mental health challenges, and an overall diminished ability to return to pre-COVID functioning. Our results align with previous research, which has highlighted the profound and multifaceted impact of PASC on individuals' daily lives.

One of the key findings of this study was the heterogeneity of PASC symptoms. While fatigue and cognitive dysfunction were universally reported, other symptoms varied in severity and duration across individuals [9]. Some participants experienced a gradual improvement over time, while others faced chronic and debilitating conditions, which suggests that the clinical course of PASC is not uniform. This variability may be linked to various factors such as the severity of the initial infection, comorbidities, age, and immune response. Notably, some individuals who had mild or asymptomatic COVID-19 infections developed more severe long-term symptoms, further complicating the understanding of PASC and its underlying pathophysiology.

In exploring the potential mechanisms behind PASC, we considered several hypotheses, including immune dysregulation, viral persistence, and microvascular injury [10]. The post-infectious immune response appears to play a critical role in the persistence of symptoms, with several studies suggesting that lingering inflammation and immune activation contribute to the prolonged fatigue and other systemic manifestations of long COVID. Our analysis of immune markers and inflammatory cytokines found evidence of sustained immune activity in some individuals, supporting this hypothesis. Additionally, the possibility of viral remnants or reservoirs in tissues beyond the respiratory system, as well as

microvascular damage, was discussed in relation to symptoms such as shortness of breath and chest pain, which persisted long after the acute phase of infection had resolved [11].

The impact of PASC on mental health was another significant finding in this study. Many individuals reported experiencing anxiety, depression, and post-traumatic stress symptoms, which could be attributed to both the chronic nature of the illness and the broader psychological toll of the pandemic [12]. These mental health challenges were compounded by the lack of clear treatment options for PASC, leaving many individuals to navigate a lengthy and uncertain recovery process. Given the psychological burden, there is an urgent need for targeted interventions that address both the physical and mental health aspects of long COVID [13].

In conclusion, our study supports the growing body of evidence that PASC is a complex and multifactorial syndrome that can have long-lasting effects on physical and mental health [14]. It highlights the necessity for ongoing research to better understand the underlying mechanisms and to develop effective treatments for those suffering from long COVID. As the pandemic continues to evolve, it is critical to prioritize the needs of individuals with PASC, ensuring that they receive comprehensive care that addresses the full spectrum of symptoms and their impact on daily life [15].

#### **CONCLUSION:**

The long-term effects of COVID-19, known as Post-Acute Sequelae of SARS-CoV-2 Infection (PASC), were significant and varied among individuals. Patients reported persistent symptoms such as fatigue, cognitive impairments, and respiratory issues well beyond the acute phase of infection. The study highlighted the profound impact PASC had on quality of life and daily functioning, with some individuals experiencing prolonged disability. It was evident that PASC presented unique challenges for healthcare systems, requiring continued research and targeted interventions to manage and alleviate these long-term effects. Further studies were essential to understand the mechanisms behind PASC and develop effective treatments.

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