

# SINTOMATOLOGÍA PERSISTENTE POSTERIOR A INFECCIÓN POR SARS-COV-2. REVISIÓN DE LA LITERATURA.

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## Resumen

**Introducción:** una proporción de pacientes que ha sido infectada con SARS-CoV-2 continúa teniendo síntomas a corto y largo plazo, después de su recuperación de la fase aguda de Covid-19.

**Objetivo:** describir la sintomatología persistente posterior a la infección por SARS-CoV-2.

**Métodos:** artículo de revisión científica, tomando como fuente de información la literatura actual publicada en bases de datos como: Biomed Central (BMC), PubMed, Google Scholar, ScienceDirect, y Lilacs. Se hace énfasis en publicaciones con diseño observacional, revisiones sistemáticas, metaanálisis y estudios de revisión, en relación a los síntomas persistentes después de la infección por SARS-CoV-2. Se considera cualquier gravedad, en pacientes adultos, que estuvieron o no hospitalizados, con o sin comorbilidades.

**Resultados:** se analizaron 32 artículos, con una población de pacientes adultos que superaron la fase aguda de la infección por SARS-CoV-2. Los síntomas persistentes postcovid-19 descritos con más frecuencia fueron: fatiga crónica (55.2%), cefalea (52%), disnea (39.5%), trastornos del sueño (35.5%), depresión/ansiedad (31.2%), mialgias (30.1%), dolor torácico (26.9%), palpitaciones (21.5%), tos (20.5%), artralgias (20.2%), ageusia/anosmia (12.4%), alteraciones de memoria y concentración (3.6%).

**Conclusión:** la sintomatología postcovid-19 es diversa, con prolongación de síntomas físicos y neuropsiquiátricos, que persisten durante 12 semanas o más, sin una explicación alternativa. Entre un 10 a 65% de pacientes que sobrevivieron a la etapa aguda de la infección presentan este cuadro clínico. Por lo tanto, las afectaciones del SARS-CoV-2 en la sociedad van más allá de la fase aguda.

**Palabras clave:** Covid-19, SARS-CoV-2, coronavirus, post, viral.

## PERSISTENT SYMPTOMS AFTER SARS-COV-2 INFECTION. LITERATURE REVIEW.

### Abstract

**Introduction:** a proportion of patients who have been infected with SARS-CoV2 continue having short- and long-term symptoms after recovery from the acute phase of Covid-19. **Objective:** to describe persistent symptomatology following SARSCoV-2 infection.

**Methods:** scientific review article, taking as a source of information the current literature published in databases such as: Biomed Central (BMC), PubMed, Google Scholar, ScienceDirect, and Lilacs. It emphasizes on publishing with observational design, systematic reviews, meta-analysis and review studies, in relation to persistent symptoms after SARS- 2 CoV-2 infection. Any severity is considered, in adult patients, who were or were not hospitalized, with or without comorbidities.

**Results:** 32 articles were analyzed, with adult patients who overcame the acute phase of SARS-CoV-2 infection. The most frequently described persistent postcovid-19 symptoms were: chronic fatigue (55.2%), headache (52%), dyspnea (39.5%), sleep disorders (35.5%), depression/anxiety (31. 2%), myalgias (30.1%), chest pain (26.9%), palpitations (21.5%), cough (20.5%), arthralgias (20.2%), ageusia/anosmia (12.4%), memory and concentration disorders (3.6%).

**Conclusion:** postcovid-19 symptomatology is diverse, with prolongation of physical and neuropsychiatric symptoms, persisting for 12 weeks or more, without an alternative explanation. Between 10 to 65% of patients who survived the acute stage of infection present this clinical picture. Therefore, the impact of SARS-CoV-2 on society goes beyond the acute phase.

**Keywords:** Covid-19, SARS-CoV-2, coronavirus, post, viral.

## INTRODUCTION

On March 11, 2020, the World Health Organization (WHO) declared the global pandemic by Covid-19, caused by a new coronavirus, called SARS-CoV-2. From inception to October 23, 2020, more than 50 million cases have been reported worldwide. And until October 1, 2021, in Ecuador there are 512,000 confirmed cases and 32,836 deaths<sup>(1)</sup>.

Despite the significant proportion of people who have been infected with Covid-19, the clinical course of the associated respiratory pathology, including the prevalence and persistence of symptoms, has not been fully described. There are patients who recover enough to be discharged from the hospital within seven to ten days, but may not yet be free of symptoms. Others progress to a hyperinflammatory state and Adult Respiratory Distress Syndrome (ARDS), which is associated with high mortality, attributed to respiratory or cardiac failure<sup>(2)</sup>.

*"The long-term effects of COVID-19 have been called "long-term COVID-19", "long-term COVID-19" or Long -COVID, determined as the symptoms present after the acute stage of the disease has been overcome. pathology, after four and even*

*twelve weeks, this was observed in a proportion of patients surviving the SARS-CoV-2 infection"*<sup>(3)</sup>.

In the context of patients recovered from Covid-19, the persistence of symptoms, radiological abnormalities and compromised respiratory function are evident. It is estimated that there are more than fifty signs and symptoms that may occur, among which are: chronic fatigue, dyspnea, cough, chest pain, myalgia and arthralgia. Older adults and those patients with comorbidities are the ones who, to a greater extent, present this problem, without neglecting the report of cases in young and healthy people<sup>(4)</sup>.

The follow-up of patients who have overcome the Covid-19 infection and persist with symptoms is a new healthcare need, which requires a multidisciplinary, protocolized and equitable approach. For this reason, it is considered opportune to carry out a scientific consensus

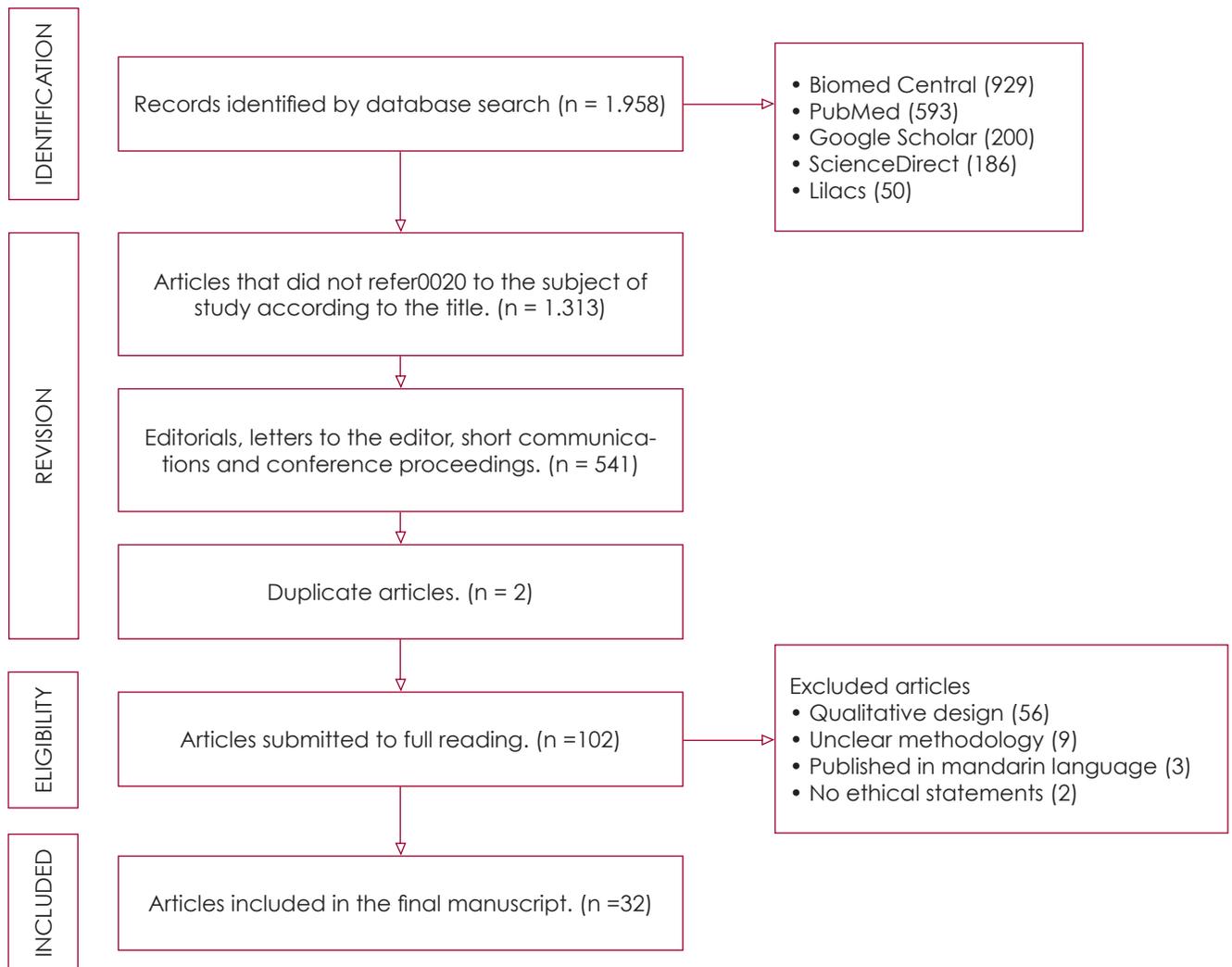
reflection, establishing how adequate clinical management should be organized and managed (6). Despite the vast availability of data on the clinical picture of acute Covid-19, there is little information on the persistence of signs and symptoms in patients who have overcome the acute stage of this infection.

Consequently, the present work aims to describe the persistent symptoms after SARS-CoV-2 infection. This, regardless of having required hospitalization or not, with or without previous comorbidities. In addition, it seeks to analyze the duration and evolution of these symptoms. In this way, it is oriented towards the implementation of therapeutic, rehabilitative and individual care plans that contribute to improving the quality of life of these patients. Its clinical relevance is that the new knowledge acquired may be the scientific evidence that supports more appropriate care.

## METHODS

A scientific review article was carried out, taking as a source of information the current literature published in databases such as: Biomed Central (BMC), PubMed, Google Scholar, ScienceDirect, and Lilacs. The search strategy was to use MeSH terms and Boolean operators such as: "Covid-19" OR "SARS-CoV-2" OR "coronavirus" AND "post" AND "viral", in Spanish or English.

were identified (BMC: 929, PubMed: 593, Google Scholar: 200, ScienceDirect: 186 and Lilacs: 50). Through selection criteria, 1,856 of them were eliminated (1,313 articles that did not refer to the subject of study according to the title, 2 duplicate articles, 541 editorials, letters to the editor, brief communications and conference proceedings). Ultimately, of the remaining 102 articles, 70 were



**Figure 1.** Flowchart for the search and selection of literature included. **Source:** Made by the authors. Year 2021.

eliminated (56 for having a qualitative design, 9 for not clearly describing the methodology or instruments used, 3 for being published in Mandarin, and 2 for not having ethical statements).

At the end of the selection process, 32 articles were included in this research, with an emphasis on scientific publications with an observational design, clinical studies, systematic reviews, meta-analyses, and review studies. These are related to persistent symptoms, after SARS-CoV-2 infection, of any degree of severity. The characteristics correspond to adult patients, who were hospitalized or not, with or without comorbidities and in whose structure evolution, analysis and discussions related to their behavior, in the short and long term, as well as the impact on quality of life, were expressed. The posts were from January 2020 to October 2021.

Letters to the editor, unpublished research, clinical study in the acute phase of Covid-19 or with conflicts of interest were excluded. A review of the titles and the abstract was carried out. Those publications that passed the described filters were considered for further reading and exhaustive analysis. With the information collected, systematized and analyzed, the present review work was carried out, answering the following research question: what is the persistent symptomatology after SARS-CoV-2 infection?

## RESULTS

### Persistent symptomatology after SARS-CoV-2 infection

The evidence of persistent symptoms, after the acute phase of the SARS-CoV-2 infection has been overcome, has led to the description of the postcovid or Long covid syndrome, which occurs in between 10% and 65% of patients who survived the infection, disease. It is characterized by diverse clinical manifestations for 12 weeks or more, without an alternative explanation. This could be attributed to the hyperinflammatory state, immunological deregulation, the sequelae of organ damage, the variable extent of the injury, the immune response with the generation of autoantibodies, the permanence of the virus, the post-intensive care syndrome or adverse effects of the medications administered<sup>(6,7)</sup>.

Sykes et al described three groups of patients who presented post-Covid-19 symptoms: group A included myalgia and fatigue; group B presented asthenia, anxiety and sleep disorders; while in group C memory impairment, attention deficit and cognitive impairment were identified<sup>(8)</sup>. On the other hand, it was determined that the fact of experiencing more than five symptoms during the first week of illness was associated with prolonged Covid-19, characterized by diverse symptoms such as: anosmia, ageusia, chronic fatigue, headache, severe dyspnea, asthenia, weight loss, chest pain, palpitations, skin signs, arthralgia, myalgia, digestive disorders and fever<sup>(9)</sup>.

### General symptoms and signs

Among the most frequent symptoms in the post-Covid-19 stage are chronic fatigue, headache, dyspnea and cough. In addition, alterations in chest X-ray images, elevation in D-dimer and concentration of C-reactive protein (CRP)<sup>(10)</sup>. In reports

made to evaluate long-term manifestations, after SARS-CoV-2 virus infection, it is indicated that patients also perceived palpitations, myalgia, depression and, less frequently, anosmia and/or ageusia, around thirty and forty days post-infection<sup>(11,12)</sup>.

In follow-up studies, the most prevalent clinical manifestations have been determined to be chronic fatigue, headache and dyspnea, with a partial recovery in around three months, after the acute stage of the infection. Furthermore, it is considered that when fatigue persists for six months or more, it is chronic fatigue syndrome or postviral fatigue<sup>(13)</sup>. This is attributed to the fact that the SARS-CoV-2 virus functions as a major stressor, targeting the paraventricular nucleus - hypothalamic axis, in genetically susceptible people. Thus, dysfunction at this level acts as the epicenter of neuroinflammation, which is driven through localized activation induced by microglia<sup>(14)</sup>.

### Neurological and psychiatric symptoms

The presence of SARS-CoV-2 in the cerebrospinal fluid (CSF) shows its neuroinvasive capacity, which induces a possible alteration of the microstructural and functional brain integrity in patients recovered from the acute phase of the infection<sup>(15-17)</sup>. Consequently, post-Covid-19 neurological symptoms are heterogeneous and manifestations such as: headache, chronic fatigue, attention deficit, difficulty concentrating (brain fog), insomnia, anxiety and depression are described<sup>(17)</sup>.

In addition, focal or multifocal peripheral nerve injury, acquired in those patients who received prone ventilation for ARDS, can cause myopathies, peripheral neuropathy, and delirium<sup>(18)</sup>. As additional data, the reports on Guillain-Barré (GBS) and axonal or demyelinating variants associated with Covid-19, in general, are presented as a post-infectious pattern, with a period of five to ten days after the infection is overcome<sup>(19)</sup>.

Together, the hypothesis about neurodegeneration has been raised, since coronaviruses have been found in people with pathologies such as: multiple sclerosis and acute disseminated encephalomyelitis, as well as in Alzheimer's and Parkinson's diseases. Previous studies raise the probability that SARS-CoV-2 chronically affects the Central Nervous System and that this triggers or accelerates neurodegenerative disorders<sup>(20,21)</sup>.

### Cardio-respiratory symptoms

Due to cardiac symptoms in the acute phase of the infection, postcovid-19 cardiovascular

manifestations may occur. Among them are dyspnea, in 45%, especially in patients who required an Intensive Care Unit (ICU); pulmonary embolism, heart failure, orthostatism, fatal arrhythmias, and sudden cardiac death. A possible interstitial lung injury was also evidenced, with total or partial return to normal lung function within six to twelve months, and the diffusing capacity for carbon monoxide (DLCO) remained abnormal for more than a year, after recovery (22).

### Other symptoms

Other symptoms that occur less frequently are: odynophagia, nausea, vomiting, anorexia, generalized tremor and inflammatory arthralgia. The latter must be differentiated from other similar conditions such as rheumatoid arthritis and systemic lupus erythematosus (SLE). Severe SARS-CoV-2 infection can cause autoreactivity against a variety of autoantigens (5,7,13,17,23).

**Table 1** shows a summary of persistent post-Covid-19 symptoms.

### Literature review

The purpose of this scientific review was to describe persistent post-Covid-19 symptoms, emphasizing that sequelae can be multiple and of variable severity. The analyzed literature agrees that the clinical manifestations are diverse, however, chronic fatigue predominates in most of the findings, followed by headache and dyspnea (4,5,8-14).

Afrin and collaborators propose that the post-covid-19 or Long - covid syndrome is due to the hyperinflammatory state, caused by a storm of cytokines that give an atypical response to SARS-CoV-2 infection, with which activation acquires an important role. of mast cells (24). This is consistent with Huang 's theory , for whom this syndrome is attributed to immune, autonomic and metabolic deregulation in postviral chronic fatigue , which would also explain other symptoms described (25). Thus, the results of Verstrepen et al. determine that if fatigue persists for six months or more, it is called chronic fatigue syndrome or postviral fatigue (26).

Regarding anosmia, it is believed that it may be related to a lesion of the pseudostratified olfactory epithelium. This is supported by the reports by Butowt et al., who suggest that damage to support cells in the olfactory epithelium could be an acceptable mechanism to explain this symptom (27). On the other hand, Wostyn relates the damage of the olfactory sensory neurons with a reduction in the outflow of cerebrospinal fluid (CSF), through the cribriform plate and the congestion of the glymphatic system, with the consequent toxic accumulation within the Nervous System. Central (CNS) (28).

According to the findings of Paterson and collaborators, post-covid-19 neurological symptoms appear due to the cytokine storm and chronic viral invasion of the CNS. The role of factors such as hydroelectrolytic alterations, acid-base, hypo or hyperglycemia can be added, which favor the appearance of a wide spectrum of neurological

symptoms such as: headache, anxiety, attention deficit depression, brain fog, insomnia and neurodegenerative disorders (29).

In relation to cardio-respiratory symptoms, dyspnea was the most frequent clinical manifestation. This is consistent with reports by Halpin and collaborators, which indicate that 45% of patients recovered from Covid-19 have dyspnea, essentially those who were in the Intensive Care Unit (ICU), in which evidence of pulmonary fibrosis was found in the chest x-ray (30).

Several of these manifestations have been explained by Dani et al as an expression of the dysfunction of the autonomic system. The Covid-19 cytokine response storm results from sympathetic activation that induces the release of proinflammatory cytokines. On the contrary, vagal stimulation results in anti-inflammatory responses, which explains different symptoms such as: orthostatism, tachycardia, or respiratory distress (31).

Regarding pulmonary manifestations, Ahmed and colleagues agree with studies that analyze long-term health problems in survivors of infections by other types of coronavirus. Reduced lung function and abnormal diffusing capacity for carbon monoxide (DLCO) were reported in these up to six to twelve months after hospital discharge (32).

The main limitation of this research was that the literature analyzed describes a great heterogeneity of symptoms, as well as in the criteria to define them and in the designs used in each study. However, it is considered that it has been possible to include the most relevant and current knowledge in relation to the current problems on this topic.

## CONCLUSIONS

Post-covid-19 symptomatology is diverse, with prolonged physical and neuropsychiatric symptoms, which can persist for 12 weeks or more, without an alternative explanation. Between 10% and 65% of patients who survived the acute stage of the infection present this clinical picture. Therefore, the effects of SARS-CoV-2 on society go beyond the acute phase.

Covid-19 symptomatology is chronic fatigue, followed by headache and dyspnea, which persist in the short or long term, regardless of whether or not there was hospitalization during the acute phase of the infection. Therefore, the heterogeneity of the clinic leads to the need to continue the study of this health problem, with a view to unifying the criteria to establish and implement management and rehabilitation protocols that are continuously updated, according to the need for this group of patients.

## Referencias

- Maguiña C, Gastelo R, Tequen A. The new Coronavirus and the Covid-19 pandemic. *Rev Medica Hered* [Internet]. 2020;31(2):125-31. doi: 10.20453/rmh.v31i2.3776. Available from: [http://www.scielo.org.pe/scielo.php?script=sci\\_arttext&pid=S1018-130X2020000200125](http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S1018-130X2020000200125).
- Park SY, Yun SG, Shin JW, Lee BY, Son HJ, Lee S, et al. Persistent severe acute respiratory syndrome coronavirus 2 detection after resolution of coronavirus disease 2019-associated symptoms/signs. *Korean J Intern Med*. 2020 Jul;35(4):793-796. doi: 10.3904/kjim.2020.203.
- Deer RR, Rock MA, Vasilevsky N, Carmody L, Rando H, Anzalone AJ, et al. Characterizing Long COVID: Deep Phenotype of a Complex Condition. *EBioMedicine*. 2021 Dec;74:103722. doi: 10.1016/j.ebiom.2021.103722. Epub 2021 Nov 25.
- Tejerina F, Garcia D, Gracia MA. Post-COVID-19 or persistent COVID-19 syndrome: a case with detection of SARS-CoV-2 RNA in plasma. *Med Gen and Fam*. 2021;10(2):91-4. doi: 10.24038/mgyf.2021.022. Available from: [www.mgyf.org](http://www.mgyf.org)
- Bianchi JL, Martin I, Medrano FJ. Prolonged COVID-19 syndrome: a new challenge for Internal Medicine. *Current Med*. 2020;105(811):253-5. doi: 10.15568/am.2020.811.ami01.
- Dos Santos A, Lima A. Covid longa e pos-covid. *Subsec Saúde Gerência Strategic Information in Saúde CONECTA-SUS*. 2021;02:1-7.
- Raveendran AV, Jayadevan R, Sashidharan S. Long COVID: An overview. *Diabetes Metab Syndr*. 2021 May-Jun;15(3):869-875. doi: 10.1016/j.dsx.2021.04.007. Epub 2021 Apr 20. Erratum in: *Diabetes Metab Syndr*. 2022 May;16(5):102504.
- Sykes DL, Holdsworth L, Jawad N, Gunasekera P, Morice AH, Crooks MG, et al. Post-COVID-19 Symptom Burden: What is Long-COVID and How Should We Manage It? *Lung*. 2021 Apr;199(2):113-119. doi: 10.1007/s00408-021-00423-z.
- Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. *Nat Med*. 2021 Apr;27(4):626-631. doi: 10.1038/s41591-021-01292-y. Epub 2021 Mar 10. Erratum in: *Nat Med*. 2021 Jun;27(6):1116.
- Mandal S, Barnett J, Brill SE, Brown JS, Denny EK, Hare SS, et al. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. *Thorax*. 2021 Apr;76(4):396-398. doi: 10.1136/thoraxjnl-2020-215818. Epub 2020 Nov 10. PMID: 33172844;
- Townsend L, Dyer AH, Jones K, Dunne J, Mooney A, Gaffney F, et al. Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection. *PLoS One*. 2020 Nov 9;15(11):e0240784. doi: 10.1371/journal.pone.0240784.
- Carvalho-Schneider C, Laurent E, Lemaignan A, Beauflis E, Bourbao-Tournois C, Laribi S, et al. Follow-up of adults with noncritical COVID-19 two months after symptom onset. *Clin Microbiol Infect*. 2021 Feb;27(2):258-263. doi: 10.1016/j.cmi.2020.09.052. Epub 2020 Oct 5.
- Goërtz YMJ, Van Herck M, Delbressine JM, Vaes AW, Meys R, Machado FVC, et al. Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? *ERJ Open Res*. 2020 Oct 26;6(4):00542-2020. doi: 10.1183/23120541.00542-2020.
- Mackay A. A Paradigm for Post-Covid-19 Fatigue Syndrome Analogous to ME/CFS. *Front Neurol*. 2021 Aug 2;12:701419. doi: 10.3389/fneur.2021.701419.
- Kamal M, Abo Omirah M, Hussein A, Saeed H. Assessment and characterisation of post-COVID-19 manifestations. *Int J Clin Pract*. 2021 Mar;75(3):e13746. doi: 10.1111/ijcp.13746. Epub 2020 Nov 3. PMID: 32991035;
- Osikomaiya B, Erinoso O, Wright KO, Odusola AO, Thomas B, Adeyemi O, et al. 'Long COVID': persistent COVID-19 symptoms in survivors managed in Lagos State, Nigeria. *BMC Infect Dis*. 2021 Mar 25;21(1):304. doi: 10.1186/s12879-020-05716-x.
- Stavem K, Ghanima W, Olsen MK, Gilboe HM, Einvik G. Persistent symptoms 1.5-6 months after COVID-19 in non-hospitalised subjects: a population-based cohort study. *Thorax*. 2021 Apr;76(4):405-407. doi: 10.1136/thoraxjnl-2020-216377.
- Varatharaj A, Thomas N, Ellul MA, Davies NWS, Pollak TA, Tenorio EL, et al. Neurological and neuropsychiatric complications of COVID-19 in 153 patients: a UK-wide surveillance study. *Lancet Psychiatry*. 2020 Oct;7(10):875-882. doi: 10.1016/S2215-0366(20)30287-X. Epub 2020 Jun 25. Erratum in: *Lancet Psychiatry*. 2020 Jul 14:;
- Woo MS, Malsy J, Pöttgen J, Seddiq Zai S, Ufer F, Hadjilaou A, et al. Frequent neurocognitive deficits after recovery from mild COVID-19. *Brain Commun*. 2020 Nov 23;2(2):fcaa205. doi: 10.1093/braincomms/fcaa205.
- Rogers JP, Chesney E, Oliver D, Pollak TA, McGuire P, Fusar-Poli P, et al. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry*. 2020 Jul;7(7):611-627. doi: 10.1016/S2215-0366(20)30203-0.
- Myall KJ, Mukherjee B, Castanheira AM, Lam JL, Benedetti G, Mak SM, et al. Persistent Post-COVID-19 Interstitial Lung Disease. An Observational Study of Corticosteroid Treatment. *Ann Am Thorac Soc*. 2021 May;18(5):799-806. doi: 10.1513/AnnalsATS.202008-1002OC.
- Sonnweber T, Sahanic S, Pizzini A, Luger A, Schwabl C, Sonnweber B, et al. Cardiopulmonary recovery after COVID-19: an observational prospective multicentre trial. *Eur Respir J*. 2021 Apr 29;57(4):2003481. doi: 10.1183/13993003.03481-2020.
- Ahmed H, Patel K, Greenwood DC, Halpin S, Lewthwaite P, Salawu A, et al. Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: A systematic review and meta-analysis. *J Rehabil Med*. 2020 May 31;52(5):jrm00063. doi: 10.2340/16501977-2694.
- Afrin LB, Weinstock LB, Molderings GJ. Covid-19 hyperinflammation and post-Covid-19 illness may be rooted in mast cell activation syndrome. *Int J Infect Dis*. 2020 Nov;100:327-332. doi: 10.1016/j.ijid.2020.09.016. Epub 2020 Sep 10.
- Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet*. 2021 Jan 16;397(10270):220-232. doi: 10.1016/S0140-6736(20)32656-8.
- Verstrepen K, Baisier L, De Cauwer H. Neurological manifestations of COVID-19, SARS and MERS. *Acta Neurol Belg*. 2020 Oct;120(5):1051-1060. doi: 10.1007/s13760-020-01412-4. Epub 2020 Jul 21. Erratum in: *Acta Neurol Belg*. 2020 Jul 21:
- Butowt R, von Bartheld CS. Anosmia in COVID-19: Underlying Mechanisms and Assessment of an Olfactory Route to Brain Infection. *Neuroscientist*. 2021 Dec;27(6):582-603. doi: 10.1177/1073858420956905.
- Wostyn P. COVID-19 and chronic fatigue syndrome: Is the worst yet to come? *Med Hypotheses*. 2021 Jan;146:110469. doi: 10.1016/j.mehy.2020.110469.
- Paterson RW, Brown RL, Benjamin L, Nortley R, Wiethoff S, Bharucha T, et al. The emerging spectrum of COVID-19 neurology: clinical, radiological and laboratory findings. *Brain*. 2020 Oct 1;143(10):3104-3120. doi: 10.1093/brain/awaa240.
- Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, et al. Postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection: A cross-sectional evaluation. *J Med Virol*. 2021 Feb;93(2):1013-1022. doi: 10.1002/jmv.26368.
- Dani M, Dirksen A, Taraborrelli P, Torocastro M, Panagopoulos D, Sutton R, et al. Autonomic dysfunction in 'long COVID': rationale, physiology and management strategies. *Clin Med (Lond)*. 2021 Jan;21(1):e63-e67. doi: 10.7861/clinmed.2020-0896.
- Ahmed S, Zimba O, Gasparyan AY. COVID-19 and the clinical course of rheumatic manifestations. *Clin Rheumatol*. 2021 Jul;40(7):2611-2619. doi: 10.1007/s10067-021-05691-x.