



## The lasting impact of covid-19: autonomic dysfunctions and their implications for future healthcare

Dipanshu Aggarwal<sup>1</sup>, Mahendra Pratap Singh<sup>2\*</sup>, Anoop Velayudhan<sup>3</sup>, Safayet Jamil<sup>4</sup>, Carlos Quispevicuna<sup>5</sup>, Afukonyo Shidoiku Daniel<sup>6</sup>, Joseph Clement<sup>7</sup>, Kumbha Gopi<sup>8</sup>, Pooja Sindwani<sup>9</sup>

<sup>1</sup> Department of Oral Pathology and Microbiology, Shree Bankey Bihari Dental College, Ghaziabad, India.

<sup>2</sup> Evidence for Policy and Learning, Global Center for Evidence Synthesis, Chandigarh, India.

<sup>3</sup> Indian Institute of Health Management Research University, Jaipur, India.

<sup>4</sup> Department of Public Health, Daffodil International University, Dhaka, Bangladesh.

<sup>5</sup> Red De Eficacia Clinica Y Sanitaria Redecs, Lima, Peru.

<sup>6</sup> Global Health and Infectious Diseases Control Institute, Nasarawa State University, Keffi, Nigeria.

<sup>7</sup> School of Social and Health Sciences, Millenium University, Blantyre, Malawi.

<sup>8</sup> Department of Epidemiology, South Asia Field Epidemiology and Technology Network Safetynet National Centre for Disease Control, Delhi, India.

<sup>9</sup> Department of Community Medicine, Teerthanker Mahaveer Medical College and Research Center, Moradabad, India.

\*Correspondence: [thesinghmp@gmail.com](mailto:thesinghmp@gmail.com)



### Cite this Article

Aggarwal D, Singh MP, Velayudhan A, Jamil S, Quispevicuna C, Daniel AS, Clement J, Gopi K, Sindwani P, The lasting impact of covid-19: autonomic dysfunctions and their implications for future healthcare. *The Evi.* 2024;2(1):1-. DOI:10.61505/evidence.2024.2.1.55

Available From

<https://the.evidencejournals.com/index.php/j/article/view/55>

**Received:** 2024-04-26

**Accepted:** 2024-05-28

**Published:** 2024-06-11

### Evidence in Context

- Many long COVID patients develop Postural Orthostatic Tachycardia Syndrome (POTS) and other autonomic dysfunctions.
- Symptoms include tachycardia and fatigue, with diagnostic challenges due to symptom overlap.
- Not all patients show clear POTS, complicating management.
- Advocates for specialized clinics and healthcare system adaptations.
- Emphasizes the need for further research to improve understanding and treatment.

To view Article



### Abstract

The prevalence of autonomic dysfunction, including postural orthostatic tachycardia syndrome (POTS), in patients with long COVID is significant. Studies have shown that a high proportion of long COVID patients develop POTS, with symptoms such as tachycardia, orthostatic intolerance, fatigue, and cognitive impairment. Autonomic testing in long COVID patients revealed that a considerable number exhibited autonomic dysfunction, with some showing abnormal results affecting parasympathetic cardiac function. Additionally, the majority of long COVID patients did not display specific evidence of POTS or other clear autonomic dysfunction, with only a small percentage meeting the criteria for POTS diagnosis. These findings highlight the importance of evaluating autonomic symptoms and dysfunction, including POTS, in patients with long COVID to guide appropriate management strategies for improved health outcomes. This article explores various aspects of these conditions, focusing on understanding POTS and related autonomic dysfunctions, their management, and the implications for future healthcare.

**Keywords:** *postural orthostatic tachycardia syndrome; autonomic dysfunction; long covid; cardiovascular implications; immune response; healthcare adaptation; diagnostic challenges*

### Introduction

As the world grapples with the aftermath of the COVID-19 pandemic, an emerging health crisis in the form of autonomic dysfunctions, particularly Postural Orthostatic Tachycardia Syndrome (POTS) and associated disorders, is becoming increasingly evident [1]. This article highlights the significant impact of COVID-19 on autonomic function and the implications for health-related quality of life, emphasizing the importance of further studies and targeted healthcare responses to manage these conditions effectively.



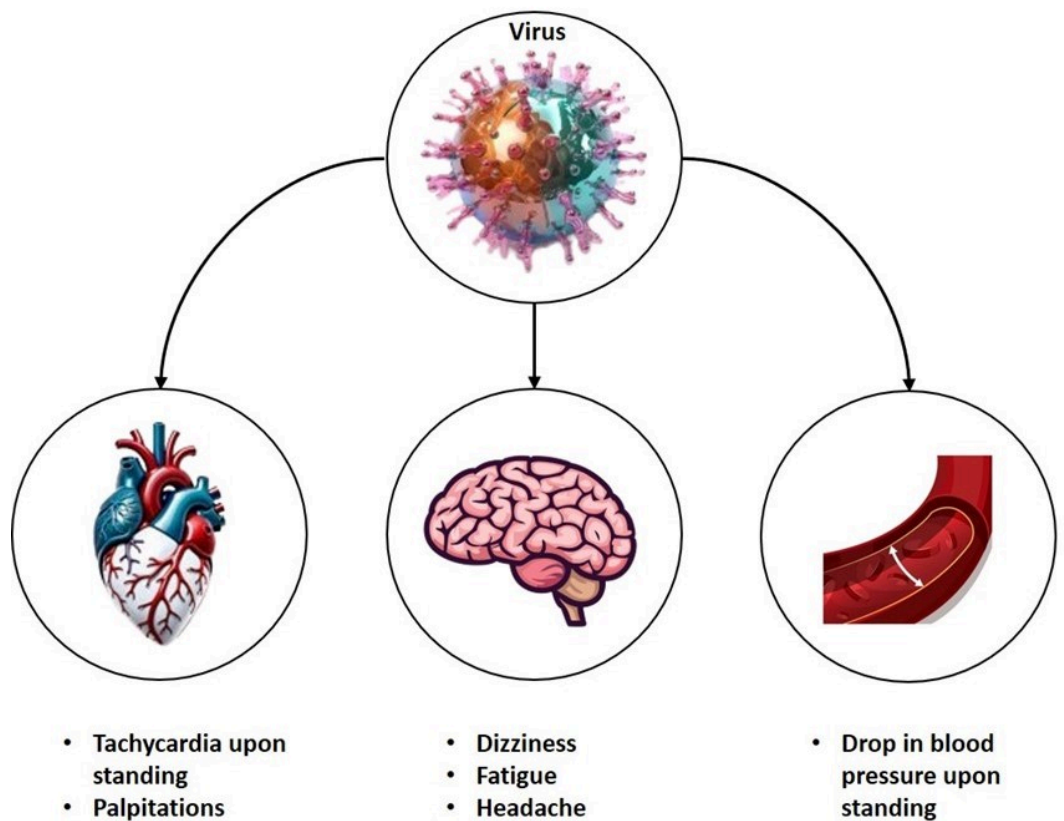
**Understanding POTS and Related Autonomic Dysfunctions**

POTS is a medical condition characterized by an abnormal elevation in heart rate when transitioning to a standing position and is often accompanied by a range of symptoms including dizziness, fatigue, and heart palpitations. Its prevalence worldwide is not well established with estimates ranging from 0.2% to 1% affecting mostly young adults and women [2]. POTS has been shown to significantly affect Health-related Quality of life including problems with usual activities, pain and discomfort, mobility, sports, standing, anxiety and depression, and self-care [3,4]. Research shows that POTS and other autonomic dysfunctions have become more common following COVID-19 [3], suggesting a direct correlation between the virus and lasting autonomic issues. These conditions reflect a dysfunction of the autonomic nervous system, which controls autonomic processes like heart rate and blood pressure.

**The COVID Connection: Pathophysiology and Prevalence**

Several studies, such as Allendes et al [4] and El-Rhermoul et al [1], indicate that autonomic dysfunction may result from the body's response to the SARS-CoV-2 virus. These responses could involve direct viral damage to autonomic nervous pathways or secondary immune-mediated mechanisms. For instance, Gómez-Moyano et al [5] discuss the occurrence of POTS following COVID-19 infection and even post-vaccination, emphasizing the role of the immune system in triggering these dysfunctions.

The prevalence of these conditions is alarmingly high among long COVID patients. Seeley et al [3]. reported a significant incidence of autonomic dysfunction among such individuals, which has substantial implications for management and healthcare planning. **Table 1** summarizes important studies examining the link between COVID-19 and autonomic dysfunctions. This high prevalence underscores the need for healthcare systems to adapt and prepare for a new wave of patients experiencing these debilitating symptoms. **Figure 1** provides a visual overview of the lasting autonomic dysfunctions associated with COVID-19, including cardiovascular problems like tachycardia and palpitations, neurological symptoms such as dizziness, fatigue, headaches, and vascular issues, notably a drop in blood pressure when standing.



**Figure 1: The long-term autonomic effects of COVID-19 on cardiovascular, neurological, and vascular systems**

**Diagnostic and Management Challenges**

The diagnosis of POTS and related autonomic dysfunctions is challenging. The condition's symptoms are often subjective and can overlap with those of other disorders, leading to underdiagnosis or misdiagnosis. Hupin et al [6] highlight the diagnostic value of 24-hour ECG recording in identifying autonomic dysfunction in long COVID patients, suggesting that more sophisticated diagnostic tools may be necessary to diagnose and manage these conditions accurately.

Management of POTS involves a multifaceted approach, including lifestyle changes, medication, and, in some cases, physical therapy. However, symptoms and responses to treatment vary, making management highly individualized. The literature suggests a growing need for tailored therapeutic strategies that address both autonomic symptoms and underlying causes of COVID-19.

**Implications for Future Healthcare**

The emergence of POTS and other autonomic dysfunctions as post-COVID conditions suggests several implications for future healthcare [3]. First, healthcare providers need to be more aware and educated about these conditions. Early recognition and appropriate management can significantly improve patient outcomes.

Secondly, healthcare systems must adjust in order to cater to the enduring requirements of individuals who have survived COVID-19. This encompasses the establishment of dedicated clinics and services as well as the undertaking of research on efficacious treatments. Moreover, the potential increase in healthcare demand due to these chronic conditions could strain already burdened healthcare systems, necessitating efficient resource allocation and perhaps even rethinking healthcare delivery models.

Lastly, the unclear mechanism of COVID-19 and POTS poses a significant challenge in managing and preventing these conditions in affected patients. Therefore, it is essential to investigate the underlying mechanisms and pathophysiology to understand their pathways and identify potential modifications to reduce their incidence.

**Conclusion**

As the world continues to recover from COVID-19, it is crucial not to overlook the secondary health crises emerging in its wake, such as POTS and related autonomic dysfunctions. The documents reviewed provide compelling evidence of the link between COVID-19 and these conditions, highlighting a pressing need for comprehensive strategies to diagnose, manage, and mitigate the impact of these disorders. Only with a proactive and informed approach can we hope to address the complexities of post-COVID healthcare challenges effectively.

**Table 1: Summary of Key studies on COVID-19 and Autonomic Dysfunctions**

Study	Characteristics	Key findings
Seeley et al., (2023)[3]	In this study, the extent of dysautonomia among individuals experiencing post-acute sequelae of COVID-19 (PASC) was not compared with individuals with POTS and individuals in good health.	<ul style="list-style-type: none"> <li>· PASC and POTS exhibited a decrease in respiratory sinus arrhythmia.</li> <li>· The prevalence of POTS was notable within individuals experiencing post-acute sequelae of SARS-CoV-2 (PASC), leading to a decline in Health-related Quality of Life (HrQoL).</li> </ul>
Hupin et al., (2023) [6]	An examination of 24-hour ECG recordings from a group of individuals identified the existence of autonomic dysfunction in patients diagnosed with POTS in contrast to those who did not have POTS.	<ul style="list-style-type: none"> <li>· LC patients with POTS exhibited a reduction in HRV parameters.</li> <li>· LC patients with POTS demonstrated an increase in the number of HR spikes.</li> </ul>
Bryarly et al., (2023) [7]	The authors examined autonomic symptoms, their degree of severity, and quantifiable indicators of autonomic performance in individuals afflicted with post-COVID syndrome. These include fatigue, orthostatic intolerance, cognitive dysfunction, and syncope.	<ul style="list-style-type: none"> <li>· The majority of individuals with long-COVID exhibited either normal results in autonomic function tests or presented with mild abnormalities.</li> <li>· Merely 12% of long-COVID patients showed test results that were indicative of POTS.</li> </ul>

<p>Zanini et al., (2023) [8]</p>	<p>The Schirmer test and Valsalva test were employed to assess parasympathetic cardiac function in individuals with SARS-CoV-2 infection.</p>	<ul style="list-style-type: none"> <li>· 37.5% of individuals with persistent symptoms following COVID-19 infection exhibited autonomic function test outcomes irregularities.</li> <li>· The average Valsalva score demonstrated a notable decrease in patients compared to the control group.</li> </ul>
<p>Fleischer et al., (2023) [9]</p>	<p>In this study, the authors assessed cardiovascular autonomic (CAN) function in a cross-sectional analysis involving 47 adults suffering from long COVID-19. Among them, 21 individuals had type 2 diabetes mellitus (T2DM) with a mean age of 61 years, 43% being women, and a mean A1c level of 6.2%. The study also included a comparison with individuals having T2DM but not affected by COVID-19.</p>	<ul style="list-style-type: none"> <li>· COVID-19 worsens cardiac autonomic neuropathy in patients with a diagnosis of type 2 diabetes mellitus.</li> <li>· COVID-19 affects cardiac autonomic neuropathy in individuals without type 2 diabetes mellitus in a comparable manner to those with the condition.</li> </ul>
<p>El-Rhermoul et al., (2023) [1]</p>	<p>Orthostatic intolerance and several other syndromes of autonomic dysfunction are identified as distinct groups of symptoms within Long Covid. Furthermore, a variety of autoantibodies are detected in both autonomic disorders related to Covid and those unrelated to Covid, indicating the existence of a possible autoimmune mechanism.</p>	<ul style="list-style-type: none"> <li>· Several autoantibodies have been identified in individuals with Long Covid and POTS.</li> <li>· An autoimmune connection has been proposed, although the precise significance remains uncertain.</li> </ul>
<p>Isaac et al., (2023) [10]</p>	<p>The author discussed the results of the Lean Test (NLT) conducted by the National Aeronautics and Space Administration (NASA) and juxtapose these results with the symptoms of LC as documented in the C19-YRS.</p>	<ul style="list-style-type: none"> <li>· Evidence of orthostatic intolerance in individuals with Long COVID has been observed.</li> <li>· The reported symptoms show a lack of correlation with the results obtained from the NASA Lean Test.</li> </ul>
<p>Allendes et al., (2023)[4]</p>	<p>In the present article, the authors focus on the enduring cardiovascular and autonomic consequences that manifest after an individual contracting COVID-19. Furthermore, they delve into the possibilities both traditional and innovative cardiovascular rehabilitation schemes present in addressing the prolonged health issues that endure/emerge after the usual recuperation timeframe.</p>	<ul style="list-style-type: none"> <li>· Prolonged COVID-19 has been associated with cardiovascular consequences and disturbances in autonomic regulation.</li> <li>· Participation in cardiac rehabilitation initiatives could potentially enhance results among individuals with persistent COVID-19 symptoms.</li> </ul>
<p>Minhas et al., (2023)[11]</p>	<p>A 53-year-old female individual received a diagnosis of POTS after a comprehensive autoimmune evaluation. This patient also had a history of being in the recovery phase after a long COVID 19 infection.</p>	<ul style="list-style-type: none"> <li>· POTS is associated with autonomic dysfunction following a COVID-19 infection.</li> <li>· The treatment regimen consists of modifications in lifestyle and the administration of pharmaceutical agents, yielding favourable outcomes.</li> </ul>
<p>Hira et al., (2023) [12]</p>	<p>The authors analyzed the enduring or fleeting nature of autonomic irregularities noted in patients post a COVID-19 infection. This inquiry involved assessing hemodynamic parameters during the initial evaluation and subsequent follow-up visits.</p>	<ul style="list-style-type: none"> <li>· Autonomic dysregulation continues to manifest in individuals experiencing Post-Acute Sequelae of COVID-19.</li> <li>· The prevailing abnormalities often encountered include Initial Orthostatic Hypotension (IOH) POTS.</li> </ul>

**Supporting information**

None

**Ethical Considerations**

None

**Acknowledgments**

None

## Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

## Author contribution statement

All authors contributed equally and attest they meet the ICMJE criteria for authorship and gave final approval for submission.

## Data availability statement

Data included in article/supp. material/referenced in article.

## Additional information

No additional information is available for this paper.

## Declaration of competing interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## References

1. El-Rhermoul F-Z, Fedorowski A, Eardley P, Taraborrelli P, Panagopoulos D, Sutton R, et al. Autoimmunity in Long Covid and POTS. *Oxford Open Immunol.* 2023;4(1) [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
2. Kim DH, Park JY, Kim SY, Lee NM, Yi DY, Yun SW, et al. Awareness of postural orthostatic tachycardia syndrome is required in adolescent syncope. *Medicine.* 2022;101(45) [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
3. Seeley M-C, Gallagher C, Ong E, Langdon A, Chieng J, Bailey D, et al. High Incidence of Autonomic Dysfunction and Postural Orthostatic Tachycardia Syndrome in Patients with Long COVID: Implications for Management and Health Care Planning. *Am J Med.* 2023 [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
4. Allendes FJ, Díaz HS, Ortiz FC, Marcus NJ, Quintanilla R, Inestrosa NC, et al. Cardiovascular and autonomic dysfunction in long-COVID syndrome and the potential role of non-invasive therapeutic strategies on cardiovascular outcomes. *Front Med.* 2023;9: 1095249 [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
5. Gómez-Moyano E, Rodríguez-Capitán J, Gaitán Román D, Reyes Bueno JA, Villalobos Sánchez A, Espíldora Hernández F, et al. Postural orthostatic tachycardia syndrome and other related dysautonomic disorders after SARS-CoV-2 infection and after COVID-19 messenger RNA vaccination. *Front Neurol.* 2023;14:1221518 [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
6. Hupin D, Pichot V, Back M, Nygren Bonnier M, Reistam U, Runold M, et al. Diagnostic value of 24-h ECG recording in Long COVID patients with postural orthostatic tachycardia syndrome. *Europace.* 2023;25(Supplement\_1) [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
7. Bryarly M, Cabrera J, barshikar s, Vernino S. Minimal Objective Autonomic Dysfunction in Long-COVID (S43. 004). *Neurology.* 2023;100(17\_supplement\_2) [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
8. Zanin A, Amah G, Chakroun S, Testard P, Faucher A, Le TYV, et al. Parasympathetic autonomic dysfunction is more often evidenced than sympathetic autonomic dysfunction in fluctuating and polymorphic symptoms of "long-COVID" patients. *Sci Rep.* 2023;13(1) [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]

9. Fleischer J, Gunaratnam SVG, Huang Y, Ang L, Charles M, Katona A, et al. 487-P: Cardiovascular Autonomic Function in Long COVID-19 Individuals With and Without Diabetes. *Diabetes. 2023;72(Supplement\_1)* [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
10. Isaac R, Corrado J, Sivan M. Detecting Orthostatic Intolerance in Long COVID in a Clinic Setting. *Int J Environ Res Public Health. 2023;20(10)* [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
11. Minhas R, Bharadwaj AS. COVID-19-Induced Postural Orthostatic Tachycardia Syndrome and Dysautonomia. *Cureus. 2023 Jun;15(6)* [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]
12. Hira R, Siddiqui T, Baker J, Bourne K, Ranada S, Soroush A, et al. Objective cardiovascular autonomic abnormalities persist over time in patients with Post-Acute Sequelae of COVID-19 (PASC). *Physiology. 2023;38(S1)* [[Crossref](#)][[PubMed](#)][[Google Scholar](#)]

### **Disclaimer / Publisher's Note**

The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of Journals and/or the editor(s). Journals and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.